Goran Augustin

Acute Abdomen During Pregnancy

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To my father, an abdominal surgeon, whose ability to make an accurate diagnosis in emergency abdominal surgery only with history taking and physical examination was never outperformed. He taught me great things in this "clinical magic"

To my wife Katarina (now pregnant with Lukas), who despite having a small baby (Lara), understood the importance of this work to me, and sacrificed several years of many weekends, evenings, nights, and journeys to allow me and provide me enough time to create this book

To my daughter Lara, who reminds me every day that teaching others is a great opportunity and pleasure that cannot be substituted

To my mother, whose mathematically functioning brain is fascinating, and now I realize that it is a fortune that I inherited most parts of it

And… to all pregnant women… who are healthy… and to all that need the clinicians' consultations from this book, whose lives and lives of their future babies will be saved and normal….

Preface

The art and science of asking questions is the source of all knowledge.

Thomas Berger

What has given me the most joy in my life is the establishment of a school that carries on my aspirations and aims, be it scientific or humanitarian thereby ensuring a legacy for the future.

Theodor Billroth, 1893

Earlier diagnosis means better prognosis.

Zachary Cope, 1921

How did the idea for the book come? Here is the answer. Acute abdomen is still one of the most exciting conditions in (emergency) surgery and medicine in general. The clinician needs to make the diagnosis and the indication for the operation as fast as possible, and then the operator should perform the operation with the lowest possible morbidity and mortality. This is known for over a century. Additional difficulty arises when that clinician has a pregnant patient with acute abdomen. Now he or she is dealing with two human beings at the same time. Also the pregnant patient has slightly changed intraperitoneal anatomy and physiology, making the diagnosis more difficult.

During the last 7 years, I started to study more about cases of acute abdomen during pregnancy. Searching through the literature, I found very little reviews on the subject. Unfortunately, that was expected because acute abdomen during pregnancy is a rare group of conditions. If one excludes the most common causes such as acute appendicitis and acute cholecystitis, the clinician can deal with only one pregnant patient having acute abdomen in several years, sometimes once in a career. When I comprehended that, I started to study, write, and publish articles about different topics of acute abdomen during pregnancy. When I tried to find some texts covering the whole topic, I could not find these. Then it came to me that I need to write a book about *Acute Abdomen During Pregnancy* to, first, help myself and then to help all the clinicians dealing with this rare subject. It is interesting that some names in medicine, gynecology, and surgery that are not so famous or known were the first to treat such cases in medical history. It was interesting for me to read about them and to put them in the book. Mostly, these persons were more famous for other achievements in their medical fields.

There are two problems in writing a book that should have guidelines and recommendations on the topics included. First, it is the (extreme) rarity of these diseases. Second, acute condition is unpredictable in the severity and the time

of presentation. Both these facts preclude the possibility for randomized studies that are needed for validated guidelines and recommendations in medicine. Therefore, some of the recommendations in the book are not adequately validated, but due to the rarity (some diseases have less than 50–100 cases published in 100 years), I tried to combine the recommendations from acute abdomen in general population and from the opinions of the authors (and myself) of published case reports. Therefore, many facts from these case reports are copied into this textbook. Also the comprehensiveness of the chapters is not equal and mostly depends on the frequency of specific condition during pregnancy. Therefore, the most extensive are chapters about acute appendicitis and acute cholecystitis, conditions which present most of the cases of acute abdomen during pregnancy. I tried to include as much as possible case reports so the reader can have his or her own opinion about the topic and also can develop ideas for further research on the subject. After completing the manuscript, I read it thoroughly and then I realized that there are many things that could be written better. What motivated me to go further is Margaret Atwood's tip for writers: "If I waited for perfection, I would never write a word." Therefore, if I waited for perfection, I would never write this book.

Additionally, it should be mentioned that possibly any cause of acute abdomen can occur during pregnancy, and detailed description would lead to an enormous number of unnecessary pages; therefore, in conditions that have only one or several cases published, a short description of the disease is presented. It is difficult to say if this book is more suitable for the gynecologist or general/abdominal surgeon. Some parts will be more interesting to the surgeon, while others more to the gynecologist, especially therapeutic considerations. Diagnostic workup will be interesting to every reader.

Some photos (figures) in the text are not of the excellent quality, but because of the extreme rarity of some conditions, it is impossible to obtain other figures of similar or same pathology.

And my final plea… to every reader… please contact me about any type of errors, misinterpretations, and any medical/surgical mistake in the text because it would improve (further editions of) this interesting subject. Contact me if you have any questions about the subject. Also any reader dealing with this subject could feel free to contact me to be an author of one of the chapters in (possible) further editions of this book. My other plea to the reader is to publish cases of acute abdomen during pregnancy so the medical community could have a better insight into the incidence, etiology, diagnosis, treatment, and maternal and fetal outcome for all causes of acute abdomen during pregnancy.

I hope that the reader will enjoy reading the book as much as I enjoyed creating it!

Zagreb, Croatia

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1.1 History

It proves fatal to a woman in a state of pregnancy, if she be seized with any of the acute diseases.
Hippocrates

In 1848, Henry Hancock (Fig. 1.1), President of the Medical Society of London, presented a paper to that society describing the treatment of a 30-year-old female in the 8th month of pregnancy in the Charing Cross Hospital in London [1]. She developed abdominal pain, miscarried on the fourth day, and developed a tender mass in the lower right abdomen. She was seen by Hancock 12 days after the disease started. She had distended, tender abdomen, particularly in the lower right abdomen. Hancock prescribed opium and poultices. Two days later her condition was much worse with palpable mass in the lower right abdomen. Then incision was made above and parallel to Poupart's ligament. When the abdomen was opened, offensive pus and bubbles of gas escaped, followed a couple of weeks later by two fecaliths which Hancock postulated had escaped by ulceration from the diseased appendix. From that time her improvement was rapid and she made a good recovery. Therefore, Hancock is the author of the first reported and successfully operated appendicitis complicating pregnancy.

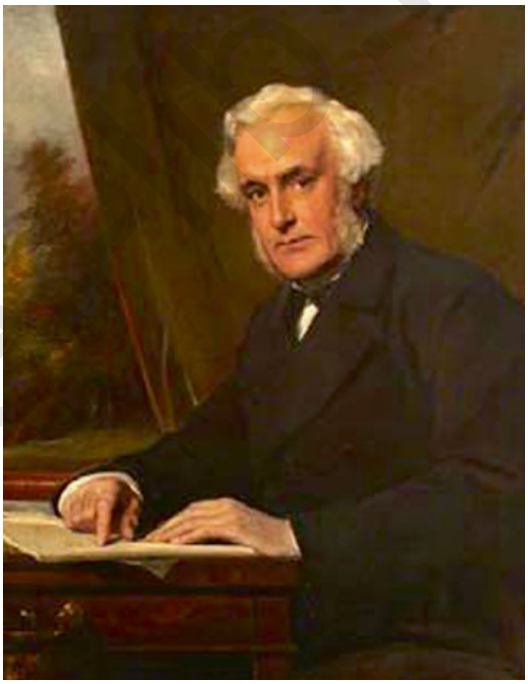

Fig. 1.1 Henry Hancock (oil on canvas, 91 × 71 cm, painted by *George Richmond* in 1874; collection: The Royal College of Surgeons of England)

1.2 Incidence, Etiology, and Pathogenesis

The study of the influence of pregnancy on the incidence of appendectomy and appendicitis is a methodological challenge. The incidence of

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appendectomy and appendicitis and childbearing are strongly related to age, with a peak in the middle of the second decade for appendicitis and appendectomy and a peak in the third decade for childbearing. The incidence of appendicitis and appendectomy shows regional variations and a secular trend with a decreasing incidence. Secular and regional variations are also seen for the incidence of childbirth. The influence of these variations on the incidences of appendectomy, appendicitis, and pregnancy is complex which makes it difficult to determine the expected incidence of appendectomy and appendicitis during pregnancy for comparison purposes. Although there are no references that specifically address postpartum appendicitis, most studies group appendicitis of pregnancy and the puerperium together because of the anatomic and physiological continuum [2]. Up to 1960 there were 373 cases collected [3].

Acute appendicitis or epityphlitis (*epi-* + Greek *typhlon* = cecum + -itis, inflammation) is the most common non-obstetric cause of acute abdomen (surgical emergency) in pregnancy. It is present in 1/500–2,000 pregnancies and amounts to 25 % of operative indications for the acute abdomen in pregnancy [4–9]. This high incidence has a multifactorial etiology. Early marriage and repeated pregnancies till menopause make the probability of an acute appendicitis occurring in pregnancy higher. Appendicitis seems to be more common in the second trimester with incidence of 35–50 % [9–11], but there are no proven data that that pregnancy affects the overall incidence of appendicitis [12]. Others claim that there is reduced incidence especially in third trimester because of protective effect of pregnancy [13]. During pregnancy a range of physiological changes take place that may influence the pathogenesis of appendicitis. The immune system is shifted toward a T-helper cell type 2 (TH_2)-dominated immunity with a depressed cellular inflammatory response and increased humoral immunity [14]. A decrease in T-helper cell type 1 (TH_1)-mediated chronic inflammation, as in rheumatoid arthritis and multiple sclerosis, is observed during pregnancy [15, 16]. Appendicitis is an inflammatory process, and the inverse relation between appendicitis and pregnancy may suggest that the inflammatory response in appendicitis is mediated by a TH_1-mediated inflammatory response. It is explained by suppression of TH_1-mediated inflammatory response during pregnancy. Appendicitis is an inflammatory process, and this observation indirectly proves that appendicitis is mediated by TH_1 inflammatory response [15]. Authors' comment suggest that the aforementioned mechanism influence only the inflammatory causes and not obstructive which causes gangrene due to obstruction as a secondary event. Other explanations are hormonal influences because there are incidence variations during menstrual cycle [13].

The development of appendicitis may be more fulminating in pregnancy for various reasons. Increased pelvic vascularity and displacement of the appendix by the uterus may hasten strangulation, and increased local lymphatic drainage together with interference with omental migration may favor systemic spread of the inflammatory process.

It is still not possible to presume when appendicitis would develop because etiology and pathogenesis are not completely known and understood [17, 18]. According to the most favored theory, appendicitis is caused by mechanical obstruction of the appendix lumen, because of either fecal stasis, kinking, peritoneal adhesions, or infection-induced swelling of the mural lymphoid tissue. Other possible mechanisms include a breakdown of the mucosal barrier in the appendix by the direct invasion of a pathogen or by an inflammatory response that has been triggered by an infectious agent or some other stimulus. Geographical differences in the incidence in appendicitis and secular trends in general population have been related to the differences and changes in the dietary intake of fiber and in standards of hygiene [19, 20].

A relation with female sex hormones has been proposed because of a lower incidence among women and incidence variations during the menstrual cycle, but studies have given inconsistent

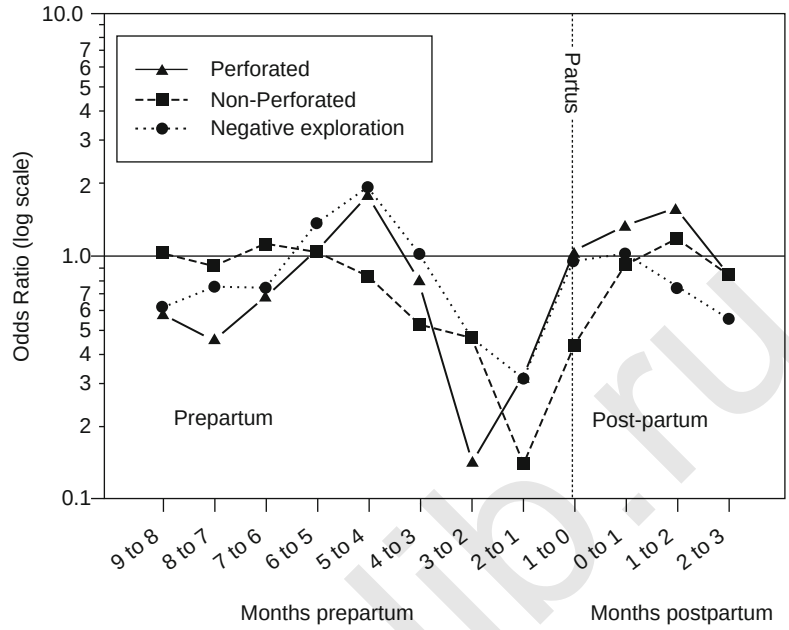

Fig. 1.2 Comparison of pregnancy status at the time of surgery in women who had an appendectomy compared with matched controls. The relation is expressed as the odds ratios according to conditional logistic regression [13]

results [21–23], and childbearing constitutes a period of increased concentration of female sex hormones. Figure 1.1 illustrates a comparison of pregnancy status at the time of surgery in women who had an appendectomy compared with matched controls in the largest epidemiological study on the subject [13].

This study by Andersson and Lambe shows that patients who had undergone appendectomy were less likely to be pregnant at the time of the operation compared with controls. This inverse relation was dependent on the period of gestation and the underlying diagnosis at the operation. Corroborating results from previous reports, the highest incidence of appendicitis and appendectomy was found in the second trimester of pregnancy. This pattern was seen for perforated appendicitis and negative explorations, whereas for non-perforated appendicitis, the strength of the inverse relation increased continuously throughout the pregnancy. This result does not support the commonly expressed opinion that the incidence of appendicitis is the same in pregnant as in nonpregnant women but rather suggests that pregnancy may protect against appendicitis (Fig. 1.2) [13].

1.3 History Taking and Clinical Examination

The approach to pregnant patients with severe abdominal pain is similar to that for nonpregnant patients. However, the physiological changes associated with pregnancy must be considered when interpreting findings from the history and physical examination. The uterus enlarges about 20 times during the pregnancy as compared to the nonpregnant state, and this results in stretching of supporting ligaments and muscles, as well as pressure on other intra-abdominal structures and layers of the anterior abdominal wall (Fig. 1.3).

The abdominal wall also undergoes significant change during pregnancy, with muscle tone reduction and skin elasticity to accommodate the enlarging uterus. The abdominal wall tone remains lax for several weeks postpartum, returning to a near-nonparous level in 6–7 weeks. The hallmarks of acute surgical disease, abdominal guarding and rigidity, do not occur or are attenuated during the early puerperium. Immediately after delivery, the uterus assumes a 15–16-week size [24]. At 1 week postpartum, the uterine fundus returns to the pelvis and is the size of a 12-week gravid uterus. After

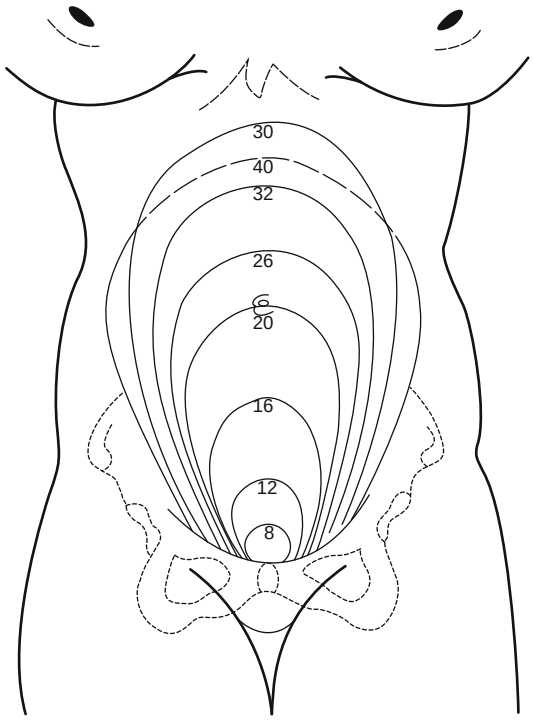

Fig. 1.3 Height of the fundus at comparable gestational dates varies greatly from patient to patient. Those shown are most common. Convenient rule of thumb is that at 5 months gestation, fundus is usually at or slightly above the umbilicus [2]

the first week, uterine involution occurs more slowly, reaching prepregnancy size within 6 weeks. There is a high circulatory level of adrenocorticoids in pregnancy which tends to diminish the tissue response to inflammation and to mask the early signs of infection and hinder localization. Therefore, the difficulties in diagnosis of appendicitis in pregnancy are due to:

- Blunting of signs and symptoms due to abdominal wall distension, dislocation of intra-abdominal organs, and diminished tissue response to inflammation
- Possible changes in appendiceal location as pregnancy advances
- Nausea, vomiting, and abdominal pain which are present in normal pregnancy especially in the first trimester
- Extensive differential diagnosis

It is important to note that there is not one, completely reliable sign or symptom that can aid in the diagnosis of appendicitis in pregnancy, and some of the classic signs of appendicitis such as Rovsing's and psoas signs have not been shown to be of clinical significance in diagnosing an acute appendicitis in pregnancy [25].

Constant abdominal pain is the most common symptom, and pain in the right lower quadrant (present in 75–84 % of patients) is the most reliable symptom [5, 6, 26, 27]. Classical pain migration is highly suspicious of acute appendicitis and is present in around 50 % of patients [26]. After the 3rd month of pregnancy, the pain could change location and move progressively upward and laterally reaching the level of the right iliac crest at the end of the 6th month of pregnancy. Baer et al. [28] showed by barium enema that the growing uterus progressively displaces the appendix after the 3rd month in a counterclockwise rotation out of the pelvis, into the upper right quadrant, by as much as two fingerbreadths above McBurney's point (Fig. 1.4). The appendix returns to its normal position by postpartum day 10. Original description by McBurney is that pressure is applied by one finger "exactly between 1½ and 2 in. from the anterior spinous process of the ileum on a straight line drawn from that process to the umbilicus" (McBurney's point). This landmark was believed to correspond to the areas of the inflamed appendix irritating the abdominal peritoneum over the T11 and T12 dermatome segments.

Others have found no evidence of upper displacement of the appendix using similar techniques [11, 29–31]. Hodjati and Kazerooni compared patients in the third trimester undergoing elective Cesarean section and appendectomy for appendicitis and did not find statistically significant difference in the change in the position of the appendix. These groups were compared to female nonpregnant patients undergoing appendectomy. The results were similar, and the significant change (more than 2 cm) in the position of the appendix was found in 15–23 % of patients [30]. This discrepancy is probably due to the different extents of cecal fixation. In other words, a growing uterus could displace a mobile cecum with the appendix but not the completely fixed cecum. Also, due to increased separation of

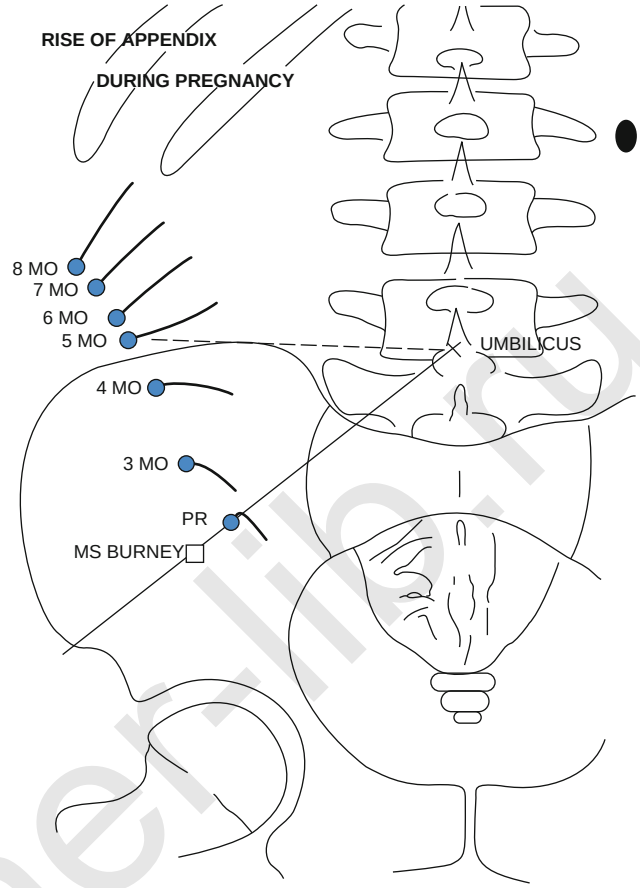

Fig. 1.4 Change of the location of the appendix during pregnancy according to Baer et al. [28]

parietal and visceral peritoneum by an enlarging uterus, there is decreased perception of somatic pain and localization; thus clinical localization of inflamed appendix is unreliable.

Nausea is nearly always present, and vomiting is present in two-thirds of patients. This is due to progesterone-induced delayed gastric emptying and pressure of enlarged uterus on intra-abdominal structures. These symptoms should be evaluated with caution because many women with normal pregnancies have these symptoms especially in early pregnancy [26]. Suspicion should be raised if new-onset nausea is present (the period of nausea and vomiting in early pregnancy is mostly self-limiting and confined to the first trimester).

Anorexia is present in only one-third to two-thirds of pregnant patients, while it is present almost universally in nonpregnant patients [4, 5, 32]. If new-onset anorexia is present, it should raise suspicion, especially if present with other signs and symptoms suggesting appendicitis.

An atypical clinical picture is most commonly present in the second trimester [9]. Right upper quadrant pain, uterine contractions, dysuria, and diarrhea could also be present [11, 12, 25].

1.4 Examination

An *abdominal mass* may be missed on physical examination because of the presence of the enlarged gravid uterus [33].

Abdominal tenderness in the right lower quadrant on direct palpation is almost always present [34].

Rebound tenderness is present in 55–75 % of patients [32, 35].

Abdominal muscle rigidity is present in 50–65 % of patients [36]. These two signs are more likely to be present during the first trimester then later in pregnancy, when laxity of the abdominal wall musculature makes this more difficult to detect [12, 37].

The psoas sign (*Obraztsova's sign*) is pain on passive extension of the right thigh when the inflamed appendix is in a retrocecal/retroperitoneal location in contact with the psoas muscle. The psoas muscle is stretched by this maneuver. The psoas sign is observed less frequently during pregnancy when compared with nonpregnant patients with appendicitis [4].

Rectal or pelvic tenderness may occur in early pregnancy but is unusual in late pregnancy as the appendix migrates from its pelvic location [37, 38]; therefore, less than half of patients had tenderness on rectal examination [35].

Alders' sign is used to differentiate between appendicitis and tubo-ovarian pathology in right lower quadrant (RLQ) pain in pregnancy and puerperium [39]. The practitioner should find the point of maximal tenderness while the patient is supine. Then roll the patient onto the left side. If pain shifts toward the center, then it may be tubo-ovarian. The problem in pregnant patients in third trimester is that the enlarged uterus does not allow the tubo-ovarian complex to shift its position. It is obvious that this sign can be of use only if the uterus is large enough to be palpable abdominally and that it may be misleading in the rare case in which a uterine lesion has become fixed by adhesions to the anterior abdominal wall. In acute salpingitis, which does occur in pregnancy, the result of the test will depend on the presence or absence of perisalpingitic adhesions. In the study by Chen et al. [40], 36 % of patients with positive appendicitis had positive Alders' sign. Unfortunately there was no comparison by trimesters of pregnancy.

Aaron's sign is a referred pain or discomfort felt in the precordial or epigastric region when continuous firm pressure is applied over McBurney's point [41].

Arapov's sign (*contracture*) is a pain reflex contraction of the right hip joint in appendicitis [42, 43].

The *mean maximal axillar temperature* for proven appendicitis is between 37.2 and 37.8 C but could be over 39 C in cases of perforation and diffuse peritonitis. Unfortunately only 50 % of pregnant patients with acute appendicitis have low-grade fever [44, 45]. In one series 72 % of patients who had appendicitis (with or without perforation) had temperatures of less than 37.5 C (99.6 F) [35]. This incidence of elevated temperature is not different from normal pregnant population and the finding is also true for *tachycardia* [44, 46], and both are not sensitive signs [11, 47]. Also if normal pregnant patients have low-grade fever, they have leukocytosis, a finding that further complicates definitive diagnosis [45]. Some studies showed an increased rate of adverse outcomes if the temperature was over 38 °C [48].

In conclusion, it should be stressed that clinical signs and blood indices are unreliable for the diagnosis of appendicitis in pregnancy and lead to an unacceptable rate of false-negative appendectomy, and a false-negative rate of up to 50 % has been reported when imaging studies are not used [49].

1.4.1 Scoring Systems

There are several scoring systems developed for a more precise diagnosis of acute appendicitis in nonpregnant population.

1.4.1.1 Modified Alvarado Score

The most commonly used is the *Alvarado score* described in 1986 [50] and has been extensively validated in nonpregnant population. The mnemonic is MANTRELS (Table 1.1). Currently there is no scoring system for pregnant patients, and this scoring system was modified keeping in mind the symptoms of normal pregnancy and named *Modified Alvarado Score for pregnant patients* [51]. The difference in comparison to the standard Alvarado score is that migration of pain is not included and the number of points just for

Table 1.1 Comparison of Alvarado score and modified Alvarado score for pregnant patients

Alvarado score		Alvarado score for pregnant patients	
Symptoms	Score	**Symptoms**	Score
Migratory RLQ pain	**1**	RLQ pain	**2**
Anorexia	1	Anorexia	1
Nausea/vomiting	1	Nausea/vomiting	1
Signs		**Signs**	
Tenderness in RLQ	2	Tenderness in RLQ	2
Rebound tenderness in RLQ	1	Rebound tenderness in RLQ	1
Elevated temperature			
(≥37.3 °C/≥99.1 °F)	1	Elevated temperature	
(≥37.3 °C/≥99.1 °F)	1		
Laboratory		**Laboratory**	
Leukocytosis (>10,000/mm^3)	2	Leukocytosis (>10,000/mm^3)	1
Shift to the left (>75 %)	1		
Total score	**10**	**Total score**	**9**

the pain in RLQ is 2 in comparison of 1 point in the standard Alvarado score for nonpregnant population. Leukocyte left shift is not included, and leukocytosis (which could be present in normal pregnancy) has only 1 point in Modified Alvarado Score for pregnant patients, and total score is lower for 1 point (9 vs. 10) (Table 1.1). Positive predictive value was 60 % in Alvarado score range of 5–7 and 100 % in a score range of 7–9. In the same study the sensitivity of ultrasound was 78.6 %.

1.5 Differential Diagnosis

Differential diagnosis is more difficult than in nonpregnant patients because of:

- Less reliable history and physical examination (see Sect. 1.3)
- Higher incidence of some pathologic conditions that mimic acute appendicitis

These conditions could be divided into non-obstetric/non-gynecologic and gynecologic/obstetric conditions (Table 1.2).

Table 1.2 Differential diagnosis of acute appendicitis during pregnancy and puerperium

Non-obstetric/non-gynecologic conditions	Gynecologic/obstetric conditions
Gastroenteritis	Ruptured/hemorrhagic ovarian cyst
Urinary tract infections	Adnexal torsion
Pyelonephritis	Salpingitis
Nephrolithiasis	Tubo-ovarian abscess
Acute cholecystitis/ cholelithiasis	Threatened abortion
Acute pancreatitis	Placental abruption
(Incarcerated) hernia	Chorioamnionitis
Bowel obstruction	Pelvic inflammatory disease
Carcinoma of the large bowel	Degenerative fibroid
Mesenteric adenitis	Ectopic pregnancy
Rectus hematoma	Preeclampsia
Pulmonary embolism	Round ligament syndrome/pain
Right lower lobe pneumonia	Varicose veins in the parametria
Meckel's diverticulitis	Preterm labor
Sickle cell disease	Pelvic endometriosis
Stump appendicitis	

1.5.1 Round Ligament Pain/ Syndrome

Round ligament pain or syndrome (RLP) is one of the most common discomforts of pregnancy and usually starts at the second trimester of gestation and continues until delivery. It usually resolves completely after delivery, although cases of postpartum RLP, e.g., RLP that persisted for a few days after delivery, have been reported. The most

common symptoms of RLP are sudden pain in the lower abdomen, usually in the right side of the pelvic area that can extend to the groin, and shooting abdominal pain when performing sudden movements or physical exercise. Pain is sudden and intermittent and lasts only for a few seconds. The pathogenesis of RLP is varied. Although very common during pregnancy, non-gestating women can also experience RLP. The most common causes of RLP are the following: (1) RLP may be caused by a spasm or cramp when the ligament contracts involuntarily. The ligament pulls on nerve fibers and sensitive structures of the female reproductive system. Since the uterus tends to be oriented toward the right side of the body, the pain is also often felt on the right side. This leads to frequent confusion with appendicitis [52]; (2) during pregnancy, the uterus expands to accommodate the growing fetus. This increase in size and weight of the uterus puts stress on the ligament that holds it, causing it to stretch. During physical exertion or sudden movements, the ligament is overly stretched, causing pain; (3) varicosities [53], e.g., enlargement of the blood vessels of the round ligament, can occur during pregnancy, causing pain and swelling. The varicocele starts at the veins draining the round ligament and the inguinal canal and is associated with engorgement of the veins of the ovaries and the pelvis during pregnancy; (4) endometriosis [54, 55] that infiltrates or borders the uterine round ligament can cause RLP in fertile, non-gestating women; and (5) other pathologies that involve the uterine round ligament can cause RLP. However, diagnosis of RLP is problematic. Some of the conditions that may present symptoms similar to those of RLP are appendicitis, ectopic pregnancy, kidney stones, urinary tract infection, uterine contractions, inguinal hernia, ovarian cysts, and endometriosis. If abdominal pain is continuous and accompanied by vaginal bleeding, excessive vaginal discharge, fever, chills, or vomiting, then it is most unlikely to be RLP, and immediate consultation with a health-care provider is warranted [55]. Physical examination, ultrasonography, and blood and urine tests may be able to pinpoint the actual cause of abdominal pain. In some cases, however, RLP was only diagnosed during exploratory surgery [53, 56, 57].

1.5.2 Ovarian Vein Thrombosis

Ovarian vein thrombosis typically presents with symptoms suggestive of acute appendicitis, and color Doppler sonography is the favored diagnostic procedure, with CT being a supplementary tool [58].

Special consideration should be placed on *stump appendicitis*. It is an acute inflammation of the residual part of the appendix and a rare complication of incomplete appendectomy. It can present clinically as acute appendicitis and/or as an appendiceal stump abscess. It was first reported by Baumgartner in 1949 [59], and currently 60 cases are published and found after open as well as after laparoscopic appendectomy [60]. There is only one case report in pregnancy where fimbriae of the right fallopian tube were stuck on the appendiceal stump end-to-end. Tubal abscess was drained following bridectomy. Right salpingectomy and appendectomy were performed. The chorioamnionitis resulted with preterm delivery [61].

1.5.3 Pathologic Conditions Associated with the Puerperium

1.5.3.1 Metritis

The most common of these is *metritis*, the broad group of postpartum infections of the genital tract. Metritis is often insidious in onset. Because of the vague initial manifestations, it is often a diagnosis of exclusion. Endometritis, or deciduitis, is an infection of the most superficial layer of the uterus and is the most common site of puerperal infection. The onset of endometritis is commonly 2–5 days postpartum, and the earliest manifestations are malaise, anorexia, and fever. There may be no localizing signs or symptoms in mild cases. The pelvic examination may be normal, even in the presence of severe endometritis. The disease may progress further to involve the myometrium (myometritis) and parametrial structures (parametritis) with extension into the broad ligaments, tubes, ovaries, and pelvic peritoneum [24]. Extensive infection may produce lethargy, chills, high fever, and significant lower

abdominal pain, tenderness, and rebound. An accompanying paralytic ileus may cause distention and vomiting. Myometritis and parametritis are usually accompanied by localized peritoneal signs and cervical motion tenderness; rarely will one see generalized peritonitis. In one patient, infection of the genital tract was not given serious consideration because she was 3 weeks postpartum, which is well outside the normal limits for the onset of postpartum metritis.

1.5.3.2 Perihepatitis (Fitz-Hugh-Curtis Syndrome)

Perihepatitis (*Fitz-Hugh-Curtis syndrome*) is the result of early bacteremic or retroperitoneal lymphatic dissemination of *Chlamydia trachomatis* or gonococcal pelvic infection [62]. The syndrome is most frequently seen in young women and is more common in the second and third trimesters and puerperium. Inflammation in the right upper quadrant produces perihepatic adhesions. Classically, there is sudden onset of sharp right upper quadrant pain, often pleuritic in quality. Nausea and hiccups are occasionally noted. Physical findings include tenderness under the right costal margin, an occasional hepatic friction rub, and fever. Pelvic examination may be normal or may reveal signs of cervicitis or pelvic inflammatory disease. Liver function tests and cholecystogram may be transiently abnormal. The diagnosis is suggested by a history of recent pelvic infection, but the syndrome can be a sequel of latent or asymptomatic infection. The diagnosis is further supported by isolation of gonococcus on cervical culture and improvement on appropriate antibiotics [62]. It is important to exclude other etiologies because there is no specific diagnostic marker of this syndrome.

1.5.3.3 Pelvic Thrombophlebitis/Right Ovarian Vein Syndrome

Thrombophlebitis and thromboembolic events occur significantly more often in the puerperium than in nonpregnant women. Women in the puerperium are predisposed to deep vein thrombosis attributable to sluggish circulation, trauma to the pelvic vessels during delivery, and estrogen-mediated hypercoagulability. Thrombophlebitis of the pelvic vessels is more common in puerperal females and may be difficult to diagnose. *Pelvic thrombophlebitis*, or *right ovarian vein syndrome*, commonly presents with abdominal pain, fever, and a tender midabdominal mass. It may be difficult to distinguish from metritis but should be strongly considered if there is a poor response to appropriate antibiotics (see Part 2, Sect. 1.5.2) [24].

Although *urinary tract infection* was mentioned in the differential diagnosis section, it remains a common cause of puerperal febrile illness. During pregnancy, the compressive effect of the gravid uterus on the ureters in combination with progesterone effects results in collecting system dilatation, especially on the fight side. Ureteral peristalsis is also decreased. These factors contribute to the predisposition toward urinary tract infections in pregnancy and persist to some degree in the early puerperium. The trauma of delivery may induce bladder hypotonicity; frequent catheterization is often necessary and represents an additional risk factor [24]. *Pyelonephritis* is most often either right sided or bilateral in location. Unilateral left pyelonephritis in the puerperium is uncommon [24].

1.6 Diagnosis

1.6.1 Introduction

Until recently, negative appendectomy rates of 15–25 % (and up to 50 % in pregnant women) have been tolerated, given the consequences of missing a true case of appendicitis and the understanding that no test or combination of tests existed with sensitivity and specificity above 80–85 % [48, 63]. This is one of the reasons why all investigations must occur in the hospital. All the diagnostic workups should be done on an interdisciplinary basis in cooperation with the obstetrician. Physicians may be reluctant to order a radiological study because of the potential teratogenic risks to the fetus as well as the medical-legal implications of the radiation dose causing birth defects. For acute indications, the benefits for the mother usually outweigh the small risk to the fetus. The greatest effects of radiation occur during the period of rapid cell proliferation, from approximately the first week after conception

through week 25. The recommended total dose of radiation during this time is less than 5 rad. During the first 2–3 weeks of pregnancy, while cells are not yet specialized, radiation injury will cause failure of implantation or undetectable death of the embryo. After that, injury usually occurs in the organs under development at the time of exposure. Current recommendations on radiation exposure are as follows: "No single diagnostic procedure results in a radiation dose that threatens the well-being of the developing embryo and fetus" (American College of Radiology) [64].

> *Fetal risk is considered to be negligible at 5 rad or less when compared with the other risks of pregnancy, and the risk of malformations is significantly increased above control levels only at doses above 15 rad.*
>
> National Council on Radiation Protection [65]

Exposure to less than 5 rad has not been associated with an increase in fetal anomalies or pregnancy loss [66, 67]. Also, it should be stressed that there are normal risks of pregnancy: 3 % risk of spontaneous birth defects, 15 % risk of spontaneous abortion, 4 % risk of prematurity and growth retardation, and 1 % risk of mental retardation [68]. These data should be explained to the future mother.

Another important consideration for precise diagnosis is that negative appendectomy in pregnant women is associated with fetal loss rate of 2–4 % and early delivery of 4 %, the same rate as in noncomplicated acute appendicitis during pregnancy [69].

1.6.2 Laboratory Findings

Leukocytosis (raised white blood cell count – WBC) is not diagnostic as this can go up in the second and third trimesters and can reach 20,000/mm^3 in early labor in normal pregnancy [70]. In view of the wide range of values, however, it is not possible to derive clinical relevance from these data [71]. For the orientation, the values over 16×10^9/l (16,000 mm^3) should raise serious suspicion [6, 11, 36, 47, 48]. Unfortunately only 60 % of those with perforation had values over 16,000 mm^3 [26]. If there is clinical suspicion of acute appendicitis with normal values of WBC, serial WBC counts may be helpful.

Neutrophil granulocytosis with left shift: the presence of increased proportions of younger, less well-differentiated neutrophils and neutrophil precursor cells in the blood is diagnostic of acute infection. If left shift is not present, then granulocytosis of more than 80 % should be suspicious [45].

A *raised C-reactive protein* (CRP) could be a normal finding in pregnancy and is therefore of little assistance in establishing the diagnosis [26], but with the high clinical suspicion of appendicitis it confirms the diagnosis. Some studies claim that all positive cases had negative CRP values if the patients were evaluated less than 12 h after the onset of pain [47]. Sixty-eight percent with appendicitis had CRP ± 10 mg/l, but all patients with perforation had elevated CRP (mean 55 mg/l) [26].

The *erythrocyte sedimentation rate* is physiologically elevated and thus is a less reliable monitor of inflammatory activity during pregnancy [72].

Pyuria (pus in the urine) is observed in 10–20 % of patients with appendicitis. This may also represent concurrent asymptomatic (or symptomatic) bacteriuria found frequently in pregnant population [4]. Other abnormalities such as mild proteinuria and/or hematuria could be present in up to 19 % of pregnant patients [35].

Puerperal changes in blood components may be confusing as well. During the first 10–14 days of the puerperium, WBC counts of 20,000–25,000/mm^3 are not unusual; there is also a predominant increase in neutrophils. The erythrocyte sedimentation rate may increase to 50–60 mm/h. Reliance on either the erythrocyte sedimentation rate or the WBC count for the diagnosis of acute infection may be misleading [24].

1.6.3 Transvaginal Ultrasound

There are no *Royal College of Obstetricians and Gynaecologists* guidelines about the use of transvaginal ultrasound. An observational study

suggested that it can be used to look for the following features in acute appendicitis [73]:

- Presence and size of adnexal or uterine pathology which can rule out acute appendicitis
- Free fluid in the pouch of Douglas
- Abnormal pathology in the ileocecal region, for example, appendicitis, cecal tumors, cecal diverticula, or retroperitoneal tumors

1.6.4 Graded Abdominal Ultrasound

As a noninvasive procedure, it is the diagnostic procedure of choice [74]. Abdominal ultrasound has good accuracy in the first and second trimesters but has less accuracy in the third trimester. A noncompressible, blind-ended tubular structure that is visualized in the right lower quadrant with a maximal diameter greater than 6 mm is considered diagnostic. The reported sensitivity, specificity, and accuracy (overall percentage of correct test results) vary dramatically. The reported sensitivity ranges from almost 75–100 % [72, 74–78] to only 40–50 % [45, 79]. In one large study, transabdominal ultrasound used for suspected appendicitis was nondiagnostic in 88 % of patients [80]. Because its positive predictive value was 100 %, it provides confirmation of the diagnosis when it is positive. However, the diagnosis of appendicitis could not be ruled out if negative. The use of this technique with the patient supine is difficult during the late second trimester and third trimester of pregnancy because the large size of the gravid uterus does not allow adequate compression. For women in the late second trimester or third trimester, it is recommended that the patient is placed in the left posterior oblique or left lateral decubitus position, which allows displacement of an enlarged uterus and use of the graded-compression technique without difficulty [74]. There is a significant reduction in the negative appendectomy rate in the ultrasound/CT scan group compared to the clinical evaluation group or the ultrasound group. Thus, an ultrasound followed by a CT scan in patients with a normal or inconclusive ultrasound is recommended [81].

Sometimes differentiation between (giant) Meckel's diverticulitis and acute appendicitis on ultrasonography can be difficult.

The US Food and Drug Administration (FDA) has proposed an upper limit of 720 mW/cm^2 for the spatial-peak temporal average intensity of the ultrasound beam for obstetric ultrasound [82]. Doppler sonography can produce high intensities and should be used judiciously, keeping the exposure time and acoustic output to the lowest level possible [83].

1.6.5 Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is the diagnostic modality of choice in patients for whom the risks of radiation or the potential nephrotoxicity of iodinated contrast agents is a major concern. MRI is also known to be a reliable imaging modality for diagnosing appendicitis in nonpregnant patients with a sensitivity, specificity, positive predictive value, and negative predictive value (NPV) of 97, 92, 94, and 96 %, respectively [84]. There have only been a small number of studies evaluating the utility of MRI for diagnosing appendicitis during pregnancy. Oto et al. reported a cohort of 118 pregnant patients who presented with abdominal pain who underwent MRI between 2001 and 2007. They were able to detect appendicitis in 11 patients (9.3 %) [85]. After confirmation with surgical, pathologic, and clinical follow-up, MRI was found to have an accuracy of 97.5 % for diagnosing appendicitis during pregnancy [85–89].

The MRI criteria for appendicitis include (Fig. 1.5):

- Enlarged appendix with a diameter of greater than 6 mm
- Signs of periappendiceal inflammatory changes, such as the presence of periappendiceal high signal intensity

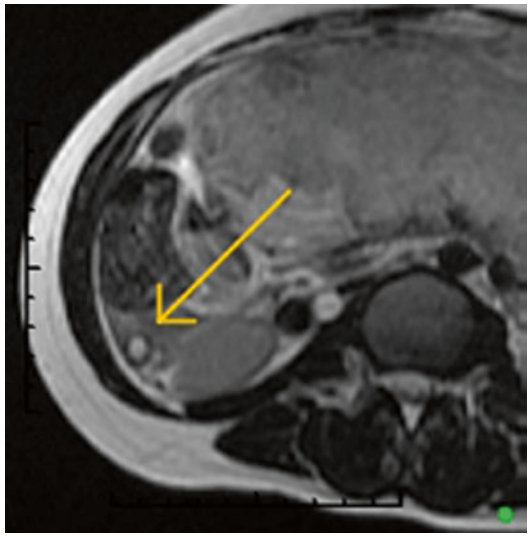

Fig. 1.5 Axial T2-weighted image demonstrating dilated appendix (*arrow*) consistent with acute appendicitis [89]

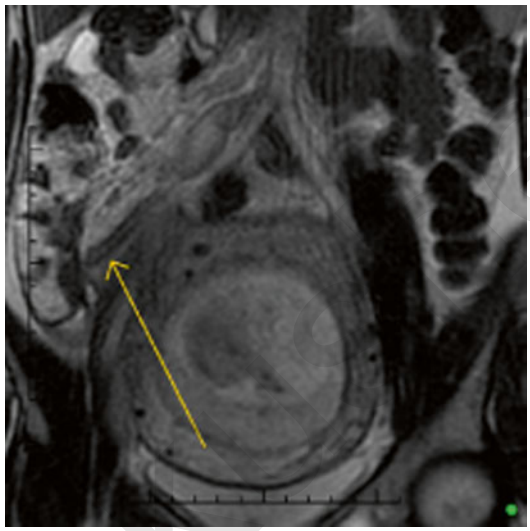

Fig. 1.6 Coronal T2-weighted image demonstrating normal appendix (*arrow*) in a 14-week gestation patient [89]

The MRI criteria that excluded appendicitis were an appendix of less than 6 mm in diameter or an appendix with a diameter of greater than 6 mm with no evidence of periappendicitis (Fig. 1.6).

It is most useful for evaluating pregnant patients with acute pain in the lower abdomen thought secondary to an extrauterine cause, such as appendicitis or ovarian torsion [90, 91]. Some recommendations for its use are:

- MRI is used when the appendix is not visualized by abdominal ultrasound.
- MRI is used when no other cause of an acute abdomen is found.
- The patient needs to give informed consent in writing; the safety of MRI for the fetus has not been proved according to the FDA guidelines and the American College of Radiology. Therefore, it is prudent to perform an MRI in pregnant patients only when ultrasound findings fail to establish a diagnosis.

The significant difference between the performance of CT and MRI was not found. However, some advantages of MRI over CT include the following [86]:

- Reduced requirement for contrast administration (CT often requires rectal, oral, and/or intravenous contrast). An entire abdomen can easily be viewed in more planes.
- No radiation exposure.

MRI is not free of theoretical risks including the potential biological effects of the static and time-varying magnetic fields, the heating effects of the radiofrequency pulses, and the acoustic noise generated by the spatial encoding gradients [92]. FDA has expressed caution over the use of MRI in pregnant women and has stated that there is no conclusive evidence to establish safety [92, 93]. However, the clinical studies that have evaluated the safety of MRI during pregnancy reported no adverse effects on the developing conceptus [93]. Thus, MRI is currently preferred by radiologists over CT [94].

There are also some limitations and recommendations. The patient should be informed that there are no known harmful effects from use of MR imaging at 1.5 T or lower magnetic field strengths [95] and that there is lack of experience with the use of field strengths greater than 2.5 T, and they should be avoided at present [96]. Also absolute

contraindications for MR are metal implants in the body that are not made of titanium or the composition is not known. Gadolinium administration should be avoided during the first trimester [97–101]. Rapid-sequence MRI is preferable to conventional MRI because of the briefer exposure [99].

1.6.6 Computed Tomography (CT) Scan

Clinicians may not be well informed of the facts relating to the use of diagnostic radiological studies in pregnancy. Lack of understanding of radiation effects on the fetus causes unnecessary anxiety in pregnant patients exposed to diagnostic radiation and may lead to unnecessary pregnancy termination. A study examining physician perceptions of teratogenic risk associated with undergoing plain radiography and CT during early pregnancy found that six of the 208 family practice physicians would recommend pregnancy termination after first trimester CT and one following radiography in the first trimester; 12 % (25/208) of physicians were not sure of the need for pregnancy termination after radiography; and 19 % (39/208) of family practice physicians were not sure about a CT scan examination. The same study reported that 8 % (5/65) of obstetricians included in the study would have recommended pregnancy termination after first trimester CT scan examination [102].

In 1998, Rao et al. published their experience with the use of a helical or spiral CT technique, and results show that the method is highly sensitive and specific for the identification of acute appendicitis in the non-obstetric population with lower costs when CT scanning was used to diagnose appendicitis with sensitivity, specificity, and diagnostic accuracy each of 98 % [103, 104]. Appendix CT scans were identified as positive for appendicitis if found:

- Enlarged appendix (>6 mm in the maximum diameter)
- Periappendiceal inflammatory changes (fat stranding, phlegmon, fluid collection, and extraluminal gas)

Table 1.3 Summary of potential in utero-induced radiation effects [105]

Conception age	<50 mGy	50–100 mGy	100 mGy
Prior to conception	None	None	None
1st–2nd weeks	None	Probably none	Possible spontaneous abortion
3rd–8th weeks	None	Potential effects uncertain and too subtle to be clinically detectable	
9th–15th weeks	None	Potential effects uncertain and too subtle to be clinically detectable	
16th–25th weeks	None	None	IQ deficits are not detectable at diagnostic dose
>25th weeks	None	None	None applicable to diagnostic medicine

Unfortunately, there are instances where the findings at CT scan are not so clear. Several authors comment on “equivocal” readings. In all instances, the “equivocal” readings influence on the sensitivity and specificity of CT scan, depending on how these readings were handled. It is preferable to use the multidetector row CT scan with high-speed mode in pregnant patients since it has half the radiation dose of the high-quality mode and its scanning parameters are otherwise identical. Radiation exposure using this test is 300 mrad, which is below an accepted safe level of radiation exposure in pregnancy of 5 rad. Table 1.3 shows potential dose-dependent radiation effects during fetal development.

Sensitivity and specificity in a pregnant population with acute appendicitis are similar to general population with values reaching 100 % [106]. Limitations include small number of patients (seven), retrospective study, and study performed in a tertiary care institution; therefore, these findings may not be universally applicable. CT

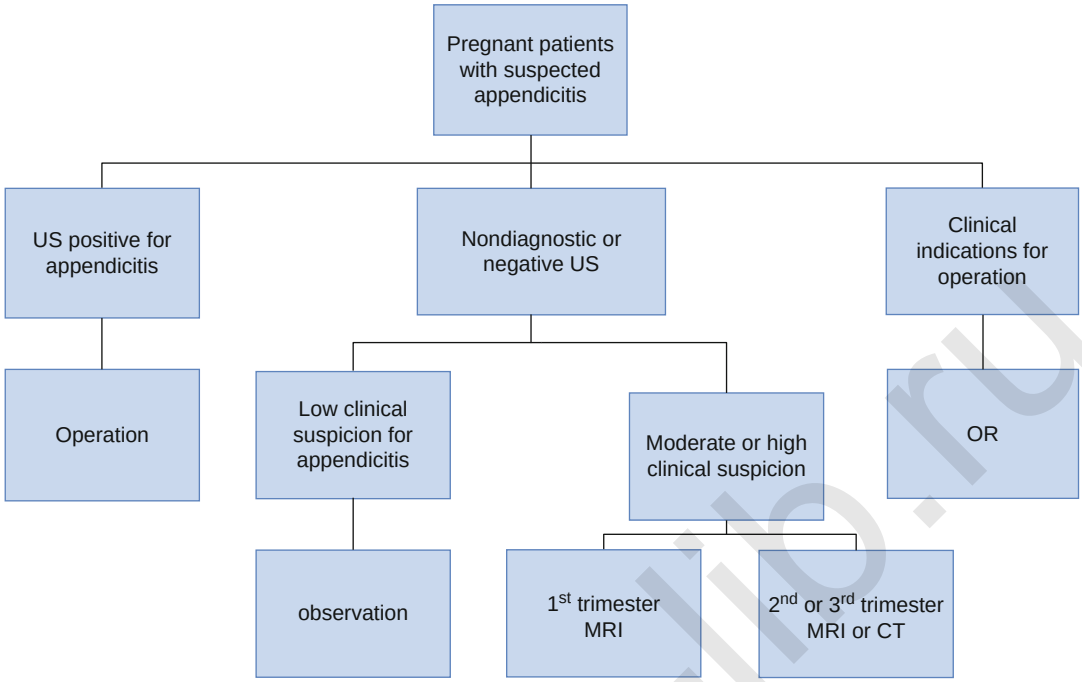

Fig. 1.7 Algorithm for the evaluation of pregnant patients with suspected appendicitis [80]

established a diagnosis in 30 % of cases with an initial negative ultrasound scan proving the accuracy of CT as well as its superiority over sonography for this indication [107]. In a letter to the editor in response to that series, CT scan was not helpful in the diagnosis in a single patient. Author's comments on the aforementioned study included the advanced appendicitis with periappendicitis and laparotomy with a paramedian incision. Indirectly, this meant that the 100 % sensitivity and specificity was because of significant pathologic changes in advanced appendicitis [108].

The conclusion and recommendation is that the CT scan should be used when there is an uncertain clinical diagnosis or equivocal laboratory or ultrasound findings or where access to MRI or MRI expertise is limited.

1.6.7 Chest Radiograph

It may be useful in identifying right lower lobe pneumonia from appendicitis in pregnant patients with right-sided abdominal pain. A plain abdominal radiograph can be used to identify air fluid levels or free air but indicated according to signs and symptoms of perforation (sudden sharp and severe pain) or obstruction (significant or feculent vomiting, no stool and flatus evacuation for several days).

Simplified diagnostic algorithm is presented on Fig. 1.7 [80].

1.7 Negative Appendectomy

1.7.1 Incidence

Negative appendectomy rates in the gravid patient vary considerably (4–55 %) [7, 26, 79, 80, 109–112]. In comparison, the rate of negative appendectomy in the general population ranges 10–15 % and as high as 26 % among the reproductive age females. Of interest is that only 15–20 % of patients undergoing negative appendectomies had another pathologic diagnosis (e.g., ovarian cyst, ovarian torsion, mesenteric adenitis, fibroids, and salpingitis) identified as the cause of their abdominal

pain [80]. These high negative appendectomy rates may be due to the surgeon's propensity for early intervention to prevent perforation and avoid unnecessary morbidity and mortality. There is a decreased risk of negative appendectomies in the puerperium. This indicates that puerperal women experience abdominal pain less frequently or are less prone to seek care for abdominal pain [13]. There is no significant difference of negative appendectomy rate between laparoscopic and open appendectomy groups [109].

1.7.2 Indications for Appendectomy

There is still a dilemma to perform or not a laparoscopic appendectomy if the appendix looks macroscopically normal in the nonpregnant patient, as well as among the population with no other abdominopelvic pathology. It has been argued that retaining a normal-looking appendix allows it to be used in reconstructive procedures [113]. On the other hand, some investigators believe that the appendix should be removed to rule out appendicitis histologically, also making the diagnosis of appendicitis less likely if the patient's symptoms return [114]. It can partly be explained by the fact that gross changes are not visible if intramural, mucosal, and submucosal changes in appendix are present histologically and could be responsible for the symptoms. Van den Broek et al. reported that 9 % of their series continued to have recurrent RLQ pain after negative laparoscopy, yet they did not recommend appendectomy in these patients [115]. This is due to early intraluminal inflammation that subsequently leads to transmural inflammation, or the inflammation subsides and could lead to chronic appendicitis with recurrent episodes of right lower quadrant pain and other symptoms mimicking acute appendicitis. Several studies report 20–22 % of patients with clinical suspicion of acute appendicitis who underwent appendectomy responded very well to appendectomy in spite of a normal microscopic examination of the appendix. Explanation could be found in other underlying causes such as appendix colic, appendiceal fecalith, and functional appendiceal abnormality or functional appendicopathy that might be the contributory factors rather than acute inflammation [116, 117]. In a study from 2009 of laparoscopic appendectomy, there were 30 % of intraoperative diagnoses of normal appendix confirmed with inflammation confirmed histologically. Authors recommend appendectomy in these situations [118]. These conclusions are similar to SAGES guidelines for laparoscopic appendectomy (04/2009):

> *If no other pathology is identified, the decision to remove the appendix should be considered but based on the individual clinical scenario (Level III, Grade A). Macroscopically normal appendices may have abnormal histopathology. Several studies have shown a 19–40 % rate of pathologically abnormal appendix in the setting of no visual abnormalities. Therefore, the risk of leaving a potentially abnormal appendix must be weighed against the risk of appendectomy in each individual scenario.*

Furthermore, some neoplasms of the appendix can occur in an organ that appears grossly unremarkable [119, 120]. If pseudomyxoma peritonei is observed, the appendix should always be removed and subjected to a thorough histological examination.

Conclusion in one sentence should be: "As a surgeon you should not be deterred from removing an appendix once the diagnosis is suspected, because pregnancy is not affected by removal of a normal appendix" [121].

It should be noted that using modern diagnostic modalities, correct diagnosis of biliary origin of acute abdomen during pregnancy is very high. It can be presented as *index of wrong diagnosis*.

> *Index of wrong diagnosis* (%) = provisionally diagnosed cases – confirmed cases × 100 provisionally diagnosed cases

For acute appendicitis it is around 40 % and only 8.5 % for acute cholecystitis [7, 122]. A correct diagnosis of acute appendicitis between 1951 and 1973 was 58–68 % [124–126].

1.7.3 Perinatal Outcome

Because of the unreliability of the clinical diagnosis of appendicitis in pregnancy, an aggressive surgical approach to the disease process has been advocated to avoid progression to appendiceal perforation, which has been associated with a high rate of fetal demise [127, 128]. However, more recently it has been reported that negative appendectomies also may be associated with a significant rate of fetal demise. In a review by McGory et al. on 3,133 pregnant patients, rates of fetal loss and early delivery in patients with complicated appendicitis were 6 and 11 %, respectively [69]. In comparison, the rates for fetal loss and early delivery in patients undergoing a negative appendectomy were 4 and 10 %, respectively. This study was limited because only fetal demise and early delivery occurring during the hospitalization in which the appendectomy was performed was reported. Freeland et al. did not find any relationship of the early delivery and the fetal demise due to the appendectomy [80], while Ito et al. found similar adverse perinatal outcomes in patients with negative appendectomy and inflamed appendicitis. In this study by Ito et al., perforated appendicitis caused significantly higher adverse perinatal outcomes [129]. These adverse outcomes in negative appendectomy and inflamed appendicitis group were the same as in general population; therefore, it is questionable that negative appendectomy causes adverse perinatal results [130].

1.8 Management

Once investigations have been carried out in hospital and the diagnosis of acute appendicitis has been confirmed, management is always surgical removal of the inflamed appendix. Murphy in 1916 said for appendicitis in general population but can be adopted also for pregnant women: "Let us return to our ideal; early operation is the only safe practice." This can be performed by several different procedures simply divided into laparotomy or laparoscopy procedures.

1.8.1 Anesthetic Considerations

Anesthetic concerns in the pregnant patient can be broken down into two major categories: teratogenicity of the anesthetic agents and maternal physiological changes as a result of anesthetic agents. The teratogenicity of anesthetic agents, defined as the potential effect in chromosomal damage or in carcinogenesis in the fetus, is minimal [131]. In a consensus statement published in the *New England Journal of Medicine* in 2000, no anesthetic agents were listed as definitively causative of fetal malformations [132]. Increased oxygen consumption and mechanical displacement of the abdominal organs cause the pregnant patient to increase minute ventilation, primarily through a 30–40 % increase in tidal volume [133]. A compensatory respiratory alkalosis with a $PaCO_2$ from 30 to 35 mmHg develops. Intubation may be more difficult because of increased airway edema later in the pregnancy, and smaller endotracheal tubes should be used at this time. Because decreased lower esophageal sphincter pressure and delayed gastric emptying in pregnancy can cause an increased risk of aspiration, cricoid pressure should be used to prevent aspiration during intubation [134]. End-tidal CO_2 monitoring should be used intraoperatively. Hypotension in the pregnant patient should be treated initially with aggressive intravenous fluid resuscitation. The patient should be placed in the left lateral decubitus position, if possible, to increase venous return. Trendelenburg positioning can also be used in the hypotensive patient to increase venous return [131].

1.8.2 Open Appendectomy

As in other surgical procedures, type of incision is very important for successful completion of the operation. Despite the type of incision used,

the operation should be completed with minimal uterine manipulation. There are several incisions that could be performed. Despite the surgical approach, the most experienced abdominal surgeon should perform the procedure to shorten the operation time and possible postoperative complications as much as possible.

1.8.2.1 Muscle Splitting Incision (McBurney's Incision, Gridiron Incision)

This is the incision of choice for open approach for the removal of the appendix in pregnant patients in all trimesters. In the latter pregnancy, the incision could be positioned above McBurney's incision because of possible displacement of the appendix in the right upper quadrant. This change of the location of the incision is not necessary because the appendix was easily located in 94 % of the incisions made through McBurney's point and in 80 % of the incisions made above McBurney's point [135].

There is one case report of significant uterine injury during appendectomy in pregnancy [136]. Inadvertently, the uterine wall was incised to 3 cm in length on the right anterolateral aspect leading to bleeding and leakage of amniotic fluid from the incision site. Two topics should be discussed: first is adequacy of residual amniotic fluid and second is the contamination of amniotic fluid with purulent or feculent material. During operation the ultrasound scan should be performed to determine the presence of a fetal heart rate and to get an impression of residual amniotic fluid volume. With a live fetus and enough amniotic fluid, the gestation could be continued. The risk of chorioamnionitis is addressed by the use of perioperative broad-spectrum antibiotics. The immediate risk of preterm labor is addressed by the use of indomethacin, although a calcium channel blocker is also an option and would not affect amniotic fluid volume or potentially mask an infection. Cesarean delivery prior to the onset of labor is recommended to minimize the risks of uterine rupture [137]. If, on the other hand, significant leakage occurs or there is dilemma about fetal vitality, the baby should be delivered by Cesarean section during the same operation.

1.8.2.2 Midline Vertical Incision

This incision is used when acute abdomen with diffuse peritoneal irritation is present. This is important for two main reasons:

- Allows the surgeon to deal with unexpected surgical findings
- Allows Cesarean delivery if necessary

1.8.2.3 Right Transrectal/Pararectal Incision

These incisions are rarely used. If the diagnosis is certain, then McBurney's incision is made. If acute abdomen with diffuse peritoneal irritation is present, then midline vertical incision is made.

1.8.3 Laparoscopic Appendectomy

Laparoscopic appendectomy during pregnancy continues to be controversial especially in the latter part of the second and the third trimester. Several case reports and small series have reported success during all trimesters without complications [48, 110, 138], but in the same institutions, there is higher percentage of open approach during the third trimester [48]. Thus, there is some bias in these studies, and conclusions are not yet presented as recommendations.

In the case of appendicitis, some might argue that the laparoscopic approach exposes the fetus to excessive risks from trocar placement and the effects of carbon dioxide on the developing fetus and the long-term effects of this exposure with significant fetal loss [70, 139]. Laparoscopic procedures are approximately 50 % longer with conflicting studies showing decreased length of stay and hospitalization [140, 141], but with increasing number of laparoscopic procedures performed worldwide, the duration of open and laparoscopic operations would become the same [48]. Questions arise regarding the risk for decreased uterine blood flow due to increased intra-abdominal pressures from insufflation and the possibility of fetal carbon dioxide absorption [127]. Carbon dioxide used for the creation of pneumoperitoneum

could lead to fetal carbon dioxide absorption with potential subsequent fetal acidosis. This could be minimized with maintenance of intra-abdominal pressure <12 mmHg and minimizing operative time. Clinical and experimental studies found no substantial adverse effects for the fetus when the maximal pneumoperitoneum pressure was limited to 10–12 mmHg and duration of less than 60 min [142, 143]. Others stress the importance of the absorption of carbon monoxide, produced by the use of monopolar energy, through the peritoneum. The absorbed carbon monoxide can produce carboxyhemoglobin and metahemoglobin that compete with hemoglobin in the uptake and transport of oxygen. It is recommended to continually remove the smoke produced by tissue fulguration [144]. Harmonic scissors produce vapor-free gas, avoiding the potential effects of carbon monoxide [145]. Other negative effect of electrocautery is the potential for uterine irritation.

There are many advantages of laparoscopic technique. Authors note that laparoscopy expands the ability to explore the abdomen with less uterine manipulation [146]. Further, it increases the ability to locate and treat the ectopic appendix and results in relatively small incisions compared with the open technique or helps in detecting other unexpected sources of pain [147, 148]. With open technique of trocar placement, there is almost no possibility of injury of intra-abdominal organs. Direct uterine injury during trocar placement has been reported but without fetal loss [149]. Also reduced cecal manipulation during appendectomy with less cecal trauma causes earlier restore of large bowel function and earlier passage of the first flatus and first postoperative stool (author's clinical observation, not published results). In addition to general advantage of smaller incisions, less postoperative pain, and earlier return to normal activity, laparoscopy can result in less manipulation of the uterus while obtaining optimum exposure of the surgical field. Lower rates of dehiscence or herniation during labor are another potential benefit. Rapid return to full activity could reduce the frequency of maternal thrombosis and embolic events, which can be a source of maternal mortality in some patients, and it is known that thromboembolic events are more common in pregnancy [142, 147, 150]. Some studies found significantly shorter hospital stay in the laparoscopic group (3.4 vs. 4.2 days) [48]. A study from the Swedish Health Registry evaluated 2,233 laparoscopic and 2,491 open laparotomy cases from two million deliveries in Sweden from 1973 to 1993 [151]. Outcomes evaluated birth weight, gestational duration, intrauterine growth retardation, congenital malformations, stillbirths, and neonatal deaths with no statistically significant differences comparing the laparoscopy and laparotomy group. It appears that there was an increased risk for infants in both laparoscopy and laparotomy groups to weigh less than 2,500 g, to be delivered before 37 weeks, and to have an increased incidence of growth restriction compared with the total population.

A recent review advises prudence with the use of laparoscopy during pregnancy [152]. The outcome of that review was dictated mainly by a large observational study in which a significantly higher adverse outcome after laparoscopic appendectomy in pregnant patients was found – fetal loss with laparoscopy (5.6 %) versus open appendectomy (3 %). A recommendation for caution based on this study can be criticized for two reasons: First, an important limitation of an observational study is the risk of confounding by indication, making this study unsuitable to test if one surgical procedure is superior over the other. A second limitation is that the outcome of fetal loss (5.6 %) in that study is favorable compared to that of most of the literature on both laparoscopic and open appendectomy during pregnancy, suggesting that both procedures are relatively safe during pregnancy.

Current practical/clinical SAGES guidelines (04/2009) statement is:

> *Laparoscopic appendectomy may be performed safely in pregnant patients with suspicion of appendicitis* (*Level II, Grade B*). *Laparoscopic appendectomy can be performed safely in any trimester and is considered by many to be the standard of care for gravid patients with suspected appendicitis*.

1.8.3.1 Laparoscopic Technique

In the first and early second trimesters, the technique is similar as in nonpregnant patients. In an advanced pregnancy, the port positions are somewhat specific (see further text). The patient is placed supine on the operating room table. Restraining straps are placed across the chest and thighs, and sequential pneumatic compression devices are placed on both lower extremities. Some authors recommend a Foley catheter [109] and a nasogastric tube placement and removal at the end of the operation. A prophylactic antibiotic is administered intravenously 30 min before the skin incision. Maternal end-tidal CO_2 is monitored and should be controlled within physiological range (30–40 mmHg).

Patients are tilted to the left to displace the uterus from the inferior vena cava and to remove the small bowel from the operating field, and a slight Trendelenburg position may be added, if necessary. The procedure is always performed using three ports, and their placement is modified in accordance with gestational age. In the advanced pregnancy, the first port (5 or 10 mm – laparoscope) is placed 2–4 cm cephalad to the gravid uterus in the upper midline between the umbilicus and xiphoid process. The bigger the uterus, the more cranial the first trocar is placed for easier intraperitoneal manipulation.

1.8.3.2 Pneumoperitoneum

Pneumoperitoneum is carried out using an open (Hasson) technique for entering the abdominal cavity under direct vision. Other possibility is to use a Veress needle but with the higher risk of perforation of intra-abdominal organs or pneumoamnion [141, 153]. Schreiber reports, while carrying out a laparoscopic appendectomy, injuring the uterine wall with the mandrel of the 5 mm trocar during introduction. There was loss of a little amniotic fluid, but there was no severe bleeding. The remainder of the pregnancy was without complications [154]. An optical trocar can be used for entering the abdomen. Currently, the so-called Direct Vision Initial Ports (like the OptiView, by Ethicon, Cincinnati, OH, USA, and the Visiport, by US Surgical, Norwalk, CT, USA) are available. They can be used with or without pneumoperitoneum. These kinds of trocars are introduced under direct vision. The pneumoperitoneum pressure is maintained between 10 and 12 mmHg. There are several modifications of instrument placement and their size depending on the laparoscopic technique and equipment. Some authors recommend the second port (5 or 12 mm) is placed laterally in the right lower quadrant, and the third port (5 or 10 mm) is placed in the right upper quadrant in a more cranial location. Twelve milimeters ports are used when the linear cutting stapler is used for the transection of the appendix at its base (Fig. 1.8) [155]. Other combinations of trocar placement are presented on Fig. 1.8 depending on the degree of uterine enlargement [109].

Fetal heart rate is recorded immediately before and after surgery and during operation every 5 min in the lower left quadrant without disinflation (Fig. 1.9). Lu et al. found that external monitors of uterine contractions were variably effective in the insufflated abdomen [156]. For patients with potentially viable fetuses managed surgically, steroids were generally administered 24 h preoperatively to speed fetal lung maturation.

1.8.3.3 Intraoperative CO_2 Monitoring

Intraoperative CO_2 monitoring by capnography should be used during laparoscopy in the pregnant patient (Level III). Fetal acidosis with insufflation has not been documented in the human fetus, but concerns over potential detrimental effects of acidosis have led to the recommendation of maternal CO_2 monitoring [157, 158]. Initially, there was a debate over maternal blood gas monitoring of arterial carbon dioxide ($PaCO_2$) versus end-tidal carbon dioxide ($ETCO_2$) monitoring, but the less invasive capnography has been demonstrated to adequately reflect maternal acid-base status in humans [159]. Several large studies have documented the safety and efficacy of $ETCO_2$ measurements in pregnant women [160–162] making routine blood gas monitoring unnecessary.

1.8.3.4 Fetal Heart Rate Monitoring

Fetal heart monitoring should occur pre- and postoperatively in the setting of urgent abdominal surgery during pregnancy (Level III). While intraoperative fetal heart rate monitoring was once

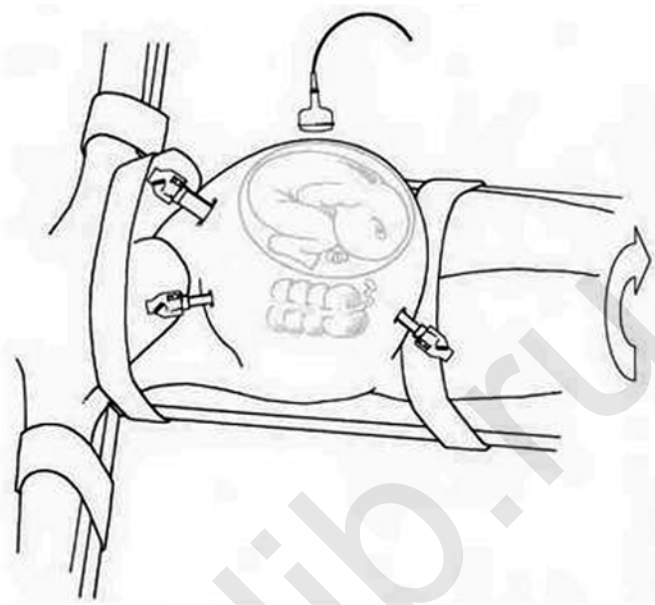

Fig. 1.8 Patient positioning, port placement, and intraoperative fetal monitoring for laparoscopic appendectomy in advanced pregnancy (see text for details) [155]

thought to be the most accurate method to detect fetal distress during laparoscopy, no intraoperative fetal heart rate abnormalities have been reported in the literature [163, 164]. This has led some to recommend only pre- and postoperative monitoring of the fetal heart rate as no increased fetal morbidity has been reported [160, 162]. The effects of general anesthesia on cardiotocography result in a reduction of beat-to-beat variation with normal baseline frequency. The decreased variability can persist until 90 min in the postoperative course due to the residual effects of anesthetic agents on the fetus. This could be misinterpreted as fetal distress leading to emergency delivery and hence adding to fetal morbidity and mortality [165]. It should be noted that transvaginal sonography must be used during the procedure because the signals from abdominal ultrasound would be lost during insufflation [166, 167].

1.8.4 Conversion from Laparoscopic to Open Approach

The question could arise about influence of conversion from laparoscopic to open approach to the mother and fetus. Studies did not show increased rate of complications and increased maternal or fetal mortality and preterm delivery. In the open approach group, preterm delivery rate was 11.8 % versus 15.8 % in the laparoscopic approach [160]. Caution should be present because of a small number of patients that had undergone such conversions [160]. Theoretically if conversion is indicated, then mostly (1) the anatomy is difficult or (2) inflammation is in an advanced stage in the form of perforation or abscess. Both situations are connected to longer operative time and higher percentage of complications.

1.8.5 Perioperative Considerations

1.8.5.1 Risk of Drug-Induced Congenital Defects

Interests of both the mother and the fetus must be considered in therapy during pregnancy. Usually, these interests do not conflict, because what is good for the mother is generally good for the fetus. Sometimes, however, maternal therapy must be modified to substitute alternative but safer therapy because of the concerns about drug teratogenicity (e.g., substituting a histamine2 receptor antagonist for misoprostol, an

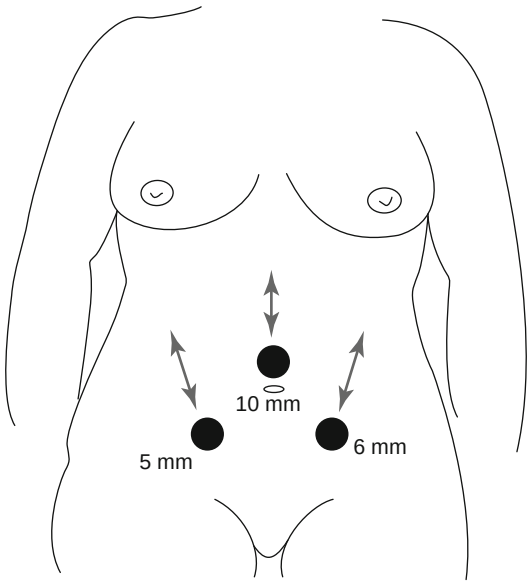

Fig. 1.9 Trocar placement for laparoscopic appendectomy in different stages of pregnancy [109]

abortifacient that is contraindicated during pregnancy) [168, 169]. Rarely, the maternal and fetal interests are diametrically opposed, as in the use of chemotherapy for maternal cancer, a therapy that is potentially lifesaving to the mother but life threatening to the fetus [33]. These conflicts raise significant medical, legal, and ethical issues.

There are many categories of drugs that could have deleterious effects on a fetus, and the detailed elaboration is out of the scope of this book. There are two main categories of medications used in all patients either prophylactically or therapeutically. All teratogenic drugs generally determine a specific pattern or single malformation during a sensitive period of gestation with a dose-dependent effect [170].

Antibiotics

Antibiotics should be administered preoperatively (30–60 min prior to skin incision) in all patients (administered to 94 % of patients found in the literature) [140]. These should be from the FDA Class B drugs which are found to be safe for the fetus. Standard antibiotics in use are second-generation cephalosporins which comprise 60 % of all classes of antibiotics used during pregnancy for acute appendicitis found in literature [140]. If a gangrenous or perforated appendix is found, cephalosporins are used in combination with metronidazole (FDA Class B) [25].

NSAIDs

Use of NSAIDs during the second and third trimesters is associated with oligohydramnios and anuria and, close to term, to precocious closure of Botallo's duct, with subsequent pulmonary hypertension, intracranial hemorrhage, and necrotizing enterocolitis [171–176]. During pregnancy the drug of choice for analgesic, anti-inflammatory, and antipyretic action is paracetamol. When appendectomy is performed with Cesarean section through median laparotomy, then all classes of medications could be used as in nonpregnant patients unless contraindicated for maternal reasons.

1.8.5.2 Thromboprophylaxis

Gestational hormones, particularly estrogen, contribute to a mild hypercoagulopathy during pregnancy by increasing the synthesis of clotting factors [177]. Thromboembolic phenomena are also promoted by intra-abdominal vascular stasis resulting from compression by the enlarged gravid uterus. Epidemiological studies estimate the annual frequency of deep venous thrombosis (DVT) in the general population is 0.16–1 % [178, 179], of which 2 % are pregnancy related [180]. Therefore, risk of thromboembolic event, either DVT or PE, during pregnancy and puerperium is estimated to be tenfold higher [181–185], reaching up to 2 % [186]. Puerperium is the period with highest VTE risk [181, 183, 184, 187, 188] which was reported to be up to 25-fold higher than that in nonpregnant women [181, 183, 184]. It has been reported that 43–60 % of pregnancy-related PE episodes take place during puerperium [184, 185]. Established risk factors for VTE during pregnancy include maternal age (1/800 for age >35 years; 1/1,600 for age <35 years) [181, 184, 187], obesity (body mass index (BMI) >30) [189, 190], preeclampsia/hypertension, parity ≥3 [186], previous VTE or congenital or acquired thrombophilia [188, 191–194], smoking, diabetes [195], multiple gestation [189], black race [196], and anemia. During the

labor there are other factors: type of delivery (with three to sixfold higher risk for Cesarean vs. vaginal delivery, higher for emergency Cesarean [184, 197, 198], and mid-cavity instrumental delivery) [197, 198], prolonged labor >12 h [189, 198, 199], immobility, major abdominal surgery for >30 min during pregnancy or puerperium [181], preterm delivery [185], excessive blood loss (>1 l), or blood transfusion. In the postpartum period, other factors may be added as dehydration, immobility, and anemia [178, 100]. The factors that contribute the most to the incidence of thromboembolic events, due to their high prevalence, are age >35 years, obesity, and Cesarean delivery [198]. Cesarean delivery increases the risk of VTE because it involves pelvic surgery that may last >30 min, adding to the prothrombotic effects of delivery, pregnancy weight gain, and other risk factors (see above). The VTE incidence rate following Cesarean section is 1.78 % [185], with an odds ratio of 2 [185]. The latest guidelines [178, 186, 200] recommend that thromboprophylaxis with low-molecular-weight heparin (LMWH) in women who undergo an emergency Cesarean section and in women who undergo an elective Cesarean section also has an additional risk factor. However, the duration of post-Cesarean thromboprophylaxis has been discussed and is an important factor, given the elevated risk of VTE during puerperium, especially during the first week postpartum [178, 200] and the trend to earlier post-Cesarean hospital discharge. So the latest guidelines [178] recommend thromboprophylaxis in these women during 7 days. However, there is no scientific evidence about the duration of the thromboprophylaxis, only clinical recommendations [178, 200, 201].

There are no recommendations for thromboprophylaxis after laparotomy or open or laparoscopic appendectomy in pregnancy; therefore, similar recommendations should apply as for general pregnant patients after obstetric operation.

1.8.5.3 Tocolysis

Although preterm contractions caused by uterine irritation from peritonitis occur in up to 83 % of the cases, preterm labor and delivery occur in only 5–14 % of the cases. However, up to 50 % of the patients in the third trimester deliver preterm [201]. Open procedures and laparoscopy do not differ with respect to the incidence of preterm delivery and other complications [160].

Different agents have been used as tocolytic agents prophylactically like magnesium sulfate, terbutaline, or 17-hydroxyprogesterone [203, 204]. Beta$_2$-receptor agonist (ritodrine) is perhaps the most used tocolytic agent. Some authors claim that tocolytic treatment after the onset of contractions could not prevent preterm labor and should be ordered for the patients with delayed presentation and advanced gestational age in order to prevent preterm labor and fetal loss [79]. No study has documented positive effects on the outcome. The current conclusion and recommendation is that the use of these agents is a matter of choice [203, 205, 206]. Current SAGES and EAES guidelines recommend tocolytics only if uterine contractions are present. In other words, tocolytics should not be used for prevention of uterine contractions. Tocolytics were thought to calm the uterus from the insult of acute abdomen and the intraoperative uterine manipulation, but their benefit is equivocal [207]. Figure 1.10 stratifies the different tocolytics used and their effect on the fetal outcome [122]. Authors show that there is no significant difference in efficacy of different tocolytics and also no significant difference in the outcome when tocolytics are used or not, the finding confirmed by others [208]. These findings are different from those which Allen et al. reported, as they recorded a 100 % success rate of tocolysis in prevention of labor [209].

Tocolytics not only fail to improve fetal outcome but also had serious maternal and fetal side effects, which could contraindicate their use, especially ritodrine and prostaglandin synthetase inhibitors. Ritodrine causes maternal and fetal tachycardia, nausea, and vomiting [122, 210], so it impairs very important signs for managing acute abdomen. Prostaglandin synthetase inhibitors are blamed for constriction of ductus arteriosus when used as a tocolytic, but recently it was found that when used between 26 and 34 weeks of pregnancy, the danger is minimal [211]. In the study by El-Amin Ali et al. [122], no teratogenesis due to prostaglandin synthetase inhibitor was detected,

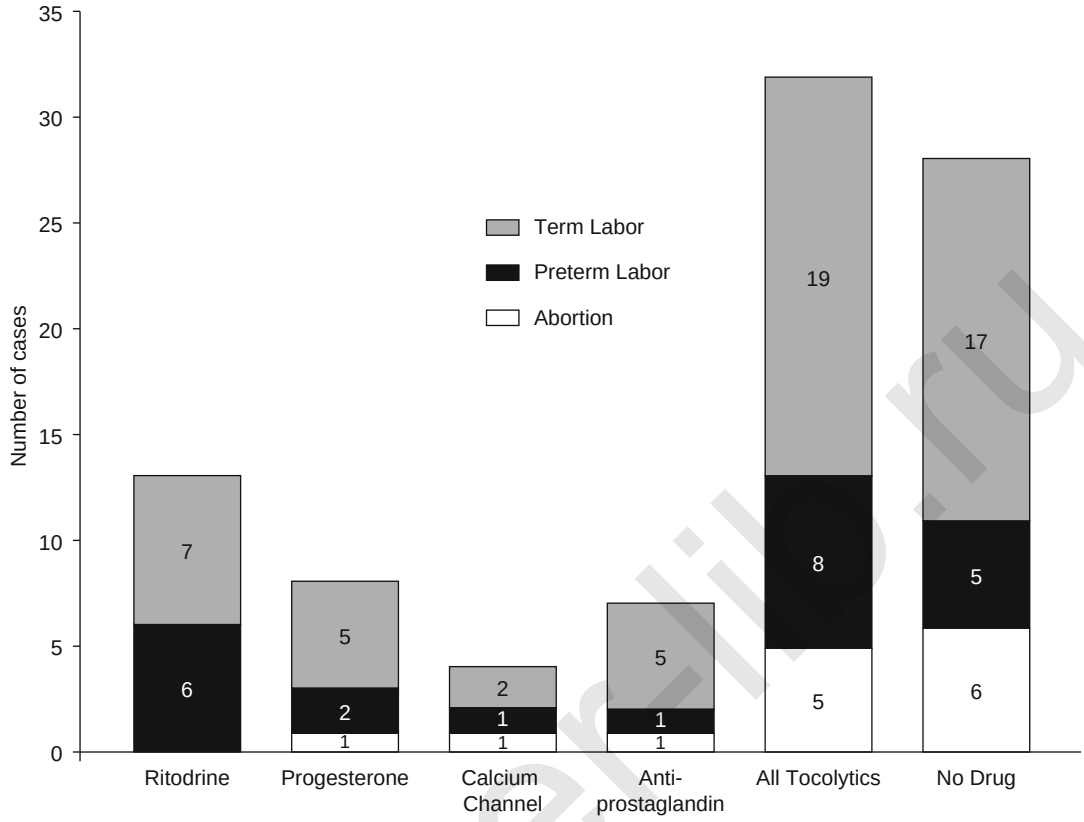

Fig. 1.10 Comparison of different tocolytics used and their effect on the fetal outcome (no statistically significant difference) [122]

and the reported complications of altered hematological indices, transient renal insufficiency, and necrotizing enterocolitis [212] were not detected. Another drawback of the use of prostaglandin synthetase inhibitor is its anti-inflammatory and antipyretic effect, which might mask important clinical parameters for acute abdomen case management and give the surgeon a false sense of security. Unlike ritodrine and prostaglandin synthetase inhibitor, nifedipine is safer and does not alter the disease symptomatology [207]. Although nifedipine was blamed for causing hypotension, this proved to be insignificant [210, 213]. Albeit feared for teratogenicity [214], the evidence is not conclusive [215], and no malformations were reported in the study by El-Amin Ali et al. [122]. In the study by Lu et al., 26 % of patients with symptomatic cholelithiasis developed preterm contractions requiring treatment with tocolytic agents. One patient with biliary colic failed tocolysis and delivered a 1,250 g infant at 32 weeks gestation, and another with acute cholecystitis had pulmonary edema as a complication of tocolysis [156]. Selective use only, when uterine contractions were present was indicated in study by Sungler et al. [216]. Both patients (25th and 32nd weeks of gestation) receiving tocolysis had preterm labor on admission for 6 and 9 days, respectively, but had complicated gallstone disease in pregnancy. Also, tocolysis, despite its efficacy when indicated, has its risks.

In conclusion, tocolytics are not only ineffective but may have serious side effects, and failure to take prompt action in such adverse conditions will be deleterious to the mother and the fetus. Tocolytics should not be used prophylactically. Maybe future studies will define high-risk groups that could benefit from such prophylactic tocolysis.

1.8.5.4 Pathohistological Examination

All the extracted specimens should be sent to pathohistological examination because in this pregnant patient group, other pathologies other than appendicitis (including carcinoid tumor) could be found [48].

Pregnancy complicated with acute appendicitis and appendiceal endometriosis is a rare condition whose frequency ranges 3–8/10,000 deliveries [217]. Only 11 cases of endometriosis causing appendicitis are published. Hematoxylin-eosin shows acute appendicitis, and the appendiceal wall has foci of endometrial implants with acute inflammation. A panel of immunohistochemical stains, including cytokeratins 7 and 20, estrogen receptor, and CD10, confirms that the intramural glands and the appendiceal mucosa are of different nature, as the former reacted as endometrial mucosa, whereas the latter reacted as a colonic-type mucosa [218]. A decidual polyp, which occluded most of the appendiceal lumen, is proposed as a rare cause of acute appendicitis during pregnancy. Commonly, most cases of endometriosis of the appendix are discovered as a result of incidental appendectomy. Data show that 30 % of these cases were complicated by perforation at the time of surgery; that there were no maternal or fetal complications in 45 % of the cases; and that there was one case of preterm labor with infant death. All complications occurred in the third trimester of pregnancy [219–229]. It may be speculated that decidual reaction in pregnancy affects decidual cells present within the appendix as well. Changes in intra-appendiceal decidual cells would induce more inflammatory response, which, in turn, may increase the risk of perforation. There is even a case of intussusception of the appendix mimicking the appendicitis described [230].

1.8.5.5 Postoperative Course

Potential advantages of laparoscopic appendectomy in the pregnant patient include decreased fetal depression due to lessened postoperative narcotic requirements, lower risks of wound complications, and diminished postoperative maternal hypoventilation [231]. Nasogastric tube is extracted after the operation and early ambulation after several hours. Oral intake is started on the first postoperative day.

1.9 Specific Considerations

1.9.1 Incidental Meckel's Diverticulum

Symptomatic Meckel's diverticulum (MD) during pregnancy is exceptionally rare. Walser et al. in 1962 published the first report of Meckel's diverticulitis in a pregnant woman [232]. Only 24 cases of MD-complicated pregnancy have been reported up to date [233–235]. In the pregnant patient, the average maternal age of all reported cases of symptomatic MD was 24 years (14–31 years). The most common complication was perforation (57 %), maternal mortality was 16 %, fetal mortality was 13 %, and incidence of preterm deliveries was 25 % [234]. Given the high incidence of perforation resulting in an enormous rate of maternal and fetal mortality, removal of incidentally found MD is justified in the pregnant patient [234]. An epidemiological, population-based study from the Mayo Clinic demonstrates that the benefits from removal of an incidental MD in general population are far superior to the risk of developing complications. Authors found that if the patient in general population fulfills any of the following criteria (or combination), then there is an indication for the incidental MD to be removed:

- Patient age younger than 50 years
- Male sex
- MD length greater than 2 cm
- Ectopic or abnormal features within a diverticulum

The same indications should be used in pregnant patients. Author's data show that when one criterion is met, the overall proportion of symptomatic MD was 17 %. When two, three, or all four criteria were met, the proportion increased to 25, 42, and 70 %, respectively [236].

During open approach, if the asymptomatic MD or symptomatic Meckel's diverticulitis is found, *diverticulectomy* or *wedge small bowel resection* with subsequent bowel continuity is performed. Laparoscopic surgical technique is

the same as in nonpregnant population. An endoscopic linear cutting stapler is introduced through a 12 mm trocar and applied to the base of the MD, perpendicular to the base of the MD but transverse to the longitudinal axis of the bowel. The stapler is fired and the MD resected off the ileum. Small bleeding points at the edge of the staple line, if present, are sutured intracorporeally with 3-0 Vicryl. All the specimens are delivered through 12 mm port with the use of an endobag. A wedge resection is not necessary in these incidental findings because the base of the MD is not inflamed. If suture techniques are used after excision, bowel continuity is achieved by placing intracorporeal sutures with 2-0 or 3-0 resorptive sutures. Pathologic specimen should always be sent for pathohistological examination.

1.9.2 Acute Appendicitis and Ectopic/Heterotopic Pregnancy

Ectopic pregnancies occur at a frequency of approximately 16/1,000 patients [237]. Ectopic pregnancy has been rarely reported in conjunction with appendicitis; there are 24 such cases in the medical literature since 1960 [238–241].

One of these cases is maybe not really concurrent appendicitis because the patient presented 1 week after termination of ectopic pregnancy [237]. It is unknown whether appendicitis is coincidentally associated with ectopic pregnancy. A causal relation between ectopic pregnancy (EP) and AA has been postulated. Some authors postulate that ectopic pregnancy may cause an initial contiguous inflammatory reaction in the adjacent appendix, which creates a portal for infection in the appendix by normal colonic bacterial flora, so-called periappendicitis [241]. In the opposite direction, an antecedent AA with spontaneous resolution could also conceivably result in peritubular inflammatory adhesions favoring the development of the ectopic pregnancy. It is of particular interest that 75 % of tubal pregnancies involve the right tube [8]. Previously reported cases of concurrent ectopic pregnancy and appendicitis have indicated a predilection for right tubal ectopic pregnancy (75 %) versus left tubal ectopic pregnancy (16 %) [241]. The rarest form is AA with heterotopic pregnancy. This is the most difficult situation because the patient has three potential causes of abdominal pain: appendix, normal intrauterine fetus, and extrauterine pregnancy [242]. Details on the subject are presented in the next Sect. 1.9.3.

Although advances in pelvic sonography by transvaginal and high-frequency sonogram [243] and highly sensitive tests for βHCG have facilitated earlier diagnosis of ectopic pregnancy before the onset of clinical symptoms, differences in operator technique and obscuring bowel and gas may render preoperative diagnosis of appendicitis and/or ectopic pregnancy inconclusive. A corollary of this is that lack of definitive findings on sonography (such as free pelvic fluid, echogenic adnexal mass for ectopic pregnancy, and noncompressible appendix >6 mm with free fluid for appendicitis), in the presence of high clinical suspicion from a complete history and physical examination, should not preclude a differential diagnosis including appendicitis and ectopic pregnancy in the workup of acute abdomen in a pregnant patient [12, 26, 241, 242].

Because of the uncertainty in diagnosis and to improve the maternal prognosis, emergency exploratory must be practiced. Recently, confirmation of the diagnosis and the management of both ectopic pregnancy and acute appendicitis could have been made by performing a laparoscopy, either microlaparoscopy or classic laparoscopy, prior to preceding to an open laparotomy as many authors recommend [26, 241, 244, 245].

1.9.3 Acute Appendicitis in Patients with In Vitro Fertilization and Embryo Transfer

1.9.3.1 In Vitro Fertilization (General Considerations)

In vitro fertilization (IVF) is now widely used for the treatment of infertility, and validated age-stratified national success rates and outcomes are published annually [246–248]. To facilitate patient counseling, clinical decision making, and

access to health-care provision, prediction models for live birth after IVF have been constructed [249]. However, these studies have been limited by their sample size, development before the introduction of intracytoplasmic sperm injection (ICSI), or lack of validation in external populations [250–254]. Established multivariable prediction models may therefore not be applicable to contemporary couples seeking treatment. Consequently, clinicians and regulatory bodies have not adopted prediction models and predominantly quote age-related success rates [246–248]. Given the known complications with multiple gestations and prematurity, the focus has moved to defining the most appropriate IVF outcome variable as a singleton term live birth [255–257]. Low birth weight and macrosomia are also known to be associated with immediate and long-term risk to offspring health [258], and IVF singletons are at increased risk of these complications [259, 260]. It is now recognized that factors leading to infertility may be responsible for adverse perinatal outcome rather than the process itself [261–264]; however, which parental characteristics of infertile couples contribute to adverse perinatal outcomes in IVF singletons and can thereby be targeted for intervention remain unknown. Nelson and Lawlor developed the most comprehensive model, which encompasses a series of new measures including the use of donor oocytes, ICSI, cycle number, and whether there had been a previous spontaneous or IVF-related live birth or fetal loss. Using this novel model, there is statistically significant improvement in the overall prediction of live birth [265]. Maternal characteristics, in particular maternal age, source of the oocyte, and cervical causes of infertility are strongly associated with the risk of low birth weight and preterm delivery in singleton live births resulting from IVF. Notably, some of these associations were in the opposite direction to those seen for successful live birth. Thus, in women who successfully have a singleton live birth with IVF, the risk of low birth weight is reduced in older compared with younger women, and both low birth weight and preterm are reduced when the woman's own embryo has been used [265].

1.9.3.2 Published Reports

In cases of IVF-ET techniques, the complication of ectopic/heterotopic pregnancy is relatively common, reportedly occurring in 1–3 % of these pregnancies [266, 267], while heterotopic pregnancy has been estimated at 1/30,000 non-IVF pregnancies [268, 269]. Transfer of four or more embryos poses an additional risk for heterotopic pregnancy [270]. There are five cases of acute appendicitis in IVF-ET pregnant patients which is significant incidence in comparison to the incidence of non-IVF pregnancies (24 cases – see Sect. 1.9.3). Of these, three cases are spontaneously developed acute appendicitis. One developed simultaneous heterotopic pregnancy (9 weeks) undergoing rupture and acute appendicitis. Right salpingectomy and appendectomy were performed. The patient delivered dizygotic male twins at 37 weeks gestation by Cesarean section [245]. Another similar case developed appendicitis and heterotopic pregnancy (6 weeks), and appendectomy and right salpingectomy were performed. The patient delivered a male neonate at 38 weeks gestation by Cesarean section insisted by the patient [271]. The third case described a woman with a perforated appendix and an ectopic pregnancy [244]. The remaining two are iatrogenic appendiceal punctuations with the needle for oocyte retrieval and subsequent development of perforated appendicitis. One case was published in 1996, and on histological examination, the appendix showed several puncture holes [272]. Another case, a first case published in a patient with IVF pregnancy in 1992, was caused by puncturation of the appendix and development of appendicitis [273].

Indicative for iatrogenic injury is the development of appendicitis (or bowel perforation) several (up to 9) days after the IVF procedure. Even a case of ovarian stimulation followed by natural intercourse and subsequent ovarian hyperstimulation syndrome (OHSS) and acute appendicitis is described [274]. Epigastric pain is not an uncommon symptom in patients with severe OHSS with massive ascites. Febrile morbidity is often observed in patients with severe OHSS without infection [275]. An elevated white blood cell count is also found both in patients with severe OHSS [276] and

in those with appendicitis. The possibility is raised that OHSS might affect the course of concurrent appendicitis. An increased rate of infectious disease was reported in patients with OHSS, possibly due to immunodeficiency as a consequence of hypoglobulinemia, a frequent occurrence in patients with severe OHSS [275]. Severe stress associated with symptoms of OHSS, a hospital stay, multiple monitoring, and therapies might also impair immunoprotective status [277, 278]. In a recent report of perforated duodenal ulcer with OHSS, severe stress was suggested to be a causative factor [279]. Following this logic, it may be that appendicitis with OHSS could be more aggressive and is likely to rupture than without OHSS. Once bacteria are seeded into the peritoneal cavity associated with OHSS, they may grow rapidly to form abdominal abscesses, because ascitic fluid of OHSS serves as an excellent culture medium for bacteria with its rich source of nutrients including albumin [280]. It seems that OHSS, if complicated by intraperitoneal inflammatory disease, may worsen its potentially life-threatening conditions.

In patients with severe abdominal pain after both IVF and ET techniques, appendicitis and ectopic pregnancy should be included in the differential diagnosis [271]. During diagnostic laparoscopy, both appendix and adnexa should be always examined in IVF pregnant patient despite proven normal intrauterine pregnancy, especially if appendicitis is proven intraoperatively with fresh blood in the pelvis or around the adnexa or appendicitis. Additional confirmation of this rule is that βHCG in heterotopic pregnancy is elevated due to normal intrauterine pregnancy and is not diagnostic for heterotopic pregnancy.

Appendectomy for appendicitis is mandatory in all cases (Fig. 1.11), and therapeutic approach of simultaneous ectopic (EP)/heterotopic pregnancy (HP) depends on several factors:

Ruptured HP
1. Intrauterine pregnancy preserved
2. Salpingectomy or salpingotomy

Ruptured EP:
1 Salpingectomy or salpingotomy

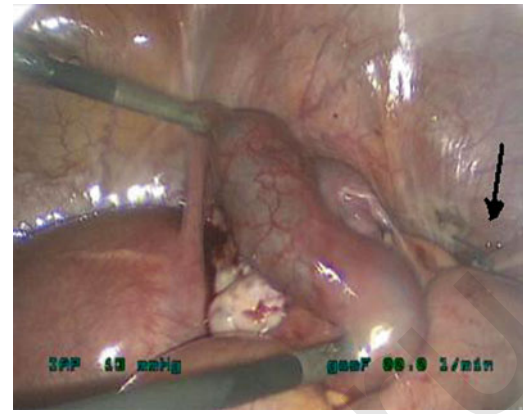

Fig. 1.11 Laparoscopic view of unruptured ectopic pregnancy in the right Fallopian tube. *Arrow* shows the knot placed on the base of antecedent appendectomy [281]

The benefits of salpingectomy over salpingotomy are uncertain. Salpingectomy may be easier and safer, especially in the presence of a live intrauterine pregnancy. It reduces the risk of complications such as the persistent bleeding or retention of trophoblastic tissue that can occur after salpingotomy [269]. Also, if Fallopian tubes are significantly damaged and not functional for further spontaneous pregnancies, salpingectomy is recommended. Salpingectomy should be considered also if contralateral Fallopian tube is healthy as this treatment does not preclude future fertility. For non-ruptured variants, therapeutic recommendations are:

Unruptured HP:
1. Intrauterine pregnancy preserved
2. Salpingectomy or salpingotomy

Unruptured EP:
1. Methotrexate

1.9.3.3 Ovarian Hyperstimulation Syndrome

For patients who appear to develop high-risk signs of ovarian hyperstimulation syndrome, such as rapidly increasing estradiol levels or massive follicular recruitment, decrease of medication dosages or alteration of the ratio of individual

medications in the regimen could be attempted, but if non-obstetric acute abdomen is suspected or proven, all these medications should be withdrawn. There is one case of OHSS with perforated appendicitis, but there is no mention of perioperative care except appendectomy and antibiotics and no mention of any complications of prolonged (37 days) postoperative course [274].

1.9.4 Acute Appendicitis and Sickle Cell Disease

There is no data available regarding the incidence of acute appendicitis and appendectomy in sickle cell disease (SCD) patients during pregnancy. It is known that incidence of acute appendicitis is lower in nonpregnant population with sickle cell disease than in general nonpregnant population [282, 283]. Also, homozygous SCD is now known to be widespread and has broad clinical variability; therefore, conclusions are difficult to be made. In the study by Al-Mulhim [284], 75 % of the SCD patients reported pain in their right lower quadrant, the same as those reported in other studies for pregnant nonsickler patients [26]. Vomiting was a common complaint (67 %), and it was comparable to other reports for pregnant nonsickler patients with acute appendicitis [285]. Only 50 % of the inflamed appendix patients had fever, while none of the sickler patients had pyrexia in the normal appendix group. In the study by Al-Mulhim, 75 % of the acute appendicitis patients with SCD had leukocytosis >16,000/mm^3. In agreement with the findings of other studies, we found a significant difference in the leukocyte counts in patients having acute appendicitis compared to those with non-inflamed appendices [206]. As with nonsickler patients, delaying the appendectomy in SCD patients with appendicitis beyond 24 h in their third trimester was associated with gangrene and perforation of the appendix [5, 286]. Pregnancies in SCD patients present a clinical challenge as maternal mortality is 1–2 % and perinatal mortality is 5–6 % [287, 288]. Maternal mortality is rarely encountered in cases of acute appendicitis in pregnant nonsickler patients [26], and there was none in the study by Al-Mulhim [284]. The fetal loss and the rate of premature delivery were 9 and 18 %, respectively, which is consistent with other reports [6, 289]. The incidence of complication in SCD patients in Al-Mulhim's study is lower than in other studies [290]. This may be because of the milder form of SCD in this area (Al-Hassa) due to the presence of high levels of HbF in the affected population. The high HbF levels protect against several clinical features associated with SCD, but the association between HbF levels and the severity of the disease process is complex [287, 291].

1.9.5 Appendiceal Endometriosis Presenting as Acute Appendicitis

Pregnancy complicated with acute appendicitis (AA) and appendiceal endometriosis (AE) is a rare condition whose frequency ranges 3–8/10,000 deliveries [217]. Endometriosis of the appendix accounts for 0.0075–0.045 % of all cases of extrapelvic endometriosis [223]. In 1999, Ortiz-Hidalgo et al. reported endometriosis of the vermiform appendix frequency as low as 1 % of all cases of pelvic endometriosis [292]. A more recent case series published by Gustofson et al. provides an estimate of the prevalence of appendiceal localization of the disease in patients with chronic pelvic pain (total of 133 and 13 of whom with previous appendectomy and 109 with history of right lower quadrant pain) and possible endometriosis who underwent laparoscopy [293]. According to this study, the prevalence of appendiceal endometriosis in patients with biopsy-proven endometriosis or with right lower quadrant pain was 4.1 and 3.7 % respectively. Notably, this was higher than the 2.8 % prevalence confirmed by literature review by Giorgakis et al. in 2012 and much higher than its prevalence in all patient population (0.4 %) [294].

When age, parity, and pregnancy duration at diagnosis, as reported by Ghazanfar et al. [295], Mourad et al. [11], and Andersson and Lambe

Table 1.4 Summary of reported cases of appendiceal endometriosis presenting as acute appendicitis during the pregnancy

Author	Age (years) gravidity/parity GA (weeks)	Symptoms and signs	WBC count per µl	Surgery/complications	Pathology
Lane [224]	34; 12; NS	NS	12,000	NS	Decidual reaction
Tedeshi and Masand [229]	30; 2/3; 12	NS	NS	NS	Decidual reaction
Finch and Lee [221]	28; NS; NS	NS	NS	Preterm labor, infant death	Decidual reaction, inflammation
Cutait et al. [219]	26; 1/0; 12	RQL pain, $t = 37.5$ °C	Leukocytosis	None	Decidual reaction, inflammation
Pigne et al. [217]	28; 2/1; 19	RQL pain, $t = 37.5$ °C	NS	Laparotomy	Endometriosis decidualization
Gini et al. [222]	23; 1/0; 35	RQL pain	NS	Laparotomy	Perforation, decidual formation in all 3 layers
Nielsen et al. [226]	NS; NS; term	NS	NS	NS	Perforation, decidual reaction
Nakatani et al. [225]	25; 2/0; 26	RQL pain, $t = 37.8$ °C	16,000	Laparotomy	Perforation, decidual cells and glands in all 3 layers
Silvestrini and Marcial [227]	28; 2/1; 21	RQL pain, diarrhea	Leukocytosis	Laparotomy	Appendiceal endometriosis, decidual polyp
Stefanidis et al. [228]	27; 3/2; 20	RQL pain, $t = 37.5$ °C	15,600	Laparotomy	Endometriosis with seromuscular involvement
Perez et al. [218]	21; 3/1; 12	RQL pain	14,700	Laparotomy	Endometriosis with stromal decidualization
Giorgakis et al. [294]	35; NA; 27	RLQ pain, $t = 38$ °C	Leukocytosis	Laparotomy	Endometriosis decidualization
Dimitriadis et al. [296]	22; 2/1; 27	RQL pain, afebrile	13,100	Laparoscopy	Endometriosis decidualization

Abbreviations: *GA* gestational age, *NS* not specified, *RQL* right lower quadrant

[13], were compared for women experiencing AE and AA during pregnancy, no differences were found between the groups. The frequency of the presenting signs and symptoms such as abdominal pain, nausea, vomiting, body temperature, and white blood cell count was not different in AE and AA and therefore not helpful in establishing the correct diagnosis (Table 1.4). In contrast, the occurrence of complications during the third trimester was higher in women with AE (Table 1.5). This difference, however, was impossible to evaluate because of the small sample size and missing variables, e.g., timing between diagnosis and surgery. It may be speculated that decidual reaction in pregnancy affects decidual cells present within the appendix as well. Changes in intra-appendiceal decidual cells would induce more inflammatory response, which, in turn, may increase the risk of perforation.

1.9.6 Surgical Considerations in the Postpartum Period

The abdominal wall also undergoes significant change during pregnancy, with muscle tone

Table 1.5 Comparison between appendiceal endometriosis presenting as acute appendicitis in pregnancy with pregnancy complicated with acute appendicitis in general [218]

Variable	Appendiceal endometriosis in pregnancy (Perez et al.) [217]	Acute appendicitis in pregnancy (Ghazanfat et al., Mourad et al.) [11, 294]
Age (years)	27	27
Primiparous (%)	27	32
Multiparous (%)	45	68
First trimester (%)	36	38
Second trimester (%)	28	52
Third trimester (%)	36	10
RLQ pain (%)	73	72
Mean temperature	37.5 °C	37.6 °C
Mean WBC (mm^3)	9,800	16,400

reduction and skin elasticity to accommodate the enlarging uterus. The abdominal wall tone remains lax for several weeks postpartum, returning to a near-nonparous level in 6–7 weeks. The hallmarks of acute surgical disease, abdominal guarding and rigidity, do not occur during the early puerperium. This single feature of the puerperium is responsible for confusion and delay in proper surgical diagnosis. Some authors found pronounced abdominal distension and acute diffuse tenderness due to peritonitis with secondary paralytic ileus, but little guarding [297, 298].

Puerperal changes in blood components may be confusing as well. During the first 10–14 days of the puerperium, WBC counts of 20,000–25,000/mm^3 are not unusual; there is also a predominant increase in neutrophils. The erythrocyte sedimentation rate may increase to 50–60 mm/h. Reliance on either the erythrocyte sedimentation rate or the WBC count for the diagnosis of acute infection may be misleading.

The enlarged uterus did not hamper exposure, even in the first week. At the time of surgery, the uterine fundus was inferior to the umbilicus. This is consistent with subsequent reports of technical success and good exposure in pregnant patients undergoing laparoscopy during the first and second trimesters [299]. There were no adhesions encountered in the Cesarean section group. The course of the procedure and recovery was identical to the remainder of patients.

The final unique consideration in the postpartum patient is the presence of a healing abdominal incision after Cesarean section. There are no published studies on outcomes for recent abdominal incisions subjected to early pneumoperitoneum. The authors did not want to unilaterally deny LC to this group, but trepidation led them to limit the pneumoperitoneum to the absolute minimum necessary for safe exposure. Pneumoperitoneum was limited to 10 mmHg pressure in the Cesarean section patients. This may have been beneficial in preventing undue mechanical strain on the healing wound, though we have no controls with the standard (15–16 mmHg pressure) for comparison. It seems prudent to utilize the minimal intra-abdominal pressure necessary for adequate exposure in these patients. Although evidence suggests fascial separation, if present, occurs early, it remains to be seen what long-term status these incisions will achieve. No hernia has developed in these patients with follow-up to 5.5 years [300].

1.10 Prognosis

The mortality of appendicitis complicating pregnancy is the mortality of delay.

Edmund Adam Babler, 1908

1.10.1 Perforation Rate

Perforation rates for pregnant patients have been reported as high as 55 % compared to 4–19 % of the general population [46, 140]. Delay in diagnosis leads to appendiceal perforation. As in nonpregnant patients, it has many potential deleterious consequences. In cases of pregnant patients, these consequences imply to both mother and fetus. Trend in overall perforation rate is lowering from 25 % [301] to 15 % during the last two decades [9]. The rate of perforation through the trimesters is increasing to 8.7, 12.5, and 26.1 %, respectively [9]. A 66 % perforation

rate has been reported when operation is delayed by more than 24 h compared with 0 % incidence when surgical management is initiated prior to 24 h after presentation [46]. This is one of the most important observations for the surgeons and gynecologists. There are several causes for the treatment delay [302]:

- *Atypical clinical picture* with uncertain diagnosis when watchful waiting is indicated
- *Time delay during consultations* between the gynecologist and surgeon if institutions are dislocated
- *Time delay during the transfer* of the patient when the departments and institutions are dislocated

The difficulty in making a clinical diagnosis particularly close to term combined with the previously quoted high incidences of fetal and maternal mortality for appendiceal perforation has led to a traditionally low threshold for surgical intervention. This is partly due to inaccurate preoperative diagnostic imaging. This has resulted in a higher negative appendectomy rate, ranging 23–55 % in pregnant women compared with 18 % in nonpregnant women [11, 13, 68, 150, 152, 206, 306]. The first trimester yields a greater accuracy, but more than 40 % of patients in the second and third trimesters will have a normal appendix [128]. Perforation can also result in an increased risk of generalized peritonitis because the omentum cannot isolate the infection [12, 304].

1.10.2 Fetal Outcome

The effects of any medical intervention on fetal mortality have to be considered in the context of certain preexisting background risks that are common to all pregnancies. These include a 3 % risk for birth defects, 15 % for miscarriage, 4 % for prematurity, 4 % for growth retardation, and 1 % for mental retardation or neurological developmental problems. Appendicitis is the most common surgical cause of fetal loss during pregnancy because of its frequency during pregnancy and frequently atypical clinical picture with delayed diagnosis and treatment [305]. In 1908, Babler reported more than 200 cases of appendicitis in pregnancy with maternal mortality of 24 % and a fetal mortality of 40 %. As a result, Babler claimed that “the mortality of appendicitis complicating pregnancy is the mortality of delay” [306]. Up to 1973 the overall fetal mortality after removal of the appendix was 20 %, and fetal mortality seems to be related to the severity of the disease rather than the period of gestation [125]. Hinshaw found a fetal loss rate of 30 % when the appendix was perforated, but only 3 % with simple acute appendicitis [307]. Black in 1960, reporting on 358 cases of acute appendicitis in pregnancy, found a fetal mortality of 0–4 % when the appendix was the only structure affected and 8–10 % when peritonitis was present [3].

Today the combined miscarriage/fetal mortality is declining; when the appendix is not perforated, fetal mortality is 0–5 % [7, 9, 27, 45, 202, 308]. When the appendix is perforated, fetal mortality raises to 20–36 % [9, 25, 45, 202, 206, 308–311]. It should be stated that the data presented in many articles have included retrospective studies for the collection of sufficient number of patients for data analysis using extended time periods. In many of these articles, fetal mortality was higher in years before 1990 at a time when the current possibilities offered by modern neonatology, fast and accurate diagnostic workup, intensive care and antibiotic therapy were limited or not available. One large study on 778 pregnant patients with appendicitis found interesting findings [7]:

- Increase in the risk of delivery the week after appendectomy when the operation was performed after 23 weeks gestation, with no further increase if the pregnancy continued beyond 1 week
- Decrease in mean birth weight of 78 ± 24 g with more infants weighing <3,000 g
- An increase of live-born infants dying within 7 days of birth
- No increase of stillborn infants
- No increase of congenitally malformed infants

The problem raised in some articles was the rate of fetal loss of 3 % after negative laparotomy and appendectomy of a normal appendix. Some of these investigators included complications in long-term follow-up after appendectomy and did not take into account the expected number of perinatal and intrauterine deaths in the total (normal) pregnant population [46, 121]. A similar observation was found by McGory et al., and there was one topic that should be discussed further. It should be noted that in 15 % of negative appendectomies, another pathology was found. Mostly these pathologic findings were of genital origin, and in this subgroup of patients with the diagnosis of leiomyoma or inflammation of the uterus, there was significantly higher incidence of fetal loss and early delivery [69]. Others concluded that if there was an effect of surgical trauma on the fetoplacental-uterine elements, it should, in uncomplicated cases, have ceased approximately 1 week after appendectomy. In some cases, however, RLP was only diagnosed during exploratory surgery [53, 56]. This increased risk of delivery the week following surgery was present when performed after 23 weeks gestation [11]. Any complication and increased risk of preterm delivery after that period in a patient without surgical complications should not be related to the operation itself [7, 206].

Premature delivery rate was often omitted in reports on appendicitis, but it ranges 15–45 % [6, 35, 312]. It is now believed that subclinical IAI is a cause of preterm premature rupture of membranes and/or preterm labor and, as such, is an important contributor to the leading cause of infant morbidity and mortality complications from prematurity [313]. Open procedures and laparoscopy do not differ with respect to the incidence of preterm delivery and other complications [109, 160]. It is more likely that the subsequent spontaneous abortions and fetal demise were associated with maternal disease severity rather than with operative technique.

1.10.3 Maternal Outcome

Overall, maternal mortality is less than 1 % [12, 25, 26, 206]. It is rare in the first trimester and increases with advancing gestational age [121]. It is associated with:

- A *delay in surgery* of more than 24 h after onset of symptoms
- Appendiceal *perforation*

The delay in surgery of more than 24 h after onset of symptoms significantly increases the perforation rate and adverse maternal and especially fetal outcome [6, 46]. If appendiceal perforation is present, maternal mortality occurs in up to 4 % of patients in contrast to less than 1 % in nonperforated appendicitis [301, 311]. Current studies have even 0 % of maternal mortality even with perforated appendicitis [308]. The risk of perforation increases with gestational age, and perforation in the third trimester often results in preterm labor [12]. The risk for premature delivery is the greatest during the first week after surgery. Others find similar risk factors for adverse outcome and also included maternal temperature greater than 38 °C, leukocytosis greater than 16×10^9/l, or more than 48 h between onset of symptoms and emergency room presentation [48]. In one series from 1973, there was no mortality [125].

The advantages of laparoscopic technique include decreased surgical trauma, decreased gravid uterine manipulation, earlier recovery of bowel function, shorter time of oral intake, shorter postoperative length of stay in hospital, and faster return to work [109, 148].

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Acute Biliary Tract Diseases

2

2.1 Acute Cholecystitis/ Biliary Colic

2.1.1 History

A notable discovery in the last century by Von Recklinghausen that 90 % of women having gallstones have been gravid at least once, and the subsequent findings by Courvoisier in autopsy studies that three times as many women have gallstones as men hinted at the possibility of pregnancy being one of the major factors in the development of cholelithiasis [1].

2.1.2 Incidence

The prevalence of gallbladder disease differs in several populations. In the United States, 10–15 % of the adult population has gallstones. In other populations, such as those of Latin American countries, the prevalence of gallstones is up to 50 % in adult women [2].

In 1910, Peterson collected 25 cases of cholecystitis during pregnancy, ten of these were during puerperium [3]. In 25 cases of gallstones complicating pregnancy, the ages of the patients were recorded in 21 instances. The age distribution of patients where gallstones complicated pregnancy was: 20–25 years, four cases; 25–30 years, eight cases; 30–35 years, six cases; and 35–40 years, three cases. The ages of the patients suffering from gallstones during the puerperium are the following: 20–25 years, three cases; 25–30 years, one case; 30–35 years, one case; 35–40 years, one case; and over 40 years, one case.

The most common causes of the gallbladder disease in pregnancy are gallstones and biliary sludge. The incidence of gallbladder disease in pregnancy is 0.05–0.3 % [4–6], and asymptomatic gallstones occur in 3.5–10 % of all pregnancies. Incidence of acute cholecystitis during pregnancy is 1/1,600–1/10,000 pregnancies [7–9], and 40 % of pregnant patients with symptomatic cholelithiasis require cholecystectomy during pregnancy [10–12]. Higher incidence of gallbladder disease of 0.39 % is found in Saudi Arabia. This is attributed to (1) high number of repeated pregnancies and (2) genetic predisposition because higher percentages (7.5 %) of pregnant women harbor silent gallstones in comparison to 3.5 % in the Western countries [13]. There is no statistically significant difference in the prevalence rates for gallstones between Mexican-born and non-Mexican-born pregnant Hispanic women in the 20-year to 49-year age group [14]. In a study by the University of Southern California, ultrasonography initially revealed biliary sludge in 15 % and gallstones in 6 % of the pregnant women examined. New sludge or stones were found in 30 and 2 % of the women, respectively, at the end of their pregnancies. Postpartum sonography revealed the disappearance of the sludge in 61 % of those women who had previously demonstrated sludge and the disappearance of stones in 28 % of those who had had stones. Therefore, some patients who have symptomatic cholelithiasis

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during pregnancy may not have it after delivery [15].

Biliary sludge, a potential precursor to gallstones, forms in up to 30 % of women during pregnancy, and gallstones form in 2–4 % [16, 17]. Biliary sludge, or microlithiasis, in pregnancy consists of clusters of cholesterol crystals in the bile. Although not all cases of sludge will necessarily evolve to become gallstones, sludge is believed to be the initial step in gallstone formation and is regarded as the earliest recognizable stage of lithogenesis [18]. Pregnancy, however, does not seem to increase the severity of gallstone complications. Most gallstones are asymptomatic during pregnancy [16, 17, 19, 20]. Despite the rarity of the condition, complications of gallstones represent the second most common non-gynecologic condition requiring surgery in pregnancy [21] with cholecystectomy performed in 1–8/10,000 pregnancies [22]. Cholelithiasis is the cause of cholecystitis in over 90 % of cases. The incidence of cholelithiasis in pregnant women undergoing routine obstetric ultrasound examinations is 3.5–12 % versus 1.3 % of non-pregnant controls [17, 19].

It should be noted that the number of children a woman has increases her risk of gallbladder disease and that compared with nulliparous women, the risk rises incrementally by 8 % with each additional birth. It is also interesting that after accounting for the number of children, 12 months of breastfeeding reduces the risk of gallbladder disease in parous women by 7 % [23]. As estrogen levels are known to fall during lactation, it is possible that the protective effect of breastfeeding could be mediated through estrogen [24], although there are other hormonal changes that occur with lactation that may also have an effect.

2.1.3 Risk Factors

2.1.3.1 Multiparity

Risk factor for cholelithiasis is multiparity due to hormonal changes that directly influence on gallstone formation [25]. Pregnancy increases prevalence from 1.3 % in nulliparous females to 12.2 % in multiparous females [26]. Early marriage and repeated pregnancies until menopause make the probability of gallstone disease occurring in pregnancy higher. A cross-sectional study found following incidence of gallstones: 21–30 years age group of 1.37 % in patients having no pregnancy, 9.62 % in patients having one pregnancy, 7.14 % in patients having two pregnancies, 6.04 % in patients having three pregnancies, and 3.3 % in patients having four and more pregnancies; in the 31–40 years age group, 0.55 % in patients having no pregnancy, 1.37 % in patients having one pregnancy, 6.04 % in patients having two pregnancies, 8.24 % in patients having three pregnancies, and 12.64 % in patients having four and more pregnancies; in the 41–50 years age group, 0.82 % in patients having no pregnancy, 0.55 % in patients having one pregnancy, 4.4 % in patients having two pregnancies, 4.4 % in patients having three pregnancies, and 12.91 % in patients having four and more pregnancies; and in the 51–60 years age group, 0.55 % in patients having one pregnancy, 1.1 % in patients having two pregnancies, 2.47 % in patients having three pregnancies, and 14.29 % in patients having four and more pregnancies. The number of pregnancies is associated with gallstone disease. The risk of developing gallstone disease increases in association with increased number of parity, particularly among the younger women [27]. Valdivieso found that 12 % of women immediately after delivery had gallstones compared to 1.3 % nulliparous control group [17]. This finding is explained by the increase in progesterone secretion which remains high during the second and third trimesters leading to smooth muscle relaxation and hence gallbladder dilatation and stasis [28]. It is important to note that the incidence of gallbladder disease in the asymptomatic category was higher in patients of higher age and parity [3, 29]. Young patients with a higher parity are more prone to gallbladder disease [29, 30].

2.1.3.2 Obesity and Diabetes Mellitus

The risk of forming gallbladder sludge or stones during pregnancy is significantly higher in obese women (BMI $\geq$30 kg/m^2) than in normal weight (BMI <25 kg/m^2) or overweight

(BMI 25.0–29.9 kg/m^2) women [4, 31]. Insulin resistance, which increases with BMI, is one possible mechanism linking obesity to gallstones [32–36]. However, not all studies confirm this association [37, 38]. Studies showing that fasting serum insulin, which may be used as a surrogate measure for insulin resistance, is a risk factor for prevalent gallstones [33, 35, 39–41]. Women who formed gallbladder sludge or stones were significantly more insulin resistant. This association remained strong even after adjusting for possible confounding factors including prepregnancy BMI, lipid and glucose levels, waist-hip ratio, and physical activity during pregnancy. This association was strongest for women whose prepregnancy BMI was <30 kg/m^2 [42]. Multiple autopsy studies have documented a statistically significant increase in the incidence of gallstones in diabetes mellitus [2, 39, 43]. Epidemiological studies in Mexican Americans [32] and in Caucasian Americans [44] have shown diabetes mellitus to be a significant risk factor for gallstones.

2.1.3.3 Oral Contraceptives

Strong association of the oral contraceptives usage and gallbladder disease shows that all pregnant patients with history of having used oral contraceptives in the past must be submitted to ultrasound examination of the gallbladder [29]. These findings are consistent with those of Thijs and Knipschild who have suggested that modern low-dose oral contraceptives may be safer than older formulas, but the safety of oral contraceptives should be evaluated by studying bile saturation and biliary function rather than waiting for gallbladder disease to develop [45].

2.1.4 Pathophysiology

2.1.4.1 Estrogens/Progesterone

As found by epidemiological and clinical investigations in every population studied, cholesterol gallstones are more common in women than men, and this gender difference begins since puberty and continues through the childbearing years [2, 46]. It has been postulated that pregnancy is associated with an increased percentage of colic acid, increased cholesterol secretion, increased bile acid pool size, decreased enterohepatic circulation, and decreased percentage of chenodeoxycholic acid [47]. The progesterone-induced smooth muscle relaxation of the gallbladder promotes stasis of the bile and increases the risk of cholelithiasis and subsequently of acute cholecystitis [48]. Ultrasound findings of the gallbladder in pregnant women show a decrease in the emptying rate and an increase in residual volume after emptying. Additionally, elevated levels of estrogen during pregnancy increase the lithogenicity of the bile, which further increases the risk of cholelithiasis and acute cholecystitis [49]. Therefore, the most common type of stones in pregnancy is yellow cholesterol stones [2, 31]. Bile becomes more lithogenic as a result of increased estrogen levels, which results in increased hepatic secretion of biliary cholesterol and cholesterol-supersaturated bile. Additionally, high levels of estrogen could impair gallbladder motility function and consequently induce gallbladder hypomotility [50]. These changes promote the formation of sludge and stones. Increased plasma levels of progesterone also reduce gallbladder motility [51, 52]. Since plasma hormone concentrations increase linearly with duration of gestation, the risk of gallstone formation is especially hazardous in the third trimester of pregnancy. Most, but not all, studies have found that the use of oral contraceptive steroids and conjugated estrogens in premenopausal women doubles the incidence of cholesterol gallstones [53–56]. In addition, the administration of estrogen to postmenopausal women and estrogen therapy to men with prostatic carcinoma displays similar lithogenic effects [57–62]. These observations support the concept that higher risks for cholesterol gallstones in women than in men are related to differences in how the liver handles cholesterol in response to estrogen [56].

Accumulated evidence has revealed that estrogen increases the risk for the formation of cholesterol gallstones by promoting hepatic secretion of biliary cholesterol that induces an increase in cholesterol saturation of the bile [57, 59, 61, 63, 64]. In addition, studies show that high levels of estrogen significantly enhance the activity of

3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in hepatic cholesterol biosynthesis, even under high dietary cholesterol loads [64–67]. These findings suggest that there could be an increased delivery of cholesterol to the bile from de novo synthesis in the liver. Furthermore, some studies show that estrogen could augment the capacity of dietary cholesterol to induce cholesterol supersaturation of the bile [65, 68–70]. It is also found that high doses of estrogen augment intestinal cholesterol absorption [68] contributable in part to an upregulated expression of intestinal sterol influx transporter Niemann-Pick C1-like 1 protein (NPC1L1) via the intestinal ESR1 pathway [71]. Furthermore, studies show that during estrogen treatment, mice continue to synthesize cholesterol in the face of its excess availability from the high cholesterol diet. It suggests that there is a loss in the negative feedback regulation of cholesterol biosynthesis, which results in excess secretion of newly synthesized cholesterol and supersaturation of the bile that predisposes to cholesterol precipitation and gallstone formation [64]. In addition, estrogen could decrease plasma low-density lipoprotein (LDL) cholesterol and increase plasma high-density lipoprotein (HDL) cholesterol because high doses of E2 amplify expression levels of HDL receptor SR-BI and LDL receptor [72–75]. The decrease in plasma LDL is a result of increased hepatic LDL receptor expression, which increases the clearance of plasma LDL. Therefore, the increased uptake of LDL by the liver may result in increased secretion of cholesterol into the bile. These alterations could induce an apparent increase in hepatic output of biliary cholesterol derived from circulating lipoproteins such as HDL and LDL, although LDL cholesterol could have a less effect on biliary secretion. These observations suggest that the hepatic estrogen receptor ESR1 is an important, selective target for the treatment of cholesterol gallstones. Figure 2.1 illustrates the potential lithogenic mechanisms of estrogen through the ESR1 pathway in the liver. Complete discussion of molecular mechanisms of estrogen effect on gallstone formation that are out of scope of this topic could be found in Wang et al. [76].

It is interesting that there is a high rate of gallstone/sludge dissolution in the 1st month after delivery. The rate of disappearance of gallstones and biliary sludge is 15–28 % and 39–68 %, respectively [16, 77]. Observation is that spontaneous disappearance of gallstones after delivery is significantly more frequent in older women [16]. Speculation is that a few young women eject small gallstones from the gallbladder during the postpartum period when gallbladder contraction restores, and some of these women develop an attack of acute pancreatitis (AP). In contrast, in older women with reduced gallbladder contractility, most gallstones likely remain in the gallbladder until dissolved by less lithogenic bile. Thus, AP associated with pregnancy usually occurs in young postpartum women and is usually due to gallstones [16].

2.1.4.2 Insulin

Apart from hormone, insulin resistance is also responsible for gallstone formation. The exact mechanisms are not clear. Cholesterol is the primary constituent of gallstones formed during pregnancy. Cholesterol gallstone formation requires several pathogenic factors, including supersaturation of hepatic bile with cholesterol and altered gallbladder motility. Hyperinsulinemia and insulin resistance may affect either of these factors. Hyperinsulinemia has direct effects on hepatic lipid metabolism, increasing cholesterol synthesis via activity of the hydroxylmethylglutaryl coenzyme A reductase enzyme [78] and increasing hepatic uptake of LDL cholesterol [79]. Insulin resistance is also associated with lower serum levels of HDL cholesterol, a known risk factor for prevalent gallstones [80]. In one study, administration of insulin in diabetics increased biliary cholesterol saturation [81]. Some, but not all, studies have shown greater degrees of biliary cholesterol saturation in patients with type II diabetes compared with controls [82, 83]. Insulin inhibits basal and cholecystokinin-stimulated gallbladder motility, and gallbladder dysmotility has been documented in patients with clinically diagnosed type II diabetes [84, 85]. In animal models, nonobese, diabetic mice have diminished gallbladder contractility and rapid

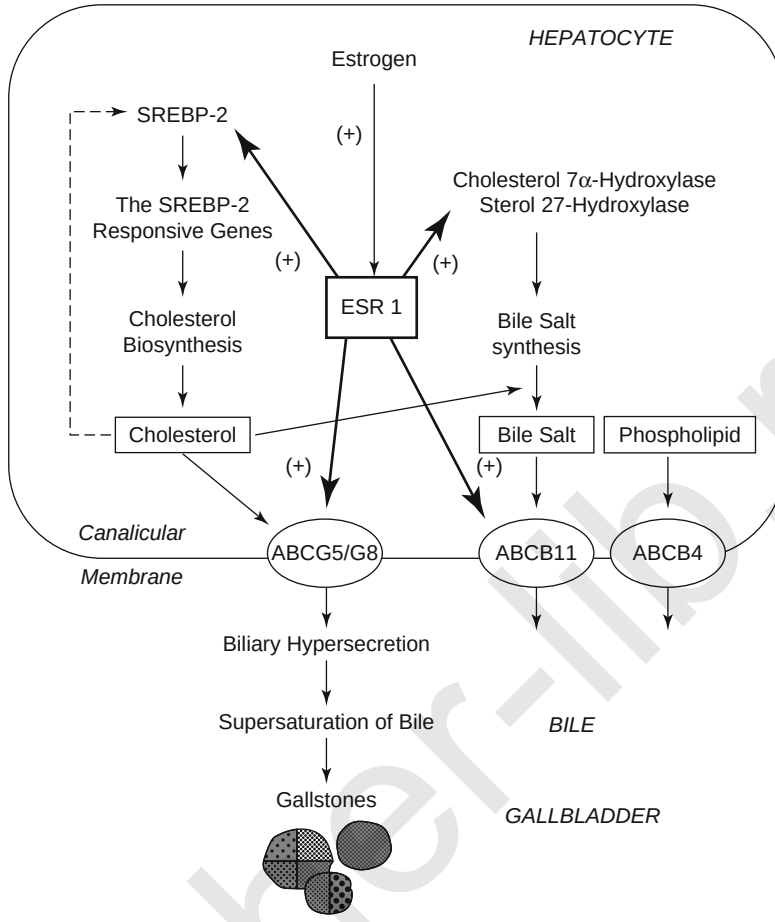

Fig. 2.1 The proposed model underlying the potential lithogenic mechanisms of estrogen through the estrogen receptor 1 (*ESR1*) pathway in the liver. In the liver there is a possible "estrogen-ESR1-SREBP-2" pathway promoting cholesterol biosynthesis and hepatic secretion of biliary cholesterol. The negative feedback regulation of cholesterol biosynthesis (as shown in a *dashed line*) is inhibited by ESR1 that is activated by estrogen, mostly through stimulating the activity of sterol regulatory element-binding protein-2 (*SREBP-2*) with the resulting activation of the SREBP-2 responsive genes for the cholesterol biosynthetic pathway. Consequently, these alterations induce excess secretion of newly synthesized cholesterol and supersaturation of the bile that predisposes to cholesterol precipitation and gallstone formation. Moreover, the hepatic ESR1 activated by estrogen could stimulate the activity of ATP-binding cassette (*ABC*) transporters ABCG5 and ABCG8 on the canalicular membrane of the hepatocyte and promote biliary cholesterol secretion. Of special note is that these lithogenic effects of estrogen are inhibited by the antiestrogenic ICI 182,780. In addition, the estrogen effects on increasing cholesterol biosynthesis and promoting cholesterol gallstone formation are, in part, blocked by deletion of the *ESR1* gene [76]

formation of cholesterol crystals [86], while gallbladder contractility correlates inversely with glucose and insulin levels in obese animals [87]. Insulin resistance is associated with gallbladder dysmotility in nonobese, nondiabetic humans [88]. Therefore, insulin resistance, even in the absence of obesity, may lead to gallbladder sludge and stone formation, either by causing gallbladder dysmotility or by altering biliary lipid secretion. Insulin resistance may be a surrogate for other, undefined pathophysiologic mechanisms that lead to gallstone formation rather than a direct underlying cause [42]. For example, other, undefined abnormalities in lipid metabolism may lead to gallstone formation and also lead independently to insulin resistance.

Diabetics have been shown to have an increased cholesterol saturation index in the bile

compared with nondiabetics [89]. In addition, gallbladder fasting volumes have been shown to be larger, and gallbladder motility is diminished in non-insulin-dependent diabetics compared with nondiabetics [90, 91]. Hyperinsulinemia is characteristically found in persons with non-insulin-dependent diabetes as a result of insulin resistance. Several authors have documented an association between hyperinsulinemia and an increased prevalence of gallbladder disease [32, 35, 36, 92]. Both hyperglycemia and euglycemic hyperinsulinemia have been shown to inhibit CCK-stimulated gallbladder motility [84]. Hyperinsulinemia may also be a key factor in these observations because insulin regulates the Na^+-K^+ pump, which may adversely affect the ionic and osmotic homeostasis of smooth muscle cells including gallbladder myocytes [93]. The Na^+-K^+ pump of presynaptic nerve terminals is also regulated by insulin [93]. Moreover, decreased Na^+-K^+ pump activity can result in increased intracellular Na^+, which in turn increases the Na^+-Ca^{++} exchange, thereby increasing intracellular calcium. Increased intracellular calcium will alter both smooth muscle tone and release of neurotransmitters. Moreover, we have demonstrated that gallbladder myocytes from obese, diabetic mice are foreshortened and respond poorly to cholecystokinin (CCK) [94]. Thus, the abnormal gallbladder emptying seen in response to a test meal in the nondiabetic lean subjects investigated in this study may be related to a state of relative hyperinsulinemia as a result of insulin resistance. Insulin resistance and/or diabetes may also affect alterations in the density or sensitivity of acetylcholine or CCK receptors or prevent neurotransmitters from accessing their receptors. Sugars can react nonenzymatically with amino groups in proteins, lipids, and nucleic acids to form advanced glycation end products [95, 96]. These products are thought to have many effects, including covalent cross-linking of collagen and protein matrix [96]. The cross-linking of the matrix may lead to stiffening of the gallbladder wall itself, limiting its contraction, or may impair CCK egress through blood vessel basement membranes, preventing CCK interaction with neural or myocyte receptors.

2.1.4.3 Obesity

One potential explanation for the differences in gallbladder dynamics observed between obese and lean individuals may be due to the differences in serum and, perhaps, gallbladder wall lipids [97–99]. As a result, the cholesterol/phospholipids ratio increases and membrane fluidity decreases. Smooth muscle cells from human gallbladders with cholesterol stones have increased cholesterol and cholesterol/phospholipids ratios [97]. In addition, this group has demonstrated decreased membrane fluidity in these gallbladders. Therefore, these obese subjects with high serum total and LDL cholesterols as well as triglycerides may also have high gallbladder lipids, which may play a role in gallbladder function.

2.1.5 Clinical Presentation

Symptoms of gallstone disease during pregnancy are the same as in nonpregnant patients [17, 20]. The following features suggest biliary colic or acute cholecystitis:

- History of previous episodes or known gallbladder stones
- Nausea, dyspepsia, and intolerance of fatty foods
- Vomiting (50 % of patients)
- Abdominal pain in the right hypochondrium or epigastrium
- Pain radiating to the back around the right scapula

During physical examination there are several signs that can be elicited:

- *Direct abdominal tenderness* in the upper right quadrant. Due to different locations of the enlarging uterus and gallbladder, there is no significant blunting of symptoms.
- *Murphy's sign* (cessation of inspiration during palpation of inflamed gallbladder) may be elicited less frequently in pregnant patients and are indicating acute cholecystitis [100].
- *Abdominal muscle rigidity* is present only with gallbladder perforation and biliary peritonitis. A rigid abdomen with rebound tenderness remains a valid indicator of peritonitis

during pregnancy, but abdominal wall laxity in late pregnancy might mask the classical signs of peritonitis [101, 102].
- *Fever* and *tachycardia* are variably present and are not sensitive signs. The more advanced the disease, the more pronounced these symptoms and signs are.

2.1.6 Differential Diagnosis

There are many diseases that can present with the pain in the upper right quadrant. But with adequate history taking and clinical examination, most of them could be easily excluded. Complete list of differential diagnoses is found in Table 2.1.

2.1.6.1 Hyperemesis Gravidarum

Hyperemesis gravidarum can be defined as persistent vomiting associated with weight loss greater than 5 % of prepregnancy body weight and ketonuria [103]. It occurs in 0.5–1.5 % of pregnancies [103, 104] and is more common in nulliparous in contrast to multiparous women that are prone to cholelithiasis and cholecystitis [105]. Hyperemesis gravidarum leads to dehydration, and hospitalization is usually required for intravenous fluid therapy. Indeed, the necessity of hospital admission is commonly included in the definition of hyperemesis gravidarum [105]. This disorder presents early in the first trimester of pregnancy, with intractable nausea and vomiting. As a rule, symptoms resolve before the second part of pregnancy, regardless of therapy. Jaundice is uncommon and, if present, is not associated with abdominal pain or fever. Abnormal liver tests are common, but the exact frequency is unknown. A frequency of 16 % has been found in a retrospective study [106]. The most striking abnormality is elevation of aminotransferases with ALT levels exceeding AST levels as it is usual in nonalcoholic and noncirrhotic liver diseases [106]. ALT levels are variable, and hepatitis serologies are useful in the differential diagnosis especially when ALT levels are above 10 times the upper normal limit or when it is the first affected pregnancy. Associated drug-liver injury should be systematically searched, especially when jaundice is present. Liver biopsy is not needed to confirm the diagnosis. Pregnancies complicated by hyperemesis gravidarum have been associated with transient hyperthyroidism, which usually requires no specific therapy [105].

Table 2.1 Differential diagnosis of right upper quadrant pain

Diaphragmatic myocardial infarction
Acute fatty liver in pregnancy
HELLP syandrome
Preeclampsia-eclampsia
Acute appendicitis
Acute hepatitis
Pancreatitis
Symptomatic/perforated peptiac ulcer
Pyelonephritis
Nephrolithiasis
Herpes zoster
Hepatitis
Perihepatitis (Fitz-Hugh-Curtis syndrome)
Hepatic vascular engorgement
Hepatic hematoma
Hepatic malignancy
Choledocholithiasis
Cholangitis
Rib fracture
Shingles
Pneumonia
Pulmonary embolus or infarct
Pleural effusion
Radiculopathy
Colon cancer (hepatic flexure)

2.1.6.2 Perihepatitis (Fitz-Hugh-Curtis Syndrome)

Perihepatitis (Fitz-Hugh-Curtis syndrome) is the result of early bacteremic or retroperitoneal lymphatic dissemination of *Chlamydia trachomatis* or gonococcal pelvic infection [107]. The syndrome is most frequently seen in young women and is more common in the second and third trimesters and puerperium. Inflammation in the right upper quadrant produces perihepatic adhesions. Classically, there is sudden onset of sharp right upper quadrant pain, often pleuritic in quality. Nausea and hiccups are occasionally noted. Physical findings include tenderness under the

right costal margin, occasional hepatic friction rub, and fever. Pelvic examination may be normal or may reveal signs of cervicitis or pelvic inflammatory disease. Liver function tests and cholecystogram may be transiently abnormal. The diagnosis is suggested by a history of recent pelvic infection, but the syndrome can be a sequela of latent or asymptomatic infection. The diagnosis is further supported by isolation of gonococcus on cervical culture and improvement on appropriate antibiotics [107]. It is important to exclude other etiologies because there is no specific diagnostic marker of this syndrome.

2.1.6.3 Costal Margin Pain

Costal margin pain and tenderness due to stretching of muscular attachments are not uncommon during pregnancy, and consequently the pain of biliary disease may be brushed aside as insignificant.

2.1.7 Diagnosis

2.1.7.1 Laboratory Findings

If there is clinical suspicion of acute biliary colic or cholecystitis after history taking and clinical examination in primary care, the patient should be sent to hospital for further evaluation. The difficulty in establishing the diagnosis is physiological leukocytosis up to 20,000/ml at labor in normal pregnancy and is not diagnostic. Only granulocytosis (left shift) indicates bacterial infection. C-reactive protein (CRP) is elevated and significant, and bacterial infection is expected if values over 40 are expected. The erythrocyte sedimentation rate (ESR) is physiologically elevated and thus is a less reliable monitor of inflammatory activity during pregnancy [108]. Serum bilirubin and transaminases may be elevated, as in nonpregnant women. Serum alkaline phosphatase is less helpful because estrogen causes its elevation (levels may double during normal pregnancy). Serum amylase levels are elevated transiently in up to 33 %.

2.1.7.2 Transabdominal Ultrasound

Successful visualization of the gallbladder itself in pregnancy is 97 % [29, 109]. The remaining 2.5 % of the patients, whose gallbladder could not be visualized initially, were diagnosed as having chronic cholecystitis with contracted gallbladder and thickened gallbladder wall on the rescan [29, 110]. Gallbladder sludge, a mixture of cholesterol and calcium bilirubinate crystals in the bile, can be detected ultrasonographically and represent a precursor stage potentially leading to the formation of actual gallstones [18]. It is sonographically visible as the accumulation of the bile and is reported in as many as 30 % of gravid patients with a similar proportion of women affected by the postpartum period [31]. Sonography performed in early pregnancy has confirmed the physiological expansion of the gallbladder and the accumulation of stones, debris, and bile. Ultrasound findings of the gallbladder in healthy pregnant women show a decrease in the emptying rate and an increase in residual volume after emptying. Gallstones are detected with accuracy of 95–98 % [111]. If gallstones are an isolated finding, then only biliary colic is present in patients with pain in the right upper quadrant. If acute cholecystitis is present, there are several characteristics present on ultrasound:

- Gallbladder calculi
- Wall thickening (>3 mm)
- Pericholecystic fluid
- Sonographic Murphy's sign (focal tenderness under the ultrasound transducer positioned over the gallbladder)

Another finding that should be ruled out is common bile duct (CBD) obstruction because confirmation or suspicion changes therapeutic approach. It is suspected or confirmed if these characteristics are present:

- CBD over 7 mm in diameter
- Dilatation of intra- and extrahepatic ducts
- Gallbladder calculi smaller than cystic duct diameter

Ultrasound and magnetic resonance cholangiopancreatography (MRCP) may be particularly helpful in differentiating choledocholithiasis from intrahepatic cholestasis of pregnancy because the clinical and biochemical presentation of these two entities overlap [112].

A patient with abdominal pain from a suspected urinary tract calculus disease is better evaluated with ultrasound. Although the diagnosis of calculus is complicated by the presence of pregnancy-related hydronephrosis, addition of color Doppler imaging of the bladder to identify ureteral jets and transvaginal ultrasound to detect stones in the distal third of the ureter has helped in the evaluation [113].

2.1.7.3 Endoscopic Ultrasound

Endoscopic ultrasound (EUS) is rarely used as a definitive diagnostic tool for identification of stones in the distal CBD. Mostly it is used before ERCP for therapeutic strategy or as confirmatory tool after sphincterotomy stone extraction.

2.1.7.4 Magnetic Resonance Cholangiopancreatography

MRCP is indicated if dilatation of intrahepatic and extrahepatic ducts (Fig. 2.2) is present on abdominal ultrasound (see "Common Bile Duct Stones, Cholangitis, and Biliary Pancreatitis"). It can also differentiate between common bile duct stones and external compression due to Mirizzi syndrome (Fig. 2.3). Additionally, because the pancreas is frequently obscured by overlying bowel gas during ultrasound evaluation, MRCP can often better evaluate the pancreas for edema, the pancreatic duct for obstruction in the setting of gallstone pancreatitis, and the peripancreatic tissues for inflammation.

The European Society of Urogenital Radiology (ESUR) established its Contrast Media Safety Committee in 1994. Table 2.2 presents the ESUR guidelines for the use of iodinated and gadolinium contrast media during pregnancy [116].

It should be noted that using modern diagnostic modalities for correct diagnosis of biliary origin of acute abdomen during pregnancy is very high. It can be presented as *index of wrong diagnosis*:

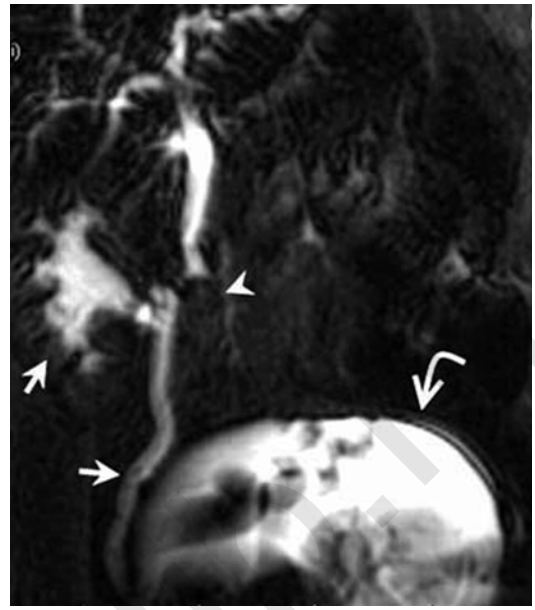

Fig. 2.2 Choledocholithiasis in a patient in the second trimester of pregnancy. Magnetic resonance cholangiopancreatography (*MRCP*) shows distal common bile duct obstruction due to a calculus (*arrowhead*), gravid uterus (*curved arrow*), and physiological right hydronephrosis and hydroureter (*arrows*) [114]

Index of wrong diagnosis (%) = provisionally diagnosed cases – confirmed cases × 100 provisionally diagnosed cases

For acute appendicitis in pregnancy, it is around 40 % and only 8.5 % for acute cholecystitis in pregnancy [117].

2.1.8 Treatment

2.1.8.1 Historical Perspective

Discussion of this pathology dates from 1890 when Robert Barnwell Rhett, Jr. (Fig. 2.4), wrote of a cholecystotomy on a pregnant woman. In 1893, Boorse mentioned a case of pregnancy complicated by the expression of biliary calculi. In 1893, Willien reported a cholecystotomy in the 3rd month of pregnancy. In 1895, Vineberg reported two cases of cholecystitis in the

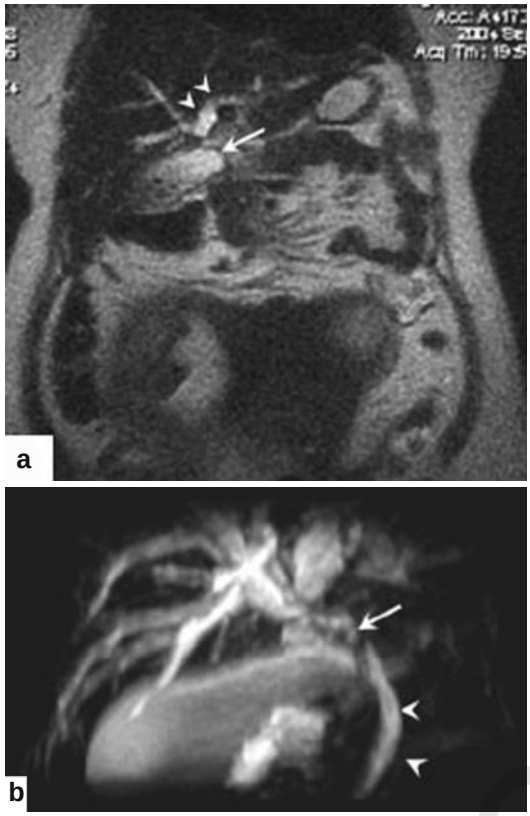

Fig. 2.3 A 27-year-old female at 36 weeks gestation who had obstructive jaundice and right upper quadrant pain. (**a**) Coronal T2-weighted single-shot fast spin-echo image shows distended gallbladder with cholelithiasis (*arrow*) and intrahepatic biliary dilatation (*arrowheads*). (**b**) Thin-slice MR cholangiopancreatography (MRCP) images showed that the distal common bile duct is normal in caliber, and the common hepatic duct was compressed by the inflamed and distended gallbladder. Maximum intensity projection reconstruction of thin-slice MRCP images demonstrates the distended gallbladder fundus compressing the proximal common bile duct (*arrow*), causing intrahepatic biliary dilatation, and a normal caliber distal common bile duct (*arrowheads*), consistent with Mirizzi syndrome [115]

puerperium and said that he was able to find but four cases previous to his article. In 1895, Davis AB reported a case of cholecystectomy in the 7th month without interrupting pregnancy. Ploger in 1910 gave a record of 42 cases, of these 22 had gallstone colic in the puerperium, and in 19 of these it was the first attack. The remaining 20 attributed the beginning or increase in the severity of their gallstone pains to some pregnancy [119]. Peterson collected 25 cases complicating pregnancy including his own case and ten complicating the puerperium. These are cases proved by operation or through finding of calculi in the stool [3]. Otherwise he could have included 20 cases of Huchard and 51 of Berline-Herwig. Since 1910, Green reported two cases following miscarriage [120]; Branson, four cases [121]; Audebert, one case; and Graham, six cases, a rather meager list when the frequency of gallstone operation is considered [122].

This relationship is suggested by the relative frequency of gallstones in para women to the occurrence in men on the one hand and virgins or sterile women on the other. Ochsner reported 50 cases in which there were four times as many females as males. Kehr reports a series of 720 laparotomies upon 655 patients of which 536 were women and 119 men. Mayo makes the statement that gallstones occur three times more frequent in women. Schroeder says that 90 % of women operated upon have borne children. Peterson found that 75 % had children. Grube proves that of 657 cases of gallstone, 613 cases had children. There were 183 married and 33 unmarried or sterile women [123]. Authur's collection tends to the same conclusions that there is sufficient evidence positively to state that pregnancy produces changes in the biliary system which favors the invasion of microorganisms. Grube concisely states that these changes are (1) stasis of the bile, (2) increase of cholesterin in the bile, (3) protein decomposition, (4) cell desquamation, and (5) hyperemia of the mucosa of the bile ducts [123]. He agrees with Hofbauer that cholelithiasis is due to the above processes plus bacterial infection and says that as a result of investigations of the livers of women who have died during or just before or after labor all of the above-named conditions are characteristic of pregnancy [124]. M'Nee says that on the basis of investigation carried on by himself and Ashoff,

Table 2.2 ESUR guidelines for the use of iodinated and gadolinium contrast media during pregnancy and lactation

	Iodinated agents	Gadolinium agents
Pregnancy	(a) In exceptional circumstances, when radiographic examination is essential, agents may be given to the pregnant female	(a) When MR examination is necessary, agents may be given to the pregnant female
	(b) Following administration to the mother, thyroid function should be checked in the neonate during the first week	(b) Following administration of agents to the mother, no neonatal tests are necessary
Lactation	Breastfeeding may be continued normally when agents are given to the mother	Breastfeeding may be continued normally when agents are given to the mother
Pregnant or lactating mother with renal impairment	No additional precautions are necessary for the fetus or neonate. Follow ESUR guidelines for contrast media administration when renal function is impaired	No additional precautions are necessary for the fetus or neonate. Follow ESUR guidelines for contrast media administration when renal function is impaired

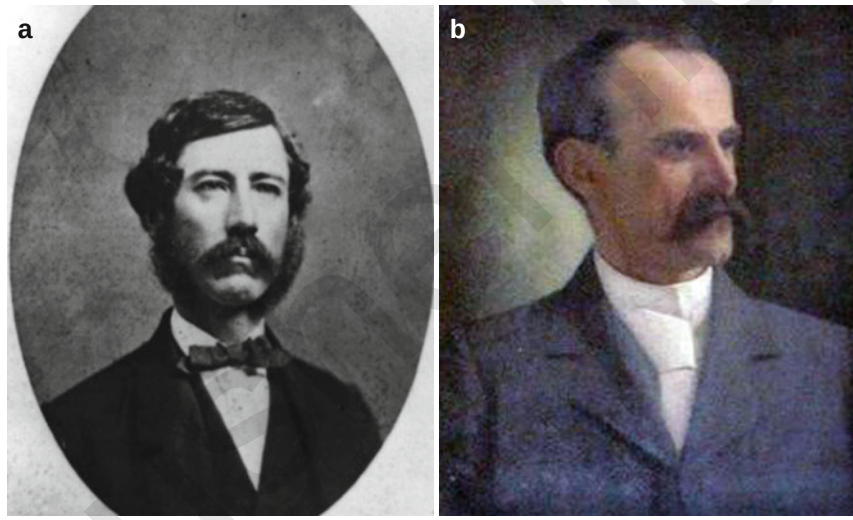

Fig. 2.4 Robert Barnwell Rhett Jr. (1853–1901), President of the Medical Society of South Carolina and Dean of the Charleston Medical School, performed first cholecystotomy on a pregnant patient [118]

some forms of stones originate in the aseptic and uninflamed bladder. M'Nee believes there is a definite relationship between gallstones and pregnancy taking into consideration that the most common age of onset corresponds to the period of childbearing and the number of cases of gallstones in women who have borne children [125]. He believed that the pressure of the uterus causes stasis. He also found that the *cholesterme* contents of the bile were greatly increased in five women who died during, just before, or after labor. These findings coincide with those of Grube. Peterson says that in pregnancy, it is significant that in nearly one-third of the cases the

period of onset is at that time of gestation when the uterus is approaching the level of the umbilicus, sending the intestines upward, and when the growing fetus is beginning to hamper the eliminative powers of the liver. In the puerperium in one-half of the cases, the attacks occurred during the first 7 days postpartum suggesting traumatism of the biliary passages during labor. He quotes Vineberg who says the great eliminative processes going on at this period, the change in the intra-abdominal pressure, and the forced rest in bed with the attendant constipation all favor these attacks.

The occurrence of jaundice is most important as its presence materially affects the uterine contents, and the nearer to term, the greater the possibility of exciting labor. Peterson found that in 15 cases of his series of 25, jaundice was present. He seems to prove by a study of the cases with reference to the location of the gallstones and jaundice that pregnancy can produce jaundice in a constitutional way without the aid of obstruction in the shape of calculi. Peterson's bibliography shows that in this country, IUoway, 1889, reported a case of icterus gravidarum.

The operative mortality is 13 %, for 23 cases [3]. This is influenced by the complications of common duct involvement and the degree and extent of inflammatory processes. The condition of pregnancy seems to have but little effect. The deaths reported were from rupture of the gallbladder, cases of empyema, or extensive or prolonged operative procedures required by the conditions found. The occurrence of miscarriage is dependent upon the pathology present more than upon the effect of the operation. In Peterson's cases, two started before operation and three after. All of the latter were cases of extreme infection with chills, fever, and jaundice. Graham reports a case in the 6th month in which the gallbladder was ruptured by a blow on the abdomen. At operation, three gallstones were found in the abdomen, one in the gallbladder and two in the cystic duct. He gives detailed histories of four others, which were operated upon during pregnancy, all of whom went to term. One other case refused operation and died 2 years later from complete obstruction of the common bile duct. Luiz in discussing Graham's paper describes a case with gallbladder rupture during labor. The patient died of general peritonitis, and postmortem, 250 gallstones were found scattered through the abdominal cavity. There is evidence to believe that operation on the gallbladder in which complications are not marked has but little effect in producing abortion and that recovery may be expected as in the ordinary case. This fact justifies us in advising removal at any time when the symptoms become frank and at any time during the pregnant state, especially when a history of frequent and recurrent attacks is obtained. The tendency of cholecystitis to subside for long periods is to be remembered so that in mild and short attacks operation may be postponed until after delivery with a minimum risk.

2.1.8.2 Conservative Treatment

Interests of both the mother and the fetus must be considered in therapy during pregnancy. Usually, these interests do not conflict, because what is good for the mother is generally good for the fetus. Sometimes, however, maternal therapy must be modified to substitute alternative but safer therapy because of concerns about drug teratogenicity (e.g., substituting a histamine two receptor antagonist for misoprostol, an abortifacient that is contraindicated during pregnancy) [126, 127]. Rarely, the maternal and fetal interests are diametrically opposed, as in the use of chemotherapy for maternal cancer, a therapy that is potentially life saving to the mother but life threatening to the fetus [128]. These conflicts raise significant medical, legal, and ethical issues.

The first available large studies on pregnancy-related gallbladder disease showed fetal loss of 12–15 % [3, 129]. A study by Greene et al. noted fetal loss of 24 % after cholecystectomy [130]. If one of four patients with fetal loss (of total 17 patients) is excluded due to postoperative peritonitis (cholecystectomy and appendectomy were performed during initial operation), then the fetal rate is 18 %. In that time 10 % of all pregnancies ended in abortion [131, 132]. Greene et al. also concluded that the causal relationship to surgery is not clear, because of the varied time lapse between surgery and abortion. Even in 1997

a study in *British Journal of Surgery* recommended conservative treatment [10].

It is known that there is significant difference between biliary colic and acute cholecystitis. The diagnosis of biliary colic requires right upper quadrant pain and gallstones documented by ultrasound in the absence of ultrasonographic signs of gallbladder inflammation. Traditionally, medical treatment is almost always used first especially in biliary colic. The therapy could be initiated or continued by primary care physician but only after the consultation with the gastroenterologist or abdominal surgeon. This recommendation is due to the fact that even after biliary colic, there were 28 % of premature contractions [133] and in the study by Dixon et al. even three fetal deaths [134]. Initially, the patients should be seen every day for the first several days then once a week. The patients with significant comorbidities should be hospitalized even for medical therapy.

Another traditional indication for medical therapy is to delay the cholecystectomy until the second trimester because spontaneous abortion rate after open cholecystectomy is 12 % in the first trimester and 5.6 % in the second trimester [135]. On the other hand, delay of surgery until the second trimester in patients with symptomatic gallstone disease during pregnancy may lead to further complications of gallstone disease such as acute cholecystitis and gallstone pancreatitis, risk of maternal malnutrition, and reduction in fetal growth rate caused by lack of maternal oral intake leading to higher spontaneous abortion rates and preterm labor [20, 136–138]. In addition, the rates of preterm labor and premature delivery are 0 % during the second trimester compared to 40 % in the third trimester [135].

Total Parenteral Nutrition

Total parenteral nutrition has been used as an effective alternative to surgical treatment of chronic cholecystitis in the second and third trimesters [139]. A study of ten pregnant patients with severe hyperemesis managed with parenteral nutrition found no adverse effect on maternal weight gain and fetal growth [140]. The growing fetus requires essential fatty acids and amino acids for development and maturity of vital organs like the brain and lungs. Parenteral nutrition provides a viable means for the fetus to receive these supplements. There has been recent trend toward the use of peripherally inserted central catheters (PICC) because of lower rate of major complications and relative ease of insertion compared to central venous catheters [141]. PICCs should always be considered particularly in high-risk populations like pregnant women. Several studies, however, have shown a higher rate of minor complications like thrombophlebitis in patients with PICCs [142, 143]. PICC insertion is highly operator dependent, and lowest complication rates have been reported in the most experienced centers [144].

Diet

Low fat diet is essential, minimizing intake of cholesterol-rich foods like foods of animal origin, pork and red meat, with slow reduction of body weight and by indulging in more fruits and fiber intake. Potent natural remedies minimize the abnormal concentration of bile acids (acids that help in fat digestion), keep cholesterol level in check, heal inflammation, clear out toxins, and eliminate excess of lipids from the body.

Beetroot juice is high in fiber and has carotenoids and flavonoids that reduce the cholesterol from entering the gallbladder and thus stops the formation of solid pear-shaped gallstones. It has betaine that supports liver function and tames high sugar level.

Apple juice has unique compound – malic acid – that helps in softening the gallstones and disintegrates.

Mix of raw juice comprises of carrot juice, cucumber juice, and beetroot juice. The maximum concentration should be of carrot juice. Cucumber juice has silica that prevents overformation of calcium stones in the body.

Analgesia

Nonsteroidal anti-inflammatory drugs are the first choice treatment for symptomatic relief:

- Ibuprofen 400–600 mg three times a day
- Naproxen 250 mg up to four times a day
- Diclofenac 25–50 mg up to three times a day

Increased risks of miscarriage and malformations are not proved with NSAID use in early pregnancy. Conversely, exposure to NSAIDs after 30 weeks gestation is associated with an increased risk of premature closure of the fetal ductus arteriosus and oligohydramnios. NSAIDs should be given in pregnancy only if the maternal benefits outweigh the potential fetal risks, at the lowest effective dose, and for the shortest duration possible. If indicated, ibuprofen is the preferred agent.

Paracetamol and weak opioids such as codeine may be used as additional treatments to help control the pain. They are also useful if nonsteroidal anti-inflammatory drugs are not tolerated or are contraindicated as in patients with peptic ulceration.

Anticholinergic Antispasmodics

Dicyclomine (Bentyl) is classified as FDA type B drug which means that it could be used in pregnancy, if clearly needed. It passes into breast milk and could affect a nursing infant. Dicyclomine can suppress the production of breast milk in nursing mothers.

Antibiotics

The US Food and Drug Administration has categorized all antibiotics according to the risks associated with their use in pregnancy. Two categories are important:

- Category A: studies in pregnant women do not demonstrate any risks to the mother or fetus.
- Category B: while animal studies show no risk, human studies are inadequate or animal toxicity has been noted, but the studies on humans show no risk

There are no antibiotics in category A. In category B are penicillins and cephalosporins. The first-line treatments are ampicillin and sulbactam or cefoxitin/cefuroxime.

There is no consensus on the duration of antibiotic use. The most precise method is to use it until the patient becomes afebrile and does not show evidence of leukocytosis or elevated CRP.

Ursodeoxycholic Acid

Ursodeoxycholic acid, a naturally occurring bile acid agent, can dissolve gallstones by changing the composition of the bile, and it has been used in nonpregnant patients for this indication. Although ursodeoxycholic acid has been administered in pregnancy in the management of intrahepatic cholestasis, its safety and efficacy for the treatment of gallstones during pregnancy has not been established [145].

2.1.8.3 Percutaneous Biliary Drainage

Pregnant patients presenting with recurrent gallbladder colic during the first or third trimester or high-risk patients could be managed with percutaneous transhepatic gallbladder aspiration (drainage). Under ultrasound guidance and local anesthesia, a pigtail drainage tube is inserted through the liver and into the distended gallbladder. Essentially, it is recommended that the drainage tube should not be extracted until a fistula forms around the tube (around 2 weeks) in severe cases where changing of the drainage tube is necessary. Major disadvantages of this procedure are bile leakage, bile duct injury, and abdominal abscess [146]. Although the patients both delivered without neonatal complications and subsequently underwent LC postpartum, not enough data are available for recommending this approach routinely [147].

2.1.8.4 Operative Treatment

Recommendations for General Population

According to Tokyo guidelines for surgical treatment of patients with acute cholecystitis [148], there are several statements that should be followed in nonpregnant population. Randomized controlled trials in the open cholecystectomy era, comparing early surgery with delayed surgery in the 1970s–1980s, found that early surgery had the advantages of less blood loss, a shorter operation time, a lower complication rate, and a briefer hospital stay (level 1b) [28, 149–151] and (level 3b) [152]. Recent randomized clinical trials (level 1b) [153–157] have addressed the timing of and surgical approach to the gallbladder in patients with acute cholecystitis, and the results have indicated that laparoscopic cholecystectomy performed during the first admission was associated with a shorter hospital stay, quicker recovery, and reduction in overall cost of treatment compared to open cholecystectomy. Early laparoscopic

cholecystectomy is now accepted to be sufficiently safe for routine use, because earlier reports of increased risk of bile duct injury (level 4) [158] have not been substantiated by more recent experience (level 1b) [154, 155, 157, 159, 160].

According to the Tokyo guidelines [148], acute cholecystitis has three grades related to severity of the disease:

- *Mild* (*grade I*): early laparoscopic cholecystectomy is the preferred procedure.
- *Moderate* (*grade II*): early cholecystectomy is performed. However, if patients have severe local inflammation, early gallbladder drainage (percutaneous or surgical) is indicated. Because early cholecystectomy may be difficult, medical treatment and delayed cholecystectomy are necessary.
- *Severe* (*grade III*): urgent management of organ dysfunction and management of severe local inflammation by gallbladder drainage and/or cholecystectomy should be carried out. Delayed elective cholecystectomy should be performed later, when cholecystectomy is indicated.

Indications in Pregnant Population

The most common cause of biliary surgery during pregnancy is repeated biliary colic in 37–70 % of cases, followed by acute cholecystitis in 20–32 %, choledocholithiasis in 7 % and acute biliary pancreatitis in the remaining 3 % of cases, and olecystitis with 32 % of cases [10, 161]. In contrast to the generally favorable published fetal-maternal outcomes following cholecystectomy during pregnancy, conservative medical management of symptomatic cholelithiasis in pregnant women often leads to suboptimal clinical outcomes. Maternal illness may pose a greater threat to the fetus than surgery. Three published studies have shown the readmission rate for pregnant patients with biliary tract disease to be greater than 50 % in patients managed conservatively, and 16 % of the patients had either spontaneous abortions or preterm births [20, 134].

Recurrence rate during pregnancy is 31–38 % for symptomatic cholelithiasis, and patients in the second trimester had the highest rate of relapse, followed with first and then the third trimester [133, 162]. There are reports with even higher recurrence rates (40–92 %) after conservative treatment confirming that it is trimester dependent [136, 163, 164]. Also, pregnant patients often had more severe disease at the time of relapse [133]. Swisher et al. [164] reported an average of 2–6 relapses during pregnancy; Elamin et al. reported an average of 4 ± 1.3 admissions for relapse [165]; and Lu et al. reported 1-3 additional admissions, each lasting 5–8 days [133]. Patients with symptomatic cholelithiasis at first presentation with each subsequent relapse had more severe disease than the previous episode [133]. The most common causes of biliary surgery during pregnancy were repeated biliary colic in 37.5–70 % of cases, followed by acute cholecystitis in 20–32 %, and choledocholithiasis in 7–17 % [10, 161]. If the disease progresses to AP, the rate of fetal loss may be increased. Jouppila et al. reported three episodes of fetal death in a series of eight pregnant patients with AP [166]. However, not all of their patients had gallstones. Another important observation is that the majority of patients with complicated gallstone disease who do not undergo antepartum cholecystectomy have recurrent postpartum symptoms often within 3 months postpartum. When appropriate, physicians should advocate for antepartum or early postpartum cholecystectomy to minimize symptom recurrence and unplanned hospitalizations [167].

Compared with patients managed surgically, nonoperative management was associated with a significantly higher rate of labor induction and preterm delivery requiring neonatal intensive care [133]. Also a recent report suggests that fetal death rate is higher after conservative treatment than after laparoscopic cholecystectomy for symptomatic benign biliary disease [163]. A spontaneous abortion rate of 12 % is associated with the nonoperative management of symptomatic cholelithiasis in the first trimester [5]. The effects of any medical intervention on fetal mortality have to be considered in the context of certain preexisting background risks that are common to all pregnancies. These include a 3 % risk for birth defects, 15 % for miscarriage, 4 % for prematurity, 4 % for growth retardation, and

1 % for mental retardation or neurological developmental problems.

Surgical advances made over the last two decades shifted the management toward a multidisciplinary and minimally invasive approach. Interventional radiology, endoscopic retrograde cholangiography (ERCP), and laparoscopic surgery are commonly employed, but their timing and indications need to be properly defined. The advantages of operative treatment could be summarized in the following:

- Lower consumption of medications
- Lower hospital stay and number of hospitalizations
- Lower incidence of potentially life-threatening complications:
  - Perforation
  - Biliary sepsis
  - Peritonitis
- Lower incidence of gallstone pancreatitis
- Lower incidence of spontaneous abortions, preterm labor, and preterm delivery

Open Versus Laparoscopic Cholecystectomy

On the basis of four retrospective studies comparing laparoscopic cholecystectomy (LC) with open cholecystectomy (OC), it is difficult to recommend any particular treatment because these studies did not specifically look at the physiological effects of pneumoperitoneum or CO_2-induced acidosis on the fetus during LC or the effects of uterine manipulation during OC [15, 135, 168, 169]. These studies did not show any significant difference in maternal and fetal outcome. There were 6.74 % preterm deliveries in the LC group compared with 2.90 % in the OC group ($p = 0.27$). One fetal death occurred in the LC group compared with two in the OC group ($p = 0.41$). The fetal death reported by Cosenza et al. occurred on postsurgical day 6. This woman underwent LC converted to OC for gallstone-induced AP in the 14th week of gestation. In a report by Barone et al. a 27-year-old woman died from postsurgical hemorrhage after undergoing LC in the 20th week of gestation. The source of bleeding was not identified. The other fetal death in this series occurred 4 weeks after surgery after the mother underwent OC in the 16th week of gestation. The absence of morbidity and mortality with the LC [15, 16] or just minor mortality including several wound infections [161] is stated in several studies. The largest study estimated a rate of 7 % for fetal mortality and by-trimester recurrence rates of 55, 55, and 40 % for nonoperative management. The rate of emergent surgery following nonoperative management was calculated to be 19.5 %. For LC the aggregate data suggest a fetal death rate of 2.5 % [163]. It should be noted that the analysis included 277 patients, and only one fetal death in the second trimester occurred.

LC in pregnant women provides all of the advantages of laparoscopic surgery – such as significantly reduced hospitalization, decreased narcotic use, and quicker return to a regular diet [135]. Other advantages of LC include less manipulation of the uterus and detection of other pathology that may be present [168]. It also decreases the possibility of postoperative deep vein thrombosis because of improved early mobility in such patients.

As in nonpregnant population, if LC cannot be completed successfully, conversion to OC is mandatory [170].

Contraindications for Laparoscopic Surgery

Contraindications for laparoscopic surgery in pregnancy are principally the same as in nonpregnant population [171]:

Absolute Contraindications

- Hypovolemic shock, massive bleeding, or hemodynamic instability
- Severe cardiorespiratory disease
- Uncontrolled coagulopathy

Relative Contraindications

- Peritonitis
- Portal hypertension
- Multiple previous procedures/extensive intra-abdominal adhesions

2.1.8.5 Specific Considerations

Symptomatic Cholelithiasis in Diabetic Pregnant Patient

The serious consequences of cholelithiasis in diabetics are well established [172–174]. There is only one article published with the analysis of

diabetic subgroup of pregnant patients with symptomatic cholelithiasis. A total of 35.8 % of the patients in this study had established diabetes mellitus. This is greater than the finding in general population of gallstone patients, among whom diabetes mellitus is only 11.1 % [172]. This may suggest that patients with diabetes have a greater tendency to symptomatic gallstones in pregnancy. A more plausible explanation is that diabetic patients, educated to the tendency of diabetes mellitus to exacerbate the seriousness of many illnesses and already accustomed to the hospital, sought medical attention more often than the nonpregnant patients. The reported prevalence of diabetes mellitus in the Saudi Arabian population varies from 4.1 to 7.2 % [175, 176]. The recommendation is to perform LC during pregnancy even if biliary colic in such patients is present.

Cholecystitis in IVF Pregnancy

The number of IVF pregnancies is constantly increasing (see "Acute Appendicitis"); therefore, it is expected that the number of cases with acute cholecystitis during IVF pregnancy will also increase, especially because patient during assisted reproduction are exposed to higher doses of female hormones which are known risk factors for the genesis and progression of biliary sludge and stones. Currently there is only one case report of laparoscopic cholecystectomy in a 16-week IVF pregnancy [177]. There were no intra- or postoperative complications, and the baby was born normal with APGAR 10/10 in the 39th week of pregnancy.

Spontaneous Biliary Tract Perforations

Biliary tract perforations are unusual causes of peritonitis in pregnancy. The symptoms and signs are often nondiagnostic, especially during pregnancy, and diagnosis may be delayed with possible fatal consequences [178]. Gallbladder or common bile duct (CBD) perforations as a cause of peritonitis in pregnancy have been rarely reported in literature, and their exact incidence in pregnancy is not known.

Gallbladder Perforation

Even when the gallbladder perforates, the usual outcome is a local abscess, on account of the adhesion that forms between the gallbladder, the greater omentum, and the parietal peritoneum [179]. Although gallbladder perforation has been reported to occur in 3–10 % cases of acute cholecystitis in adults, free gallbladder perforation into the peritoneal cavity is even rarer, occurring in only 0.5 % of the patients undergoing conservative management for acute cholecystitis. Risk factors for gallbladder perforation in adults include age greater than 60 years, immunosuppression, steroid use, and severe systemic disease [178].

The initiating event in majority of these patients is impaction of the stone leading to epithelial injury and ischemia due to distension of the gallbladder. The site of perforation is either at the fundus, which is farthest away from the blood supply, or less commonly at the neck from the pressure of an impacted stone [180].

Perforation of the Common Bile Duct

Spontaneous perforation of the CBD is even a rarer event in adults, with only 45 cases reported [178, 181]. Bile duct perforation is most commonly described in infants related to congenital biliary system anomalies. As early as 1882, Freeland [182] reported the first case of extrahepatic biliary system rupture in an adult (diagnosed at autopsy), an entity that was subsequently first described in pregnancy by Hogan in 1957 [183], and currently there are only nine case reports published in pregnancy [183–190].

Pathogenesis, Diagnosis, and Treatment

Although the pathogenesis of spontaneous biliary perforation in the adult is poorly understood, recognized mechanisms include the following: calculous perforation at the site of impaction; calculous erosion without impaction; increased canalicular pressure due to obstruction by tumor, stone, or spasm of the sphincter of Oddi; intramural infection; mural vessel infarction leading to mural necrosis; or rupture of a biliary tract anomaly such as cyst or diverticulum [189]. The obstruction leads to an increase in intraductal pressure. This leads to dilatation of the biliary tree and subsequent stasis and infection, ascending cholangitis, and thrombosis of intramural vessels. The end result is necrosis and perforation

of the duct wall. One postulated cause is increased hemodynamic changes associated with higher pressure in the vena cava during pregnancy. Overall, 70 % of cases are related to calculi [188].

Since this condition is unusual during pregnancy, accurate diagnosis and treatment may be delayed resulting in perinatal morbidity and mortality. Abdominal paracentesis is helpful in diagnosis of biliary peritonitis. It is extremely difficult to diagnose it preoperatively, but free fluid in the abdomen with signs of acute abdomen and elevated liver function test should raise suspicion [187].

The surgical management of gallbladder perforation consists of cholecystectomy, copious irrigation, and drainage of the abdominal cavity [178]. Recommended treatment for CBD perforation includes cholecystectomy and decompression of the biliary tree in the form of CBD exploration with T-tube drainage in cases of small perforations. Roux-en-Y biliary-enteric anastomosis is indicated if the ductal disruption is large [189]. If CBD perforation is detected during diagnostic evaluation, endoscopic CBD stent placement followed by biliary surgery (if necessary) is indicated [191]. If general or hepatobiliary surgeon is not reachable in emergency setting, subhepatic drainage with several large diameter drains is recommended and the patient is transferred to adequate surgical facilities [187].

2.1.8.6 Surgical Procedures

Open Cholecystectomy

There are two skin abdominal wall incisions used as in nonpregnant population:

- Right subcostal incision
- Upper midline incision

Both incisions are well known and performed in standard fashion, and the technique could be found in any abdominal surgery textbook or atlas. As in any other operation during pregnancy, it is important to eliminate or minimize uterine manipulation to exclude the possibility of uterine contractions and possible preterm labor or abortion depending on the trimester of the operation.

Laparoscopic Cholecystectomy

At the beginning of laparoscopy, cholecystectomy during pregnancy was considered as a relative contraindication, mainly because of the lack of knowledge of the effects of CO_2 to the fetus. Fear of surgical treatment was based on the potential risk of abortion or malformations if done during the first trimester or preterm labor when done in the last one. Direct uterine trauma, decreased uterine blood flow due to the pneumoperitoneum, and toxic narcotics drugs were suggested as possible causes of fetal morbidity [192–194]. In Reddick and Olsen's 1989 article [195], pregnancy was said to be a contraindication to LC. First published case of LC on a 27-year-old patient who was 31 weeks pregnant was in 1991 by Pucci and Seed [196]. Several series of laparoscopy for the management of cholecystitis have shown no negative side effects on fetal outcome [197–199].

Up to 2008 there are 277 reported cases of LC in pregnant patients in the English literature. The data from these reports are retrospective, uncontrolled, and unblinded and surely represent only a fraction of the pregnant women who have undergone LC. Nevertheless, these data provide the best evidence available to determine how to treat a pregnant woman with biliary tract disease [163]. Potential advantages of LC in the pregnant patient include decreased fetal depression due to lessened postoperative narcotic requirements, lower risks of wound complications, and diminished postoperative maternal hypoventilation [200]. A study by Barone et al. showed almost significantly lower incidence of premature contractions ($p = 0.057$) in LC compared to OC group [169]. The only significant differences between the LC and OC groups were that patients underwent laparoscopic surgery at a mean of 5 weeks of gestation earlier than those who had open procedures and the serum alkaline phosphatase was significantly higher in the open group. In a small case control study by Curet et al. 12 LC were compared with 11 OC. There were no spontaneous abortions or episodes of premature labor in the LC group and one preterm labor in the OC group [135].

Pneumoperitoneum

Despite the conventional dogma that the first and third trimesters are higher risk periods for LC, there have been no reported fetal deaths after LC was carried out in either of these trimesters. The use of LC for patients in the first trimester of pregnancy is controversial [201] because of the unknown effects of the CO_2 pneumoperitoneum on the developing fetus [202, 203], but no problems have been encountered in clinical series so far [204].

Limited published physiological data exist concerning fetal-maternal interactions during laparoscopy. As a general principle, when the fetal-maternal unit is stressed, the mother is "conserved" at the expense of the fetus. For example, the normally decreased maternal $PaCO_2$ during pregnancy may be important in assuring adequate transplacental CO_2 diffusion from the fetus to the mother for subsequent pulmonary excretion. CO_2 pneumoperitoneum may cause maternal and subsequent fetal hypercarbia, due to decreased maternal ventilation and increased transperitoneal CO_2 absorption by the mother. In a study of pregnant ewes by Hunter and Swanstrom [202], CO_2 pneumoperitoneum induced progressive, albeit reversible, fetal hypercarbia, acidosis, and tachycardia when pneumoperitoneum pressures exceeded 15 mmHg. These effects were minimized by using low pneumoperitoneum pressures or by using nitrous oxide as the insufflation gas [202]. The potential deleterious effects of short-term fetal hypercarbia are unknown. However, in high-risk mothers prone to hypercarbia (e.g., chronic lung disease, massive obesity), precautions to decrease maternal hypercarbia by using low-pressure pneumoperitoneum (12 mmHg or less) or nitrous oxide as the insufflation gas might be considered. Nitrous oxide has been safely employed during gynecologic laparoscopy. Nitrous oxide requires the presence of either hydrogen gas or methane (such as from colonic origin) to be combustible during electrosurgical procedures [202].

Introduction of gas into peritoneum (closed cavity) has two immediate effects: (1) increase in intra-abdominal pressure and (2) gaseous exchange leading to equilibrium with gases in the blood [205]. Increased intra-abdominal pressure can decrease cardiac output by several mechanisms, including direct alteration of venous resistance in the inferior vena cava, total peripheral resistance, and mean systemic pressure [205]. Impaired venous return via compression of the inferior vena cava is of particular concern in the second half of pregnancy since the enlarged uterus can also limit venous return. The uterine compression of vena cava can be minimized by slight lateral positioning of the mother [206]. The CO_2 that is absorbed across the peritoneal surface first equilibrates within the bloodstream, then with longer operative time with the skeletal muscle, viscera, and finally bone. The patients who undergo a prolonged laparoscopic procedure are at risk of maintaining hypercarbia and acidosis postoperatively until all excess CO_2 is eliminated from the tissue.

Hypercarbia and respiratory acidosis can be monitored to some extent by capnography which measures end-tidal CO_2 concentration in the endotracheal tubes. If a rise in end-tidal CO_2 is detected, CO_2 elimination via the alveoli can be increased using controlled hyperventilation. The limitation of capnography is that while it is sensitive, end-tidal CO_2 is not foolproof in estimating CO_2 arterial pressure. When ventilation-perfusion mismatch is present and the amount of ventilation is greater relative to perfusion, gas from such ventilation will contain less pCO_2 than the actual $PaCO_2$, resulting in falsely normal or low end-tidal CO_2 readings [207]. Similar discrepancy between end-tidal CO_2 and $PaCO_2$, and subsequent acidosis, has been demonstrated also in operative laparoscopy patients with compromised cardiopulmonary status [208]. For such patients, monitoring of arterial $PaCO_2$ and pH is preferable to limit the risk of hypercarbia and acidosis. The close monitoring of CO_2 is also important considering the potential direct effect of CO_2 in increasing the mean arterial pressure and total peripheral resistance index, leading to increased afterload which could limit cardiac output [209].

Limited studies of pneumoperitoneum in pregnant sheep have demonstrated increased fetal arterial blood pressure, tachycardia, and respiratory

acidosis, which were only partially corrected with alteration in ventilator settings based on maternal capnography results [202, 210, 211].

Working pressures of CO_2 are recommended to be below 12 mmHg in order to prevent fetal acidosis [212]. Hunter et al. investigated the physiological impact of a CO_2 pneumoperitoneum in these clinical settings. They concluded that a CO_2 pneumoperitoneum created minimal impact on the patient and the fetus when using intra-abdominal pressure of 15 mmHg or less, also confirmed by others [202, 213, 214]. In accordance with Steinbrook et al. [204], some authors use a pneumoperitoneum of 10 mmHg – low enough to be in the safe range and high enough to gain adequate visualization for a safe procedure [47].

Third Trimester

When LC is necessary, the recommendation is to perform it in the second trimester. This is due to the belief that in the second trimester, organogenesis is complete and the risk of spontaneous abortion as seen in the first trimester and the risk of spontaneous labor as in the third trimester are significantly reduced in the second trimester [163, 215, 216]. The third trimester, however, poses certain potential difficulties mainly in terms of the diminished working space available owing to the enlarging uterus, the risk of injuring the uterus, and the perceived risk for excessive manipulation of the gravid uterus leading to preterm labor. The most serious complication of the uterine injury includes that of fetal loss owing to pneumoamnion resulting from inadvertent injury during Veress needle insertion for pneumoperitoneum [217]. A near-term gravid uterus makes an LC technically impossible, and near-term pregnancy is the only absolute indication for OC [12,142]. Specific problem poses patients with indication for elective or emergent Cesarean section. After Cesarean section, depending on the severity of cholecystitis, one can decide between open and laparoscopic operation and conservative treatment with elective cholecystectomy after 6 weeks.

In 1991, Pucci and Seed published a case report of a successful LC for a 27-year-old patient who was 31 weeks pregnant [196]. Furthermore, in one of the largest single institution series of 15 cases of the third trimester laparoscopic surgery, Affleck et al. reported a preterm delivery rate to be similar in both the LC and OC groups [218]. There were no fetal losses, uterine injuries, or spontaneous abortions in the LC group. In fact most of the reports in the literature suggest the safety of laparoscopic approach in pregnant women including the third trimester [163, 168, 215, 216, 219–224]. Some authors are publishing data about laparoscopy in the third trimester combining acute appendicitis and cholecystitis with excellent outcome [225]. It should be stressed that appendicitis and cholecystitis as specific pathologies have different influence on uterine irritability possibly because of different nature of local peritonitis and also due to different location (the appendix is in contact with the uterus). The upper gestational limit for laparoscopic surgery is not defined. Upadhyay et al. have shown that laparoscopic surgery up to 34 weeks can be performed [216]. For patients with potentially viable fetuses managed surgically, steroids were generally administered 24 h preoperatively to speed fetal lung maturation.

Open (Hasson) Technique

According to an NIH statement, patients in the third trimester of pregnancy should generally not undergo LC, because of the risk of damage to the uterus and the difficulty presented by the large and gravid uterus, which can obstruct safe access to the abdomen and gallbladder fossa [226]. Fatum and Rojansky suggest a gestational age limit of 26-28 weeks for laparoscopic surgery in general [193]. Although in the past *Society of American Gastrointestinal Endoscopic Surgery* (SAGES) recommended an open technique of initial port placement, in a revision of their guidelines (year 2007), they have suggested that the initial access could be safely accomplished by open (Hasson) technique, Veress needle, or optical trocar technique, the location of trocar placement being adjusted according to the fundal height, earlier incisions, and experience of the surgeon [227].

When Veress needle is used for initial insufflation, it could be safely carried out by inserting it in either the left or the right upper quadrant in the midclavicular line approximately 1-3 cm below

the costal margin [216, 228]. It should be noted that there are two reports of Veress needle insufflating intrauterine cavity, resulting in CO_2 embolism [223, 229], and one during laparoscopic appendectomy, injuring the uterine wall with the mandrel of the 5 mm trocar. There was loss of a little amniotic fluid, but there was no severe bleeding. The remainder of the pregnancy was without complications [230]. After inserting a 5 mm trocar at this site, a 5 mm camera is then used to guide the insertion of the rest of the ports under direct vision [216].

The usual umbilical port for the camera is placed few centimeters cephalad beyond the fundus of the gravid uterus in the midline usually in supraumbilical position. The insufflation pressure is around 12–15 mmHg. A pressure of 15 mmHg should not be of concern as in the third trimester, as at times the uterine pressures can reach very high during spontaneous intermittent contractions [216]. Currently, optical trocars or the so-called Direct Vision Initial Ports (Optiview, by Ethicon, Cincinnati, OH, USA; Visiport, by US Surgical, Norwalk, CT, USA) have become available. They can be used with or without pneumoperitoneum. These kinds of trocars are introduced under direct vision.

Laparolift

To eliminate the possible influence of CO_2 pneumoperitoneum on the fetus, some authors used the laparoscopic technique without the use of pneumoperitoneum [231]. This method is not well accepted in pregnant as in nonpregnant population.

Local Anesthesia

Local anesthesia with prolonged duration of action could be utilized in port sites for improved postoperative analgesia, which minimizes narcotic requirements after surgery.

2.1.8.7 Perioperative Management

Intraoperative CO_2 Monitoring

Intraoperative CO_2 monitoring by capnography should be used during laparoscopy in the pregnant patient (level III). Fetal acidosis with insufflation has not been documented in the human fetus, but concerns over potential detrimental effects of acidosis have led to the recommendation of maternal CO_2 monitoring [203, 232]. Initially, there was a debate over maternal blood gas monitoring of arterial carbon dioxide ($PaCO_2$) versus end-tidal carbon dioxide ($ETCO_2$) monitoring, but the less invasive capnography has been demonstrated to adequately reflect maternal acid-base status in humans [233]. Several large studies have documented the safety and efficacy of $ETCO_2$ measurements in pregnant women [168, 193, 225] making routine blood gas monitoring unnecessary.

Fetal Heart Monitoring

Fetal heart monitoring should occur pre- and postoperatively in the setting of urgent abdominal surgery during pregnancy (level III). While intraoperative fetal heart rate monitoring (every 5 min) by surface ultrasound was once thought to be the most accurate method to detect fetal distress during laparoscopy, no intraoperative fetal heart rate abnormalities have been reported in the literature [11, 136]. Lu et al. found that external monitors of uterine contractions were variably effective in the insufflated abdomen [133]. This has led some to recommend only pre- and postoperative monitoring of the fetal heart rate as no increased fetal morbidity has been reported [168, 225].

Special monitoring precautions beyond those usually employed during general anesthesia – continuous maternal pulse oximetry, end-tidal CO_2, monitoring, electrocardiography, and pulse rate measurements, combined with frequent blood pressure measurements – have generally not been employed. Transabdominal monitoring of fetal heart rate is usually not technically feasible during laparoscopic surgery in advanced pregnancy. In high-risk pregnancy, transvaginal fetal monitoring can be employed [204]. In addition, in women predisposed to significant hypercarbia, changes in end-tidal CO_2 may lag significantly behind maternal $PaCO_2$. Frequent direct measurements of maternal $PaCO_2$ via an arterial catheter may be warranted [204].

Thromboprophylaxis

Many factors can alter postoperative coagulation changes. These include the type of operation

performed [234] and the type of anesthesia [235]. Postoperative changes in cytokine level are affected by even more factors. They include the type of procedure and anesthetic technique or anesthetic agent used [236], the duration of operation [237], and the use of autologous or allogenic transfusion [238].

Caprini et al. [234] reported a marked hypercoagulable state after LC, as seen by an increase in the thromboelastographic index, on the first postoperative day compared with preoperative values. Other reports have documented a reduction in postoperative hypercoagulability after LC compared with after OC [239, 240]. Prisco et al. reported a significant increase in F1.2 levels after LC, but these levels were significantly lower than OC [240]. Conversely, other investigators have demonstrated no difference in postoperative hemostasis between laparoscopic and open surgery [241, 242], and fibrinogen levels increased and reached maximum levels at 72 h, but significantly less so after LC than after OC, while plasminogen levels decreased postoperatively without a significant difference between groups [243]. Laparoscopic surgery is associated with a lesser degree of thromboembolic complications despite pneumoperitoneum which, by reducing venous inflow toward the heart, promotes venous stasis of the legs and predisposes to deep venous thrombosis [244, 245].

In a nonrandomized trial, Shietroma et al. [243] compared TAT, F1, FIB, soluble fibrin, and D-dimer plasma levels until 72 h after surgery between patients assigned to open or laparoscopic cholecystectomy and found that levels of the aforementioned markers were significantly higher in the open surgery group than in the laparoscopic surgery group, implying significantly higher activation of coagulation and fibrinolysis in the open surgery group. Three other nonrandomized studies compared fibrinolytic activity between OC and LC and found insignificant differences between the two groups of patients [241, 242, 246].

Results of the study by Tsiminikakis et al. showed that open surgery, as compared with laparoscopic procedures, leads to activation of the clotting system of a higher degree than in the laparoscopic surgery group, implying thus greater thromboembolic risk for patients undergoing open surgery. Subclinical fibrinolysis was also more profound in the open surgery group. Although of a lower degree, hypercoagulability is still observed in patients undergoing laparoscopic surgery. This fact, combined with the pneumoperitoneum-induced venous stasis of the legs, explains the reduced, but not negligible, rate of thromboembolic complications after laparoscopic surgery. Therefore, routine thromboembolic prophylaxis (low-molecular-weight subcutaneous heparin, elastic compression stockings, intraoperative pneumatic stockings, and early postoperative patient mobilization) should be considered for patients undergoing laparoscopic surgery [247].

Gestational hormones, particularly estrogen, contribute to a mild hypercoagulopathy during pregnancy by increasing the synthesis of clotting factors [248]. Thromboembolic phenomena are also promoted by intra-abdominal vascular stasis resulting from compression by the enlarged gravid uterus. If a laparotomy can be avoided, recovery time is greatly reduced; thus, postoperative complications due to immobilization, such as deep vein thrombosis and pulmonary embolism, are less likely. Prophylaxis with pneumatic compression devices both intraoperatively and postoperatively and early postoperative ambulation are recommended as in the nonpregnant patients.

Tocolysis

Current SAGES and EAES guidelines recommend tocolytics only if uterine contractions are present. In other words, tocolytics should not be used for prevention of uterine contractions. Tocolytics were thought to calm the uterus from the insult of acute abdomen and the intraoperative uterine manipulation, but their benefit is equivocal [249]. Figure 2.5 stratifies the different tocolytics used and their effect on the fetal outcome [117]. Authors show that there is no significant difference in efficacy of different tocolytics and no significant difference in outcome when tocolytics are used or not, the finding confirmed by others [250]. These findings are different from those which Allen et al. reported, as they recorded a 100 % success rate of tocolysis in prevention of labor [251].

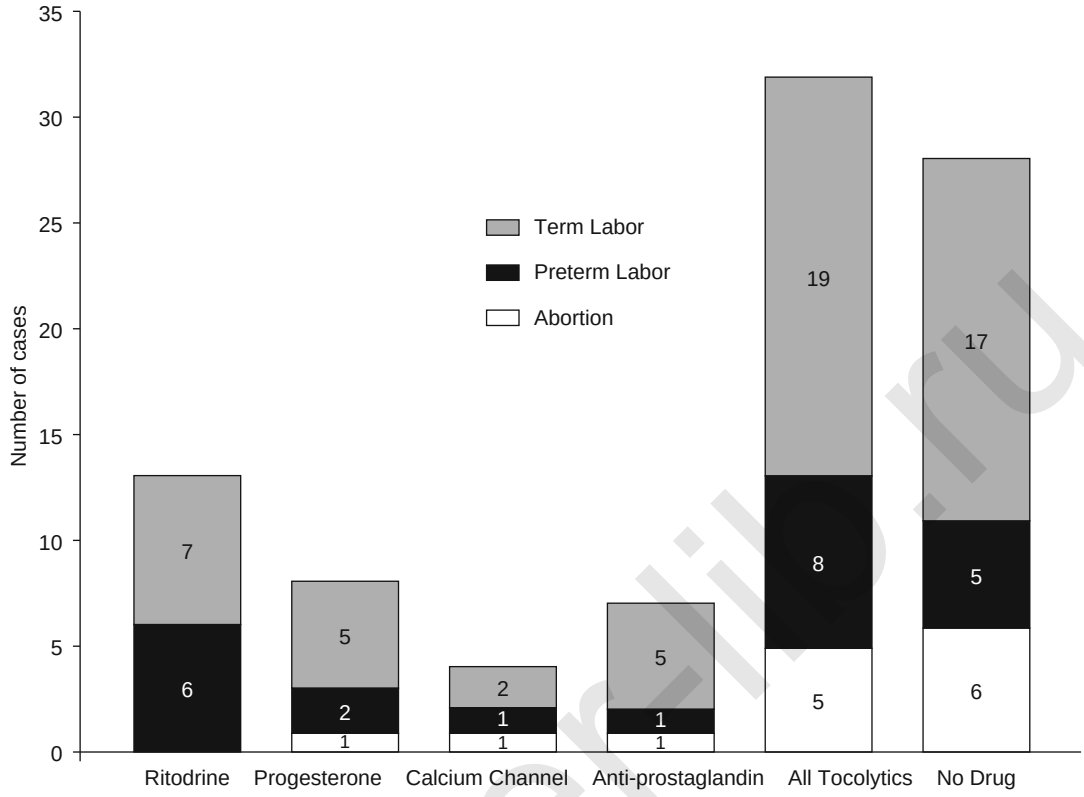

Fig. 2.5 Effects of specific tocolytics, all tocolytics, and no tocolytics on fetal outcome during acute abdomen [117]

Tocolytics not only fail to improve fetal outcome but also had serious maternal and fetal side effects, which could contraindicate their use, especially ritodrine and prostaglandin synthetase inhibitors. Ritodrine causes maternal and fetal tachycardia, nausea, and vomiting as recorded in this study, and so it impaired very important signs for managing acute abdomen. Prostaglandin synthetase inhibitors are blamed for constriction of ductus arteriosus when used as a tocolytic, but recently it was found that when used between 26 and 34 weeks of pregnancy, the danger is minimal [252]. In the study by El-Amin Ali et al. [117], no teratogenesis due to prostaglandin synthetase inhibitor was detected, and the reported complications of altered hematological indices, transient renal insufficiency, and necrotizing enterocolitis [253] were not detected. Another drawback of the use of prostaglandin synthetase inhibitor is its anti-inflammatory and antipyretic effect, which might mask important clinical parameters for acute abdomen case management and give the surgeon a false sense of security. Unlike ritodrine and prostaglandin synthetase inhibitor, nifedipine is safer and does not alter the disease symptomatology [249]. Although nifedipine was blamed for causing hypotension, this proved to be insignificant [254, 255]. Albeit feared for teratogenicity [256], the evidence is not conclusive [257], and no malformations were reported in the study by El-Amin Ali [117]. In the study by Lu et al. 14 out of 53 (26 %) patients with symptomatic cholelithiasis developed preterm contractions requiring treatment with tocolytic agents. One patient with biliary colic failed tocolysis and delivered a 1,250 g infant at 32 weeks gestation, and another with acute cholecystitis had pulmonary edema as a complication of tocolysis [133]. Selective use is recommeded, only if uterine contractions are present, as proposed in the study by Sungler et al. [47]. Both patients receiving tocolysis (25th and 32nd weeks of gestation) had preterm labor on admission for 6 and 9 days, respectively.

Folic Acid/Multivitamin Supplementation

A study by Acsa et al. showed that symptomatic cholelithiasis and/or cholecystitis in pregnant women is associated with a higher risk for neural tube defects in their offspring [258]. However, this finding was based on 11 cases, and of these cases, two had alternative possible causes (diabetes and high fever-related influenza) as well. Thus, this finding is only a signal, which needs confirmation or rejection. There is no similar report published regarding the association between symptomatic cholelithiasis and cholecystitis and neural tube defects. At the evaluation of this association, microbial agents, related drug treatments, other confounders, and chance effects should be considered. Previous studies indicated an association between neural tube defects or other congenital anomalies and high fever during the critical period [259–264]. Some pregnant women with symptomatic cholelithiasis and/or cholecystitis reported fever in the study. Currently there are no data regarding the possible association between the bacterial causes of cholecystitis and neural tube defects [164]. The drugs used for the treatment of symptomatic cholelithiasis and/or cholecystitis have no role in the origin of neural tube defects [265, 266]. The use of folic acid and folic acid-containing multivitamins was less frequent symptomatic cholelithiasis and/or cholecystitis group. Authors' hypothesis for the explanation of possible association between symptomatic cholelithiasis and/or cholecystitis and neural tube defects is based on the observation that the chronic condition of symptomatic cholelithiasis and/or cholecystitis frequently includes fever, and this fever may have a role in the origin of neural tube defects. Thus, periconceptional folic acid/multivitamin supplementation in pregnant women with symptomatic cholelithiasis and/or cholecystitis is particularly important [258, 263].

Duration of Hospitalization

In the study by Lu et al. patients who underwent LC were able to tolerate clear liquids 0.6 days sooner and regular diet 0.3 days sooner than patients who underwent OC [133]. Curet et al. demonstrated, in a retrospective study, a significant reduction in hospitalization time for LC in comparison with OC [135]. Mean hospitalization was 2 [161] to 4.5 [220] days for acute cholecystitis treated with LC and 3 days for common bile duct exploration [161].

2.1.8.8 Surgical Considerations in the Postpartum Period

The abdominal wall also undergoes significant change during pregnancy, with muscle tone reduction and skin elasticity to accommodate the enlarging uterus. The abdominal wall tone remains lax for several weeks postpartum, returning to a near-nonparous level in 6-7 weeks. The hallmarks of acute surgical disease, abdominal guarding and rigidity, do not occur during the early puerperium. This single feature of the puerperium is responsible for confusion and delay in proper surgical diagnosis. Puerperal changes in blood components may be confusing as well. During the first 10–14 days of the puerperium, WBC counts of 20,000–25,000/mm^3 are not unusual; there is also a predominant increase in neutrophils. The erythrocyte sedimentation rate may increase to 50–60 mm/h. Reliance on either the erythrocyte sedimentation rate or the WBC count for the diagnosis of acute infection may be misleading.

The postpartum patient can be operated upon without the added concerns of the fetus; however, several unique characteristics apply to this group. In the early postpartum period, the enlarged uterus is a potential technical factor. In the Cesarean section patient, the challenges of a recent surgical incision must be considered. Safe access to the peritoneal cavity and ultimate protection of the recent incision are important factors. Finally, unique features of the biliary tract disease during the postpartum period may require special consideration. Any conservative treatment course is hampered by these patients' strong desire to minimize the number of hospital days, recurrent symptoms, and disability. Physiologically, postpartum patients are still recovering from pregnancy and childbirth. In addition, separation from a newborn, combined

with varying degrees of labile emotions related to the postpartum state, serves to accentuate the usual psychological stresses of illness. If early laparoscopy can be applied to this group, the benefits will be even greater than that reported for the general population.

The enlarged uterus did not hamper exposure, even in the first week. At the time of surgery, the uterine fundus was inferior to the umbilicus. This is consistent with subsequent reports of technical success and good exposure in pregnant patients undergoing laparoscopy during the first and second trimesters [135]. There were no adhesions encountered in the Cesarean section group. The course of the procedure and recovery was identical to the remainder of patients.

The final unique consideration in the postpartum patient is the presence of a healing abdominal incision after Cesarean section. There are no published studies on outcomes for recent abdominal incisions subjected to early pneumoperitoneum. Pneumoperitoneum was limited to 10 mmHg pressure in the Cesarean section patients. This may have been beneficial in preventing undue mechanical strain on the healing wound, though we have no controls with the standard (15–16 mmHg pressure) for comparison. It seems prudent to utilize the minimal intra-abdominal pressure necessary for adequate exposure in these patients. Although evidence suggests fascial separation, if present, occurs early, it remains to be seen what long-term status these incisions will achieve. No hernia has developed in these patients with follow-up to 5.5 years [267].

Gallstone-Related Hospitalization During the First Postpartum Year

Gallbladder disease is a leading non-obstetric cause for hospitalization in the first year postpartum. Seventy-six percent were diagnosed with uncomplicated cholelithiasis, 16 % with AP, 9 % with acute cholecystitis, and 8 % with cholangitis. Seventy-three percent of hospitalized women underwent cholecystectomy and 5 % underwent ERCP. On multivariate analysis, independent risk factors for hospitalization included maternal race, age, being overweight or obese prepregnancy, pregnancy weight gain, and estimated gestational age [4].

2.1.8.9 Combined or Consecutive Operations During the Same Pregnancy

As previously reported, one unusual patient required two separate laparoscopic operations during the same pregnancy: cholecystectomy at 6 weeks gestation and later at 20 weeks appendectomy and reduction of an ovarian torsion. Another patient, at term, underwent combined Cesarean delivery (previously planned) and laparoscopic cholecystectomy. The cholecystectomy was performed first, because it was felt that it would be safer to conduct a cholecystectomy in a stable patient prior to any significant bleeding potentially encountered with child birth [268].

2.1.9 Prognosis

2.1.9.1 Fetal Outcome

All of the placental and amniotic complications occurred in patients undergoing cholecystectomy and were all in the laparoscopic group. Additionally, the incidence of placental/amniotic complications was statistically higher in those undergoing cholecystectomy compared with appendectomy [269]. The etiology of this association is not clear. Others state no fetal morbidity or mortality [161]. The incidence of preterm deliveries with conservative management was 3.5 % compared with 6.0 % in patients receiving surgical treatment. Similar figures were found for fetal mortality in conservative group (2.2 %) and operated group (1.2 %) [270].

2.1.9.2 Maternal Outcome

Prognosis after cholecystectomy during pregnancy is excellent. Most authors declare that there is no maternal mortality and complications mostly include wound infections [161]. In six reports of 310 patients comparing conservative with surgical management, all patients were initially treated conservatively. No maternal mortality was reported in either group [270].

2.2 Common Bile Duct Stones, Cholangitis, and Biliary Pancreatitis

2.2.1 Incidence

One in 1,200 pregnancies is complicated by choledocholithiasis [271]. CBD stones have been observed in 10–12.5 % of pregnant women undergoing cholecystectomy [162, 272] and account for 7 % of cases of jaundice in pregnancy [6].

2.2.2 History

Clinical presentation of pregnant patients with CBD stones is the same as in nonpregnant population. Classical symptoms include abdominal pain, jaundice, nausea, vomiting, and itching. Additional diagnostic challenge exists due to specific pathologic states that could be found only in pregnancy and should be included in differential diagnosis. Clinical presentation of biliary AP is the same as every other type of AP and is described in detail in the Chap. 3.

2.2.3 Examination

Physical examination is the same as the examination for cholelithiasis and cholecystitis with special attention on signs of icterus. If painless without elevated body temperature, then CBD stones or periampullary tumor is suspected, or if painful with fever and chills, then acute cholangitis is the most probable diagnosis.

2.2.4 Differential Diagnosis

There are several entities that should be included in differential diagnosis of CBD stones and cholangitis. Most of them could be easily excluded after abdominal ultrasound or MRCP. The two entities found in pregnancy are presented in more detail for easier determination of definitive diagnosis: intrahepatic cholestasis of pregnancy and acute fatty liver of pregnancy.

2.2.4.1 Intrahepatic Cholestasis of Pregnancy (ICP)

ICP usually occurs during the second or third trimester and disappears spontaneously after delivery. The prevalence of ICP varies widely by country [273, 274]. The highest frequencies have been reported in Bolivia and Chile. In Chile, the prevalence in 1974-1975 was reported to be 15.6 %, ranging 11.8–27.7 % according to ethnic origin [275]. For unknown reasons, the prevalence has more recently appeared to decrease (4.0–6.5 %) [275, 276]. In the United States, the prevalence has been estimated from 0.3 to 5.6 % according to ethnic origin [277, 278]. The prevalence in Europe is about 0.5–1.5 % [274]. Generally, ICP is more common in twin pregnancies [279]. Pruritus, which is the main symptom of ICP, is very uncomfortable and difficult to tolerate. It is often generalized but predominates on the palms and soles. It is more severe at night and disturbs sleep. Pruritus usually disappears within the first few days following delivery [275]. The patient may also be instructed to estimate the intensity of her pruritus on a 100 mm long visual analog scale [280]. These scales for monitoring the intensity of pruritus are particularly useful to evaluate the effect of medical treatment on this subjective symptom. The clinical examination findings are normal except for evidence of scratching. Fever, if present, is usually caused by an associated urinary tract infection. Less than 10 % of patients have jaundice. The greater frequency of jaundice in some studies may be a consequence of concomitant urinary tract infection [281]. ICP with jaundice but without pruritus is rare [282]. Patients do not experience abdominal pain or encephalopathy. Ultrasonographic examination reveals no dilatation of the biliary tract but may show gallstones. Measurement of serum ALT activity is a sensitive test for the diagnosis of ICP. Patients with ICP frequently exhibit very significant increases in serum ALT activity that suggests acute viral hepatitis, which should be ruled out with suitable serologic tests [282].

Liver histology does not reveal necrotic lesions, and the ALT elevations may be secondary to an increase in membrane permeability. The serum GGT activity is normal or only slightly increased [282]. The serum bile acid concentrations are increased and may be the first or only laboratory abnormality [282, 283]. A relationship between maternal serum bile acid levels and fetal distress has been found [284], and evaluation of the serum bile acid concentration has been suggested as a mean of fetal assessment in patients with ICP [280]. At the present time, however, no consensus has been reached concerning the usefulness of evaluating the serum bile acid concentrations in the obstetric management of patients with ICP [285]. Little or no correlation has been found between the serum total bile acid concentrations and other liver test values [282]. The serum bile acid concentration and serum ALT activity decrease rapidly after delivery and, as a rule, normalize in a few weeks. The measurement of serum glutathione S-transferase, a maker of hepatocellular integrity, has been proposed to distinguish ICP from "benign pruritus gravidarum" [286], but its use in routine is limited. The prothrombin time is usually normal. It may become abnormal in severe cholestasis with jaundice or in patients who have been treated with cholestyramine. The abnormality is caused by vitamin K deficiency, which should be anticipated and treated before delivery to prevent hemorrhage. Such therapy contributes to a good maternal prognosis. ICP has been found associated to preeclampsia [287, 288] or acute fatty liver of pregnancy (AFLP) [289]. Liver biopsy is rarely necessary for the diagnosis. Histopathology is characterized by pure cholestasis, sometimes with bile plugs in the hepatocytes and canaliculi, predominantly in zone 3. Inflammation and necrosis are not usually observed, and the portal tracts are unaffected [290].

2.2.4.2 Acute Fatty Liver of Pregnancy

AFLP was distinguished as a specific clinical entity unique to pregnancy in 1940 by Sheehan [291]. AFLP is a rare disease. Incidence has been evaluated in range 1/7,000–1/20,000 deliveries [292–295]. As a rule, AFLP is a disease of the third trimester that may occur during any gestation. The frequency of twin gestations is increased among patients with AFLP [293], and 7 % of triplet pregnancies have been reported to be complicated by AFLP [296]. The most frequent initial symptoms are nausea or vomiting, abdominal pain (especially epigastric), anorexia, and jaundice [297]. In the past, jaundice was almost always seen during the course of the disease, but because of earlier diagnosis, prompt delivery, and the diagnosis of milder cases, we now see affected patients without jaundice. The size of the liver is usually normal or small. Patients with AFLP rarely have pruritus. Hypertension and proteinuria which are the main signs of preeclampsia are found in up to half the patients [298, 299]. In severe forms, patients may demonstrate asterixis and encephalopathy, with or without coma. Esophagitis and Mallory-Weiss syndrome related to severe vomiting have been reported, as well as bleeding secondary to these esophageal lesions. Genital bleeding is frequent. These hemorrhages are exacerbated by associated coagulation disorders. Ascites may be present and is partially related to portal hypertension. Polyuria and polydipsia (without diabetes) have been noted in about 5 % of patients with AFLP [298] and are almost pathognomonic symptoms in this setting of liver disease in pregnancy. AP is a rare but a potentially severe complication [300]. The serum aminotransferase levels are raised, but usually the level is not as high as in acute viral hepatitis. The bilirubin level is almost always increased. Patients may demonstrate hypoglycemia, which is uncommon in other liver disease unique to pregnancy. In severe cases, the prothrombin time is increased and the fibrinogen level decreased. These coagulation disorders are caused by hepatic insufficiency, disseminated intravascular coagulation, or both. A low platelet count is usual in AFLP and is not always associated with other signs of disseminated intravascular coagulation. Thrombocytopenia may be the most striking laboratory feature and normalizes spontaneously after delivery. The diagnosis of AFLP should always be considered when thrombocytopenia occurs during late pregnancy and

should always prompt the performance of liver function tests. Renal failure (mainly functional) and hyperuricemia are usual. Ultrasonography of the liver may show increased echogenicity. Computed tomography may be useful for the diagnosis, and a liver density that is lower than usual may be demonstrated by Hounsfield unit values in the liver that are equal to or lower than those in the spleen [297]. The findings on imaging studies may be normal; however, a study showed that the findings on computed tomography, which is more sensitive than ultrasonography, were normal in half of patients with AFLP [301]. These complementary examinations should not delay delivery, particularly in severe cases, in which diagnosis can usually be highly suspected on clinical grounds with routine blood tests (serum liver tests, glycemia, creatininemia, electrolytes, uricemia, full blood count including platelets, prothrombin time). Liver biopsy is the best way to confirm the diagnosis of AFLP, but because it is invasive, it is not always performed. Also, we can take advantage of noninvasive procedures to demonstrate fat in the liver and exclude other liver diseases, such as viral hepatitis. Nevertheless, liver biopsy may be useful in atypical cases, especially if the appropriate treatment (delivery) is being delayed. The overall architecture of the liver is not altered. The characteristic picture is a microvesicular fatty infiltration of the hepatocytes, which are swollen. The droplets are minute and surround centrally located nuclei, so that the cytoplasm has a foamy appearance. The microvesicular fatty infiltration is most prominent in the pericentral zones and midzones (zones 2 and 3) and usually spares a rim of periportal cells. The droplets stain with oil red O, which is specific for fat. Electron microscopy confirms the presence of fat droplets and has shown nonspecific changes in mitochondrial size and shape [302]. A stain specific for fat or electron microscopy is useful for pathology confirmation of the diagnosis in patients with ballooning of the cytoplasm but no evident vacuolization [297]. Therefore, whenever AFLP is suspected, a piece of the liver biopsy specimen should be reserved before paraffin embedding and processed appropriately with special stains to confirm the presence of fat in the hepatocytes. The pathologic changes normally reverse rapidly after delivery, and AFLP is not associated with progression to cirrhosis [299].

2.2.5 Diagnosis

2.2.5.1 Transabdominal Ultrasound

Ultrasound is the imaging tool of choice for evaluation of the biliary system and is accurate in diagnosing cholelithiasis in 97 % of cases [29, 109]. Its accuracy, however, is limited in the evaluation of the common bile duct (50 %) and the pancreas (partial visualization in 60 % with unremarkable findings) [115].

2.2.5.2 MRCP

MRCP is the best diagnostic option for definitive diagnosis of biliary diseases in pregnancy if abdominal ultrasound is not diagnostic. MRCP is rarely used due to rarity of the disease and not widespread availability, and only five published case reports of MRCP in pregnant women for stones and cancer are published [115, 218, 303–305]. No maternal or fetal morbidity or mortality was noted in these reports. This imaging method is important because it can differentiate between common bile duct stones and Mirizzi syndrome (Fig. 2.3). Patient diagnosed as having Mirizzi syndrome undergo surgery, and jaundice improves after cholecystectomy without endoscopic sphincterotomy or exploration of the common bile duct. This is especially important in pregnant population because this eliminates radiation exposure during pregnancy. Recent refinements in the technique and the development of 3D MRCP sequences further improved MRCP, allowing the reconstruction of overlapping slices of less than 1 mm [306, 307]. With a reported accuracy close to 100 % in determining the presence and level of biliary obstruction, MRCP has replaced diagnostic ERCP in many institutions, and the utilization of ERCP for diagnostic purposes is steadily decreasing.

2.2.5.3 ERCP

ERCP is both a diagnostic and therapeutic modality, first reported during pregnancy in 1990 by

Baillie et al. for the treatment of complicated gallstone disease [308]. There are several important issues for the ERCP use in pregnancy.

Radiation

Clinicians may not be well informed of the facts relating to the use of diagnostic radiological studies in pregnancy. Lack of understanding of radiation effects on the fetus causes unnecessary anxiety in pregnant patients exposed to diagnostic radiation and may lead to unnecessary pregnancy termination. A study examining physician perceptions of teratogenic risk associated with undergoing plain radiography and CT during early pregnancy found that six of the 208 family practice physicians would recommend pregnancy termination after first trimester CT and 1 following radiography in the first trimester; 12 % (25/208) of physicians were not sure of the need for pregnancy termination after radiography; and 19 % (39/208) of family practice physicians were not sure about a CT scan examination. The same study reported that 8 % (5/65) of obstetricians included in the study would have recommended pregnancy termination after first trimester CT scan examination [309].

The amount of radiation used during ERCP is 18–310 mrad [310–312], which is lower than the harmful dose of 5–10 rad, which is the dose at which fetal damage occurs. Radiation risk is greatest during the first trimester. Fluoroscopy generally delivers a radiation dose of up to 20 rads/min but varies depending on the X-ray equipment utilized, patient positioning, and patient size. The fetus should be shielded during cholangiography. Other alternatives to fluoroscopy include intraoperative ultrasound and choledochoscopy. Some endoscopists have reported undertaking ERCP without fluoroscopy in pregnant women to minimize radiation risk [313, 314]. Even though the risks to the fetus during the second trimester for radiation exposure are low, it is recommended to protect the uterus with a lead shield.

ERCP Techniques

Eliminating radiation exposure can be accomplished by cannulating the common bile duct with a sphincterotome over a guidewire that can be fixed in place, performing sphincterotomy, exchanging the sphincterotome for an extraction balloon catheter over the guidewire, and sweeping the bile duct without a cholangiogram to extract any stones. The main criticism of this technique is that it provides no real-time information regarding the anatomy of the ductal system and documentation of stone clearance [313]. Axelrad et al. suggested that capturing fluoroscopic images with a videoendoscopy system provides safer ERCP procedure than using spot radiography [49]. But they had to use fluoroscopy for 45 s, 3.4 min, and 2.6 min, respectively, in ERCP applications performed three times at different times in the same patient. Llach et al. carried out sphincterotomy under ultrasound guidance in their first patient and without any imaging technique in the second one [315]. They also stressed that the aspiration of the bile after deep cannulation enabled them to confirm selective common bile duct cannulation and to carry out endoscopic sphincterotomy without radiographic control.

In one modification initial CBD cannulation was done with the help of a double lumen sphincterotome, deep cannulation was achieved, and the bile was aspirated to confirm CBD position. After deep CBD cannulation, the guidewire was passed, and complete biliary sphincterotomy was done over the guidewire. In cases where deep CBD cannulation was not possible, after two attempts, the conventional sphincterotome was removed and patients were subjected to needle-knife sphincterotomy. Once the biliary orifice was identified, a complete biliary sphincterotomy was performed using a conventional double lumen sphincterotome after confirming the location inside CBD. After the biliary sphincterotomy, a Zag guidewire was left in place and a 7Fr double pigtail stent was placed in the CBD. Patients were kept nil orally for 6 h after procedure, and i.v. fluids and i.v. cefotaxime 1 g bid was given for 1 day followed by oral antibiotics for 5–7 days. After delivery all the patients were subjected to definitive ERCP. Biliary stents were removed, and cholangiogram was obtained in all patients. All small stones were removed with

Dormia basket, while one patient with a single large stone was subjected to mechanical lithotripsy. Patient with multiple large stones was subjected to surgery [316].

Reports have shown that if certain precautionary measures are taken, therapeutic ERCP can be safely performed during pregnancy [317]. Actually, the *American College of Obstetricians and Gynecologists* (ACOG) states that risks for fetal anomalies, growth restriction, or abortions are not increased with radiation exposure of less than 5 rad, a level above the range of exposure for diagnostic procedures [318]. Aspiration technique is used to avoid pancreatography, and fluoroscopy time should be as short as possible (<1 min) and spot radiographs avoided if possible [319].

When facing more invasive operative and interventional options – surgery or percutaneous transhepatic cholangiography – ERCP may be the best therapeutic option in the setting of pregnancy. In conclusion, ERCP in pregnancy tends to be safe for both the mother and the fetus, but the procedure should be largely restricted to therapeutic indications with additional intraprocedural safety measures [312].

It should be stressed that due to the ability of amniotic fluid to conduct electrical current to the fetus, the grounding pad should be placed on the patient above the level of the uterus [311].

Sedation

Sedation in pregnancy has always been a challenge to anesthetists. Sedation during ERCP in pregnant patients has important aspects of fetal and maternal monitoring and side effects of the prone position [303, 313, 320]. Following electrocardiography, noninvasive blood pressure measurement, pulse oximetry, and fetal heart rate monitoring devices are applied. Insufflation of oxygen at a flow rate of 6 L/min is maintained throughout the procedure. The patients are placed in a left lateral to prone position. Fetal shielding was accomplished with a lead apron placed between the radiation source and the patient.

No anesthetic drug, inhaled anesthetic or local anesthetic, has been proven to be teratogenic in humans [321]. A notable exception is the benzodiazepine group, which has been linked to congenital anomalies [321, 322]. All agents that are administered during pregnancy must be used with caution and vigilance. It is clear that anesthetic effects on placental perfusion and the placental transfer of depressant drugs may influence the fetus [322]. Currently the best options are propofol, midazolam, and fentanyl. Propofol as a short-acting agent is preferred because it can be titrated easily and has a good recovery, with a low incidence of nausea and vomiting. Alternatively midazolam can be used because of its specific amnesic and anxiolytic properties. The analgesic component of this sedation regimen is the opioid. All drugs are given in incremental doses to prevent hemodynamic and respiratory changes in the mother and fetus during the procedure. The most commonly conscious sedation is achieved and maintained with intravenous midazolam 3–5 mg and duodenal hypomobility induced by hyoscine-N-butylbromide 20 mg [47, 316].

Contrast Agents

Among other considerations for ERCP in pregnancy, contrast agents that contain iodine, such as diatrizoate, have the potential to cause hypothyroidism in the baby. Risks may be minimized by using low concentrations of diatrizoate, especially the water-soluble form, thus limiting the number of intraductal injections and avoiding unnecessary pancreatography [323]. Guidelines for the use of contrast media during pregnancy are listed in the Table 2.2.

ERCP in Diabetic Pregnant Patient

There is only one case report of ERCP in diabetic patient on insulin therapy that was euglycemic during the procedure for obstructive jaundice due to residual choledocholithiasis. The patient had ERCP 1 year ago for common bile duct stones with laparoscopic cholecystectomy after 3 months [303].

Complications

In the nonpregnant patient, risk of bleeding and AP is 1.3 and 3.5 %, respectively [324]. The reported rates of complications in pregnancy due to endoscopic biliary interventions range 7–16 %.

The complications consist mainly of post-ERCP AP, preterm labor, and post-sphincterotomy bleeding [311, 312, 325–327]. Gupta et al. [325] analyzed 18 pregnant women (first trimester, four; second, six; third, eight) who the women underwent therapeutic ERCP and biliary sphincterotomy for common bile duct (CBD) stones. One woman had a preterm delivery. At follow-up after a median of 6 years, all the babies were healthy. According to the data collected from different centers by Jamidar et al. one AP, two neonatal deaths, and one abortion (3 months following ERCP) occurred in 23 pregnant patients undergoing ERCP applications with a very short period of fluoroscopy [326]. Judging by the data of 45 cases of ERCP interventions during pregnancy, laparoscopic surgery and ERCP during pregnancy appear to be safe and justified. However, ERCP during pregnancy is technically exacting and should be attempted only by experienced biliary endoscopists [47, 162, 312, 319, 325–330]. So ERCP for treatment of choledocholithiasis in pregnancy has been recommended instead of a surgical approach [308, 326, 331]. It should be stressed that there is not any randomized, controlled study comparing ERCP and open (or laparoscopic) surgery in view of the efficacy and safety at present.

2.2.5.4 Endoscopic Ultrasound

Endoscopic ultrasound (EUS), a semi-invasive procedure of the biliary tree, is an accurate modality for detecting common bile duct stones [332]. As solely a diagnostic tool, it has been shown to reduce unnecessary interventions in patients with low or moderate probabilities for choledocholithiasis [333–335]. However, EUS requires expensive equipment, intravenous sedation, and technical expertise. EUS can be considered the best imaging study to evaluate CBD, although not for gallbladder stones. In expert hands small gallstones as well as sludge can be picked up by EUS; however, it is operator dependent. EUS is appropriate prior to the consideration of therapeutic ERCP in patients where noninvasive imaging such as MRCP is not available, contraindicated, or inconclusive. EUS has a high positive predictive value around 100 % in detecting CBD stones, and in many instances EUS is superior to MRCP [333]. EUS entails no radiation exposure and is extremely safe apart from a minimal sedation-related risk. If a common bile duct stone is detected, an ERCP with sphincterotomy can be performed following the EUS study during the same sedation [336].

2.2.6 Therapy

2.2.6.1 Choledochoscopy

Choledochoscopy could be used during CBD exploration (open or laparoscopic) or after sphincterotomy. Recently several reports of successful wire-guided CBD cannulation with sphincterotomy and the removal of biliary stones or sludge were performed without fluoroscopy. Choledochoscopy can then confirm ductal clearance [337, 338]. If choledochoscopy is not available, an alternative approach is to use EUS-guided extraction balloon sweeps to achieve clearance of ductal stones.

SpyGlass Direct Visualization System (Boston Scientific, Natick, MA, USA) is presented. A 4.4 Fr sphincterotome was angled in the biliary orientation, and a hydrophilic 0.35″ guidewire was gently advanced into the major papilla resulting in bile flow around the guidewire. The sphincterotome was advanced over the wire, and aspiration of 10 ml of clear yellow bile confirmed the location within the bile duct. A biliary sphincterotomy was performed. Sweep with a 9 mm extraction balloon easily removed a single 8 mm stone from the bile duct. The SpyGlass SpyScope was exchanged over the guidewire, and cholangioscopy directly visualized the common bile duct, common hepatic duct, and left and right intrahepatic ducts. Saline lavage through the cholangioscope flushed debris and two 2 mm residual stones from the bile duct into the duodenum. No fluoroscope was used during the entire procedure. To date, seven pregnant patients undergoing SpyGlass cholangioscopy-assisted ERCP have been reported [337–339]. It is important to note that the use of non-fluoroscopy interventions may actually prolong the overall duration of the procedure due to learning curves and technical

experiences of endoscopists and hence increases the risk, especially in difficult cases. Furthermore, in daily practice, non-fluoroscopy modalities are not often used. Therefore, one should not hesitate to use fluoroscopy if required with the knowledge that limited radiation exposure is safe during pregnancy [312].

2.2.6.2 Laparoscopic Cholecystectomy After ERCP

There is no consensus if the laparoscopic cholecystectomy should be performed after successful ERCP with stone extraction. There are several options.

Selective Approach (Wait-and-See Approach)

In the study by Sungler et al. selective approach was used. Five patients underwent ERCP due to common bile duct stones (three patients had jaundice and two had AP). The remainder of the pregnancy was uneventful in three of the patients. One patient had persistent colic; therefore, laparoscopic cholecystectomy was performed 2 weeks later, in the 32nd gestational week. Another patient with severe AP, cholangitis, and cholecystitis was released symptom-free after successful ERCP on day 7, but she was readmitted for recurrent severe cholecystitis 2 weeks later [47]. It is not known which patient developed complications (with obstructive jaundice or AP). All of them had healthy babies at term with vaginal delivery.

In nonpregnant patients, prospective randomized trial by Boerma et al. demonstrated a conversion rate of 55 % in patients who were allocated to a wait-and-see policy after ERCP and a 23 % conversion rate in the elective LC group. This result implies that LC after ERCP is mandatory. The fact that there is high conversion rate in both groups is partly due to the fact that LC is undertaken in a specific subgroup of patients, having complicated gallstone disease [340].

Mandatory Cholecystectomy

The prospective randomized trial in nonpregnant patients compared selective approach and mandatory cholecystectomy and showed such a high rate of recurrent biliary events in the wait-and-see group that an elective laparoscopic cholecystectomy after ERCP seems justified [340]. In practice, some strongly advocate a cholecystectomy within 6 weeks of the initial biliary event.

In pregnant population, Simmons et al. during the 2-year interval, reported a successful ERCP in six pregnant women between 6 and 30 weeks of gestation with symptomatic acute cholangitis or AP, without radiation exposure or major maternal complications [313]. No post-ERCP complications occurred. Two patients required cholecystectomy later, one in the postpartum period, and the other 5 weeks post-ERCP. Two infants were born at term without complications. Two infants were born prematurely at 35 weeks, one with significant growth restriction and pulmonary complications, and one without developmental problems or complications.

Interval Between ERCP and Laparoscopic Cholecystectomy

There are no such studies in pregnant population. In nonpregnant population, the results suggest that there is an increased risk of conversion of an LC to an open procedure 2–6 weeks after ERCP. An important explanation for a higher conversion rate could be that ERCP leads to an inflammation around the gallbladder, including the hepatoduodenal ligament, making a laparoscopic procedure more demanding [340, 341]. Adhesions, operation time, and bile duct damage did not significantly differ between the groups, but significantly higher conversion rate due to adhesions 2–6 weeks after ERCP suggests that these adhesions are less friendly and potentially dangerous compared to the adhesions encountered at surgery within 2 weeks of ERCP [342].

Others claim that time interval is of no importance. These authors found that male gender, bilirubin levels during ERCP, severe adhesions during LC, and pre-LC CRP levels were associated with an adverse outcome for an LC after ERCP. From the previous studies and studies by Alimoglu et al. and Lai et al. the recommendations in pregnant as in nonpregnant patients is that LC should be performed 24–48 h after ERCP to shorten the hospitalization, to avoid another

hospitalization, and to reduce the possibility of recurrent biliary events [156, 343].

2.2.6.3 Common Bile Duct Exploration

Six cases of laparoscopic [136, 305, 344–346] and 20 cases of open [5, 15, 133, 135, 164] CBD exploration were described in the literature. There was no maternal or fetal morbidity or mortality. Multiple studies have demonstrated safe and effective management of CBD stones in pregnancy with ERCP and sphincterotomy with subsequent LC [15, 47, 308, 319, 347, 348]. Therefore, indications for laparoscopic CBD exploration in pregnant patients, following an episode of gallstone pancreatitis, are yet to be clearly defined. Some authors use 1 mg of glucagon intravenously for sphincter of Oddi relaxation.

Transcystic Approach

In general, laparoscopic clearance of duct calculi by means of the cystic duct approach is achieved in approximately 80-90 % of attempts, appearing to be a viable alternative to postoperative ERCP [349]. This approach seems valuable when one considers the potential teratogenic effects of radiation exposure when ERCP is performed in the first trimester and the inability to appropriately shield the fetus from radiation during the third trimester [326]. However, such recommendations for laparoscopic management of biliopancreatic disease to include laparoscopic CBD exploration in pregnancy, as stated previously, are yet to be precisely defined.

The location of the bile duct stones, size, number, as well as the anatomy should be considered when choosing between a transcystic approach and choledochotomy. Guidelines for a laparoscopic transcystic approach include [350]:

- Small (<0.8 cm) stones in the CBD
- Limited number of CBD stones (≤5)
- Absence of stones in the common hepatic duct
- Cystic duct joining the CBD on its lateral or posterior (not medial) aspect

Choledochotomy

Choledochotomy is indicated when [351]:

- Transcystic approach fails or is contraindicated.
- Biliary lithotripsy needed.
- CBD is dilated more than 7 mm.

The number of case reports describing LCBDE in pregnant women is limited, but they appear to advocate this procedure as a safe alternative to ERCP [345].

Intraoperative Cholangiography

Since Mirizzi first described intraoperative cholangiography (IOC) in 1934 [352], the technique has developed from static views to dynamic real-time fluoroscopic cholangiography, and recently to three-dimensional dynamic cholangiography [353]. However, so far this latter method has only been used experimentally in liver surgery.

In nonpregnant patients dynamic real-time intraoperative fluoroscopic cholangiogram is achieved with the help of mobile C-arm X-ray equipment (Ziehm exposcop CB7-D), using 10–40 ml Iohexol (Omnipaque, GE Healthcare, UK), 200 mg/ml as contrast medium, and 1 ml glucagon (Glucagon®, Novo Nordisk A/S, Bagsvaerd, Denmark; 1 mg/ml) intravenously to release any papillary spasm, or in cases of diabetes mellitus, 1–2 ml (20 mg/ml) intravenous butylscopolamine (Buscopan®, Boehringer Ingelheim, Ingelheim am Rheine, Germany).

IOC with LC were described in eight reports [5, 7, 9, 15, 133, 216, 354, 355]. IOC was used frequently, along with cholecystectomy, until the early 1990s. However, recent literature recommends the use of IOC only in the presence of choledocholithiasis and during exploration of CBD [216]. Radiation exposure during cholangiography is estimated to be less than 0.5 rad. Fluoroscopy generally delivers a radiation dose of up to 20 rads/min but varies depending on the X-ray equipment utilized, patient positioning,

and patient size. If the IOC is performed, the use of a shield to cover the fetus is recommended in all trimesters [9, 15]. From these reports, it is clear that there was no maternal morbidity or mortality. However, 1 spontaneous abortion was reported [354].

With the advent of ERCP and MRCP, the need for IOC is minimal, although specialized units use it routinely for demonstrating the anatomy of the biliary tree. There have been no reports investigating the safety of IOC during pregnancy. In the absence of clear evidence, potential risks should be discussed with the patient.

2.2.6.4 Postpartum Presentation

The lack of initial appreciation for the higher rate of choledocholithiasis in this group led the authors to initially (patients 1 through 24) apply selective criteria for cholangiography. In the latter part of the series, routine cholangiography was applied to the postpartum patients and led to the diagnosis of two patients with common duct stones and none of the traditional risk factors. Three patients (8.8 %) had missed common duct stones. The rate in total patient series, including the patients in this report, is 0.6 % (7/1,068) and 0.4 % (4/1,034) in the non-postpartum group (unpublished data, Diettrich and Kaplan). The high incidence of choledocholithiasis, often silent, suggests that routine cholangiography should be the norm in the postpartum patient with biliary tract disease.

Intraoperative Ultrasound

Glasgow et al. did not use IOC but described the use of laparoscopic ultrasound in six patients to exclude retained CBD stones [136].

2.2.7 Prognosis

2.2.7.1 Fetal Outcome

Prognosis after common bile duct surgery during pregnancy is excellent. Six cases of laparoscopic and 20 cases of open CBD exploration were described in the literature. There was no fetal morbidity or mortality [270].

2.2.7.2 Maternal Outcome

As for fetal outcome, maternal outcome is also excellent. In all six cases of laparoscopic and 20 cases of open CBD exploration described in the literature, there was maternal morbidity or mortality [270].

2.3 Symptomatic Choledochal Cysts

2.3.1 History

Since Vater first described the condition in general population in 1723, many cases of choledochus cyst have been recorded in the literature. Rupture of the cyst is a rare complication, only six cases having been documented by 1956 [356]; one of these, published by Friend in 1958, occurred 2 weeks after a normal delivery. The first rupture of the choledochal cyst during pregnancy was published by Saunders and Jackson in 1969 [357].

2.3.2 Incidence

Choledochal cyst is a rare congenital abnormality of the biliary tract, occurring in approximately 1/2,000,000 live births [358]. Usually diagnosed during childhood, choledochal cysts present for the first time during adulthood in 25 % of patients but rarely during pregnancy with only several case reports published [359–364].

2.3.3 Clinical Presentation

Clinical manifestations are nonspecific and variable. The classical characteristic triad (abdominal pain, jaundice, and right hypochondrial mass) occurs mostly in childhood [365] and are seldom seen in adults [366]. With all anatomic changes during pregnancy, the cyst is not easily detected in pregnant women [367]. If silent, it can be unnoticed during pregnancy. Reported complications of choledochal cyst during pregnancy include pain in the upper right quadrant due to enlarged mass or palpable mass [364], cholangitis,

jaundice, AP, cystic rupture, and malignancy [367]. The pain and jaundice caused by choledochal cyst in pregnancy may be due to hormonal effect, compression of the bile duct lumen and cyst by the gravid uterus, and increase in intra-abdominal pressure during pregnancy [361]. The symptoms are sometimes similar to the symptoms of CBD stones (see "Common Bile Duct Stones, Choledocholithiasis, and Cholangitis").

2.3.4 Diagnosis

Pregnancy makes diagnosis of this disease more difficult because similar symptoms are often encountered during a normal pregnancy, and radiographic study is limited by fetal exposure. Abdominal ultrasonography is commonly used as the initial screening examination in the evaluation of acute abdomen or hepatobiliary conditions. However, difficulties may arise due to distortion of the normal abdominal anatomy and gravid uterus during pregnancy. The cyst may be misdiagnosed as an ovarian tumor or mucocele [360]. ERCP or computed tomography (CT) may provide more accurate information, but ionizing radiation should probably be avoided in pregnancy [368]. Magnetic resonance imaging (MRI) is suggested as the preferred examination due to high resolution of the biliary tree without the problems associated with exposing the mother and the fetus to ionizing radiation [366]. MRI can even define the type of choledochal cyst preoperatively (Figs. 2.6 and 2.7).

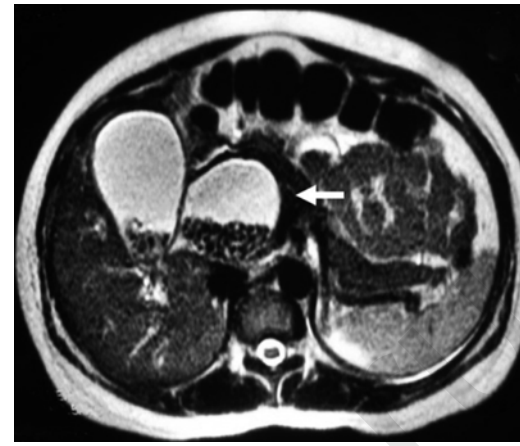

Fig. 2.6 MR of the abdomen showing pregnant patient with gallbladder calculi and choledochal cyst (*white arrow*) also filled with calculi [359]

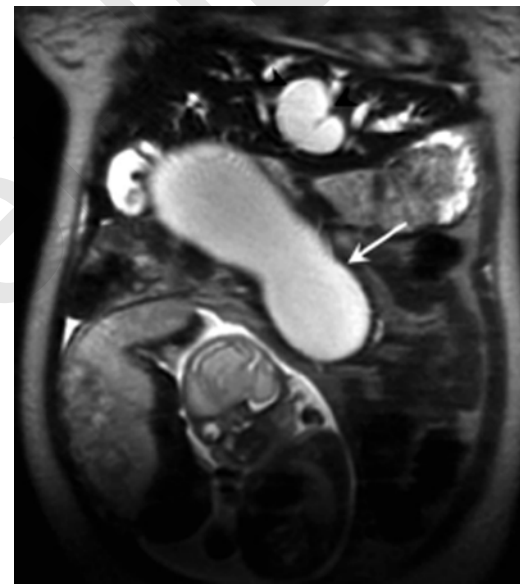

Fig. 2.7 A 17-year-old female at 27 weeks gestation who had obstructive jaundice. Coronal T2-weighted single-shot fast spin-echo image demonstrates a significantly dilated common bile duct (*arrow*) and intrahepatic biliary tree (*arrowheads*), consistent with a type IVA choledochal cyst [115]

2.3.5 Therapy

The therapeutic principles depend on the type of symptomatology (elective or emergent presentation) and the type of the cyst according to the Todani classification as in nonpregnant patients [369].

2.3.5.1 Asymptomatic Patients

If presented as asymptomatic palpable or painful mass, the patient should be checked regularly and definitive treatment postponed after labor and puerperium as elective operation. In elective settings current recommendations in nonpregnant as in a pregnant woman are complete excision of the extrahepatic duct, cholecystectomy, and Roux-en-Y hepaticojejunostomy because the risk of malignant degeneration has been reported to be

as high as 30 % [370]. Sometimes, if the cyst is large, even bilateral Roux-en-Y hepaticojejunostomy should be performed [360].

2.3.5.2 Cholangitis

Complication in the form of acute cholangitis can be treated first with percutaneous cystic decompression under US, CT, or MRCP guidance and after labor and possibly puerperium definitive surgical excision of the cyst and a Roux-en-Y reconstruction [115].

If the patient is in late pregnancy, elective Cesarean section followed by percutaneous decompression after 6 weeks is recommended [364].

2.3.5.3 Cholangitis with Biliary Obstruction or Acute Pancreatitis

However, symptoms from complications such as AP, biliary obstruction, and cholangitis require a more urgent approach. Some authors recommend, in order to avoid complications during pregnancy, definitive surgical management of the choledochal cyst should be delayed until the patient's general physiological condition becomes normal after elective Cesarean section [364].

2.3.5.4 Postpartum Presentation

The same principles as in pregnancy are recommended. If the patient presents with an emergency diagnosis, the emergency operation should follow. Otherwise the patient should be operated electively after the puerperium or even better after the termination of breastfeeding to minimize possible complications or surgery or medication therapy related to the newborn.

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Acute Pancreatitis

3

3.1 History

Acute pancreatitis (AP) during pregnancy is extremely rare. Schmitt in 1818 [1] reported the first case of pregnancy complicated by AP in a 30-year-old woman, who died in the 4th month of her eighth pregnancy, and Lawrence in 1838 [2] described the earliest series of 53 cases. Longmade and Edmondson [3] added nine cases of their own to an already existing 53 cases. In 1952 four additional cases were reported from France [4]. Acute fatty liver of pregnancy and AP were first recognized as a specific clinical entity by Sheehan in 1940. AP caused by primary hyperparathyroidism (PHPT) in general population was first described by Cope et al. in 1957 [5]. The earliest report of AP occurring in the postpartum period seems to be that of Haidlen in 1884 [6]. Another early cases were reported by Watts [7] and Deaver [8]. Joske collected personal series of six postpartum AP patients [9]. Since then there have been numerous single case reports and case series of various causes of AP during pregnancy.

3.2 Incidence

3.2.1 Incidence in General Population

Patients in general population with alcohol-related AP are the youngest (mean age: 39–41.5 years and decreases with age), while those with gallstone AP were the eldest (mean age 64.1 years) [10, 11]. The incidence of AP in general population in England, Denmark, and the United States varies: 4.8–24.2/100,000 [12]. In developing countries, alcohol abuse has been reported to be the second most common factor. In these countries, alcohol abuse is associated with approximately 35 % of the cases [13].

3.2.2 Incidence in Pregnancy

Accurate assessment of disease incidence in pregnancy is difficult since mild disease may be missed.

3.2.2.1 Age

Also more and more women become pregnant in more advanced age, and it is known that the incidence of AP in general population increases with age [14]. Literature shows varying incidence in pregnancy ranging 1/1,000–1/12,000 cases usually late in the third trimester or in early postpartum period and rarely progresses to the necrotizing form [15–21]. The wide variation in the incidence is influenced by the prevalence of its most important etiological factor – gallstone disease. While biliary AP complicated 1/3,300 pregnancies at a large public hospital in Dallas, Texas [15], in Southern California 1/1,500 women were affected [22]. Incidence is race dependent, and Hispanic population has higher incidence (0.1 %) due to higher risk for gallstone disease [23]. Discrepancy in incidence is due to [24]:

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- The rarity of disease
- Studies span different decades and countries
- Underestimation due to underreporting
- Small number of cases included in the studies

AP appears to be more prevalent with advanced gestational stage, occurring more commonly in the second or the third trimester [25–27]. Ramin et al. noted that 19 % of AP occurs in the first, 26 % in the second, 53 % in the third (consistent with a potential lithogenic effect of estrogen during pregnancy), and 2 % in the postpartum period, while some reported most of cases, 56 %, in the second trimester [15].

3.2.2.2 Hyperlipidemia/Dyslipidemia

AP secondary to hyperlipidemia/dyslipidemia has an estimated incidence of 1/25,000 births [28], or 10–50 % of all cases [29], which is much higher that the incidence of 4 % in nonpregnant population [30]. The association of hyperlipidemia with AP during pregnancy was first reported in 1818 [1]. By 1970 a total of only 101 reports had been published, the vast majority of which were case studies. Between 1.3 and 7 % of all cases of AP have been attributed to hypertriglyceridemia (HTG) [30, 31], with 1.7–6 % of cases of AP in pregnancy attributed to hyperlipidemia [32, 33]. Although there are a dozen cases of hypertriglyceridemia-induced AP in pregnancy in the literature, it is likely that the reported incidence has been underestimated secondary to lack of testing. Additionally, triglycerides universally increase during an episode of AP. Whether the elevated triglycerides are an epiphenomenon of the AP or the actual cause of the inflammation can be difficult to differentiate.

3.2.2.3 Alcohol

Idiopathic AP in pregnancy is considered in 16.5 and 12.3 % is due to alcohol consumption [24, 34]. Alcoholic AP was more prevalent in the study by Eddy et al. (17.8 % overall; 12.3 % of 89 AP cases vs. ≤7 % in other studies) [25, 35, 36], due to inclusion of chronic pancreatitis and perhaps also to selection of Midwestern states with a high prevalence of alcohol use [37].

In 1951, Lawrence and Edmondson found that there is a tendency for primipara to suffer from AP more often than the multipara. The primipara is even more subject to the disease if she has gallstones [3].

3.2.2.4 Primary Hyperparathyroidism

In general population, PHPT is considered a common disorder. Its greatest frequency is observed in postmenopausal women, in whom it reaches a prevalence of 2–3 % [38]. The incidence in women of childbearing age is approximately 8/100,000 per year [39]. The most frequent cause of PHPT in the general population is a single parathyroid adenoma (85 %), followed by parathyroid hyperplasia (15–20 %) and, albeit very rarely (less than 1 %), by carcinoma [40, 41].

The frequency of AP in pregnancy related to PHPT is higher (7–13 %) than in nonpregnant population (1–2 %) [42–44]. Others found wider incidence of PHPT-induced AP in general population of 1–12 % [45–48]. Jacob et al. have shown a 28-fold increased risk of AP in hyperparathyroid patients compared to the general population [49]. Interestingly, less than 200 of patients with PHPT have been described in gestation and during the postpartum period [42, 44, 50, 51]. The occurrence of PHPT during pregnancy was described by Hunter and Turnbul1 in 1931 [52]. It is estimated that for all women younger than the age of 40 years, eight new cases per 100,000 pregnant women occur annually [53]. This relative paucity of data may be explained by at least three different causes. Firstly, the average age of the initial manifestation of this disorder is higher than that of women of childbearing age [38, 40, 41]. Secondly, about 80 % of nonpregnant individuals with PHPT are characterized by an asymptomatic course of this disease [42]. Finally, some symptoms of PHPT may be misinterpreted as a simple consequence of pregnancy or other gestation-related disorders, while physiological changes during gestation may mask some abnormalities typical to PHPT [50, 54]. Whereas some reports – most of them based on case series – have suggested an association between PHPT and AP, a community-based study showed no increase in the incidence of AP among patients with PHPT as compared with matched controls [55].

The most frequent cause of PHPT in general population is a single parathyroid adenoma

(85 %), followed by parathyroid hyperplasia (15–20 %) and, albeit very rarely (less than 1 %), by carcinoma [40, 41]. More than 100 cases reported in the English language literature between 1930 and 1990 were found [39] and less than 200 up to date during pregnancy and postpartum [42, 50, 51]. PHPT is a rare etiology of hypercalcemic-induced AP, causing anywhere from 0.4 to 1.5 % of cases in the general population and up to 13 % of cases during pregnancy [45, 56, 57]. This relative paucity of data may be explained by at least three different causes. Firstly, the average age of the initial manifestation of this disorder is higher than that of women of childbearing age [38, 40, 41]. Secondly, about 80 % of nonpregnant individuals with hyperparathyroidism are characterized by an asymptomatic course of this disease [42]. And finally, some symptoms of PHPT may be misinterpreted as a simple consequence of pregnancy or other gestation-related disorders, while physiological changes during gestation may mask some abnormalities typical to PHPT [50, 54]. The simultaneous occurrence of PHPT and AP in pregnancy has only been reported 13 times up to 1998 [43, 58–66]. There was no single aforementioned patient with presentation during the first trimester, and more than 90 % of patients had thyroid adenoma (89 %) and there was only one thyroid carcinoma.

3.2.2.5 Preeclampsia-Eclampsia

Hojo et al. reviewed a total of 15 cases in the literature of AP thought to be associated with preeclampsia dating from 1956 to 2007 [67].

Table 3.1 Causes of acute pancreatitis in general and pregnant population

Alcohol or methanol abuse (>100 g/day for >3–5 years)
Autoimmune diseases
Choledochal cyst
Cystic fibrosis
Gallstones
Hereditary (familial) pancreatitis (including an autosomal dominant mutation of the cationic trypsinogen gene which causes pancreatitis in 80 % of carriers)
Hyperlipidemia or hypertriglyceridemia (1,000 mg/dl)
Hypercalcemia (including hyperparathyroidism)
Infection (Coxsackie B virus, cytomegalovirus, mumps)
Ischemia from hypotension or atheroembolism
Medications (ACE inhibitors, asparaginase, azathioprine, oral estrogens, antibiotics, 2′, 3′-dideoxyinosine, furosemide, 6-mercaptouride, pentamidine, sulfa drugs, valproate, thiazide diuretic, corticosteroids)
Neoplasm
Pancreatic or periampullary cancer
Pancreas divisum
Peptic ulcers
Preeclampsia-eclampsia
Post- ERCP
Postoperative inflammation
Post-renal transplant
Sphincter of Oddi stenosis
Blunt or penetrating trauma
Surgery (ischemia/perfusion/mechanical)
Tropical pancreatitis
Vasculitis
Viral infections
Idiopathic

3.3 Etiopathogenesis

3.3.1 Introduction

The role of pregnancy in the etiology of AP was stressed in the writings of the nineteenth century, for example, Mondière in 1836 [68]. In AP associated with pregnancy, Longmade and Edmondson suggested a time limit of 6 weeks postpartum [3]. In 1955, Ross suggested a rise in intra-abdominal pressure such as undue prolonged second stage of labor as etiology of AP in pregnancy [69]. Elevation of intra-abdominal pressure leading to the high pancreatic ductal pressure [70], and increased tonus of the Oddi's sphincter [71] may be other possible mechanisms to induce AP.

The list of most of the causes of AP in general population which could also be a cause in pregnant population but with somewhat different incidence is shown in Table 3.1.

Corlett and Mishell in 1972 assessed 52 patients with AP in pregnancy to classify their etiology into cholelithiasis 23 % (12/52), alcohol abuse 4 % (2/52), and idiopathic 65 % (34/52) [20]. There are too many idiopathic cases in this study.

Probably not all investigations were performed in this and some other, especially older studies and this distribution is not precise. More than half or, in some studies, nearly 70 % of cases of AP during pregnancy are secondary to biliary stones or sludge, followed by hyperlipidemia and/or alcohol abuse in approximately 20 % of cases [13, 15, 25, 27, 72]. HTG is an uncommon but well-documented cause of AP, accounting for 1–4 % of cases [30]. Moreover, HTG was listed as causative in 56 % of gestational AP cases in one study [73]. Approximately 15 cases of AP, pregnancy, and hyperlipidemia have been described from 1956 to 1996 [74]. In developed countries other causes are hyperparathyroidism, iatrogenic (diuretics, antibiotics, and antihypertensive drugs), connective tissue diseases, abdominal surgery, infections (viral, bacterial, or parasitic), and blunt abdominal injuries [15, 25, 72]. Necrotizing AP is also reported in preeclampsia due to pancreatic microvascular alterations [75]. Post-ERCP is the cause in 3.45 % [27]. Today, it is still not clear, whether the pathogenesis of AP is one entity or whether it consists of a group of distinct pathogenetic mechanisms [76]. Idiopathic AP is the cause in 10 % of cases [27]. There is one case published with AP during pregnancy caused by mucinous cystic pancreatic neoplasm. Pancreatic cystic lesions in general are rare but are difficult to treat given problems in clarifying their malignancy. Mucinous cystic neoplasms are considered premalignant lesions and resection is recommended. Receptors for estrogen and progesterone receptors in these cysts may cause cystic growth during pregnancy [77].

During pregnancy, gallstones and sludge induce most of the cases of AP, causing duct obstruction with pancreatic hyperstimulation that increases pancreatic duct pressure, trypsin reflux, and activation of trypsin in the pancreatic acinar cells. This leads to enzyme activation within the pancreas and causes autodigestion of the gland, followed by local inflammation (Fig. 3.1).

Pregnancy does not primarily predispose the pregnant woman to AP, but it does increase the risk of cholelithiasis and biliary sludge formation (see Chap. 2) [15]. Gallstone AP occurs in relatively older age (28.2 years) as compared to non-gallstone AP (24.4 years). In both groups, pregnant women were usually multiparous and AP mostly presented in the third trimester [27].

The trigger events or precipitating factors for AP in 60 % of pregnant women were associated with excess high-fat/high-protein diet. The favored explanation for it may be that large amounts of bile/trypsin release can overwhelm the defense mechanism and activate other enzymes, resulting in local and systemic complications that are commonly seen in the course of the disease [78]. Severe diabetic ketoacidosis and hyperglycemia with associated dehydration are known risk factors of AP in general population [79]. Additional pathophysiologic phenomenon in pregnancy is gestational diabetes mellitus (DM). It could be a trigger for AP in pregnancy. It should be noted that the percentage of idiopathic AP is declining as knowledge of genetic etiologies and predispositions to AP accumulates.

3.3.2 Primary Hyperparathyroidism

3.3.2.1 Calcium-PTH Metabolism in Pregnancy

Pregnancy and lactation are characterized by important alterations in calcium homeostasis, being a consequence of pregnancy-induced changes in the synthesis, metabolism, and excretion of calcium and calcitropic hormones [50, 80]. There is an interesting alteration of the calcium-PTH dynamics during pregnancy. Early reports described a *physiological hyperparathyroidism of pregnancy* with an increase in serum immunoreactive PTH levels beginning in the second trimester [81]. However, the development of more accurate and specific immunoradiometric (IRMA) methods has discredited this notion by showing a reduction, rather than an elevation, of intact PTH levels [82]. In fact, one study found mean serum PTH levels in non-pregnant women to be 72 % higher than in pregnant women [83]. These changes in PTH during pregnancy may be a response to altered calcium metabolism. Intravascular fluid expansion and hypoalbuminemia (albumin falls by 20 %) make less protein available to bind calcium, thus

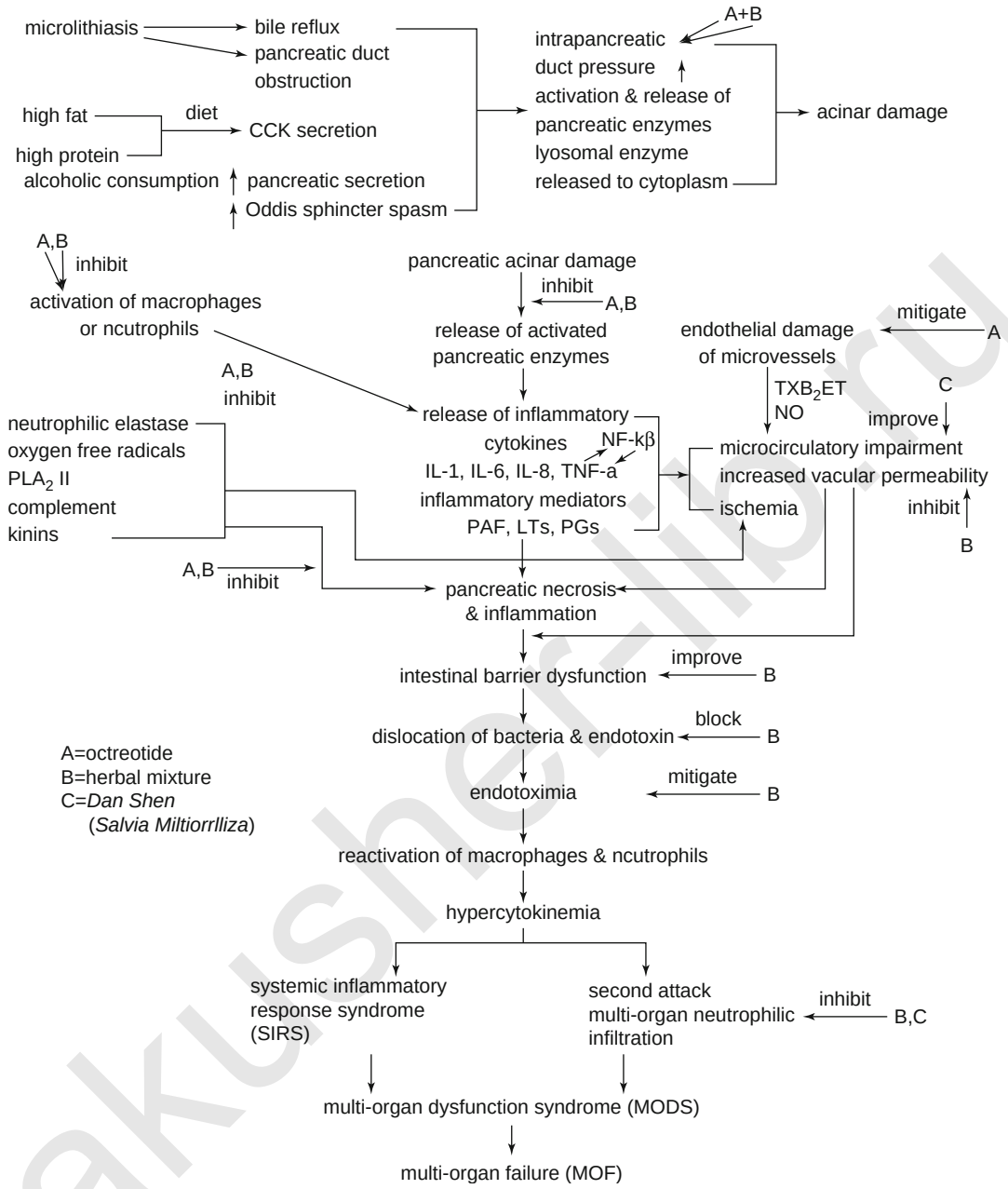

Fig. 3.1 Schematic representation of step-by-step pathogenesis of (biliary) pancreatitis with possible action of medications

lowering total (maternal serum calcium falls by about 10 %) but not ionized calcium [83, 84]. In addition, an increase in urinary excretion of calcium occurs due to increased glomerular filtration rate, and maternal calcium in the blood is actively transported across the placenta to fulfill the needs of the growing fetus [85]. Hypercalcemia is defined as a (corrected) total serum calcium above the standard laboratory reference range (2.2–2.6 mmol/l). In pregnancy, the reference range is marginally lower depending on the trimester (Table 3.2).

Table 3.2 Corrected serum calcium in pregnancy

Normal	1st trimester	2nd trimester	3rd trimester
2.20–2.60 mmol/l	2.25–2.57 mmol/l	2.30–2.50 mmol/l	2.30–2.59 mmol/l

The latter imposes an increased calcium requirement that is partly fulfilled by mobilization of calcium from the maternal skeleton. Together, these effects have a tendency to lower maternal calcium levels [86]. During pregnancy the placenta actively transports calcium ions to the fetus but does not allow transfer of parathormone [87]. Maternal hyperparathyroidism can therefore result in fetal hypercalcemia which substantially increases the risk of spontaneous abortion [88]. However, they are more than offset by a large increase in intestinal calcium absorption that occurs during pregnancy [89, 90]. Hormonal changes during pregnancy may also be responsible for an increase in the production or activity of the enzyme 1-a-hydroxylase in the kidney [91], which in turn may account for the observed differences between pregnant and nonpregnant women, including the elevation of 1,25-dihydroxyvitamin D [82], the slight increase in serum calcium levels [92], and the reduction in PTH levels [83]. Fetal 1,25-dihydroxyvitamin D, synthesized in fetal kidney and placenta, acts as the major stimulus and regulator of calcium transfer across the placenta. It increases maternal gastrointestinal absorption of calcium by 150–400 mg daily; additionally, maternal urinary excretion is also increased from 90 to 300 mg daily. Major fetal calcium demands of approximately 25–30 g are required in the third trimester for skeletal tissue mineralization. This requires an active transport of calcium across the placenta, and the fetal serum calcium remains higher than maternal blood. Conversely, after delivery, when the maternal transplacental supply of calcium ceases, neonatal hypocalcemia becomes the major problem. This may occur because the neonate is unable to mobilize calcium stores adequately as a result of prolonged parathyroid gland suppression. What is worth mentioning is that compared to the remaining subjects, pregnant ones with PHPT often experience a clinically overt course of this disease [42, 51].

3.3.2.2 Calcium-Induced Acute Pancreatitis

After eliminating all other causes, mean plasma calcium level seems to be the only predictive factor for AP development [46, 49, 93]. Its dosage must be included in the etiological work-up, although PHPT is found in <1 % of patients who present with AP [56]. Felderbauer et al. have stressed that genetic mutations constitute a greater risk factor for AP than serum calcium [48]. The pathophysiologic mechanism that leads to AP seems more related to hypercalcemia than to PHPT. It has been shown that hypercalcemia from any cause can lead to AP [94–96]. As confirmed by experimental studies, calcium ions cause calculus deposition within the pancreatic ductules, with consequent obstruction and inflammation [97]. Moreover, calcium can trigger the AP cascade by promoting conversion of trypsinogen to trypsin [98, 99].

Interrelation between AP and parathyroid function can be summarized as follows: (1) AP results in a tendency to hypocalcemia and secondary hyperparathyroidism [100, 101]. Compensation need is correlated to AP severity as shown by PTH level [102]; (2) severe and/or complicated AP can lead to overt hypocalcemia through relative deficiency in PTH secretion [101], because exogenous administration of PTH normalizes calcium level [103]; (3) in severe AP, resistance to PTH action in bones and kidneys may occur because of fluid sequestration and reduction in efficient arterial blood volume [100]; and (4) once the diagnosis of PHPT-induced AP is established, parathyroidectomy is mandatory because it prevents recurrence [46, 56].

The initiation and growth of kidney calculi may be attributed to overlapping of both increased calcium load, secondary to enhanced PTH synthesis and release, and a pregnancy-induced increase in urine calcium excretion (a typical symptom of physiological pregnancy). For these reasons clinical manifestations of parathyroid disorders in pregnancy are often different from

those observed in nonpregnant women. As the symptoms experienced by patients with parathyroid disorders are not specific, their diagnosis during gestation and breastfeeding may be sometimes very difficult [50, 80]. In opposition to the general population, four of every five PHPT pregnant patients experience clinical manifestations of this disorder. The most frequent of them is the presence of nephrolithiasis [42, 104].

The fact that AP is present in three of four pregnancies complicated by PHPT, while never occurred before and between pregnancies, supports these statistical data that gestation makes hyperparathyroid patients particularly prone to the development of this complication. It is assumed that AP occurs more frequently in primiparous than in women who underwent multiple pregnancies and occurs mainly in the first and third trimester of gestation [51, 105]. PHPT can result in calcifications occurring in the pancreatic ducts thereby blocking secretions, which then damage the pancreatic tissues and result in AP [58]. Usually, these cases present with higher calcium levels compared with cases of PHPT without AP [58]. Hyperparathyroidism can result in calcifications occurring in the pancreatic ducts thereby blocking secretions, which then damage the pancreatic tissues and result in AP [58]. Although the absolute calcium level is an important predictor, it may attenuate during the pregnant state, and individual predisposing factors may be important in the manifestation of pancreatic inflammation [66].

3.3.3 Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy (AFLP) occurs in 1/1,000–1/13,000 [106–109] pregnancies, and it usually complicates gestation as part of pregnancy-induced hypertension or HELLP syndrome [108]. In 39 % of the cases, it appears secondary to a urinary or respiratory infection [110, 111]. In all cases, multiple organs are involved.

The pathophysiology of the disease is obscure. The deficiency of long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) in the fetus may be implicated in the pathogenesis of AFLP [112, 113]. A fetus with this enzyme deficiency accumulates long-chain fatty acids that have not undergone oxidation. These fatty acids enter the mother's serum and are hepatotoxic. Furthermore, the placenta itself may produce excess fatty acids and may further elevate the level of maternal free fatty acids. Mothers who are heterozygous for LCHAD deficiency also have a greater risk of developing AFLP [112]. Studies suggest that AFLP is caused by a mitochondrial defect. The long-chain 3-hydroxyacyl-CoA-dehydrogenase deficiency in the mitochondria determines long- and medium-chain fatty acid accumulation into the cell. This defective enzyme is determined by a gene mutation (E47Q) [114] with an incidence of 1:150–1:200 in population. Alternatively, pregnancy may itself affect mitochondrial function. Other hypotheses favor above-normal (for pregnancy) level of estrogens potentiating the effects of an otherwise tolerable hormonal insult to the mitochondria in the third trimester. Clinically, the onset is between the 30th and 38th weeks of gestation. Complications cited in the literature are hepatic encephalopathy (13 %), hypoglycemia (55 %), renal failure (50 %), coagulopathy (96 %), disseminated intravascular coagulopathy (55 %), and preeclampsia (50 %) [115].

The association of AFLP and AP in pregnancy is very rare, and in the last 15 years, only a few cases have been reported in the literature [116, 117] and currently only one published case of chronic pancreatitis after AFLP during pregnancy in a patient with gestational DM [118]. It was likely due to the serious insult to the pancreas during AFLP, despite normal abdominal CT with i.v. contrast on postpartum day 5 (serum amylase and lipase levels 3× elevated and serum calcium level below lower border) after Cesarean section due to placenta previa with fetal distress when yellow amniotic fluid was found.

3.3.4 Hyperlipidemia/ Hypertriglyceridemia

3.3.4.1 Hereditary Causes

The total cholesterol and triglycerides often increase during the second and third trimester of pregnancy with triglyceride levels approximately

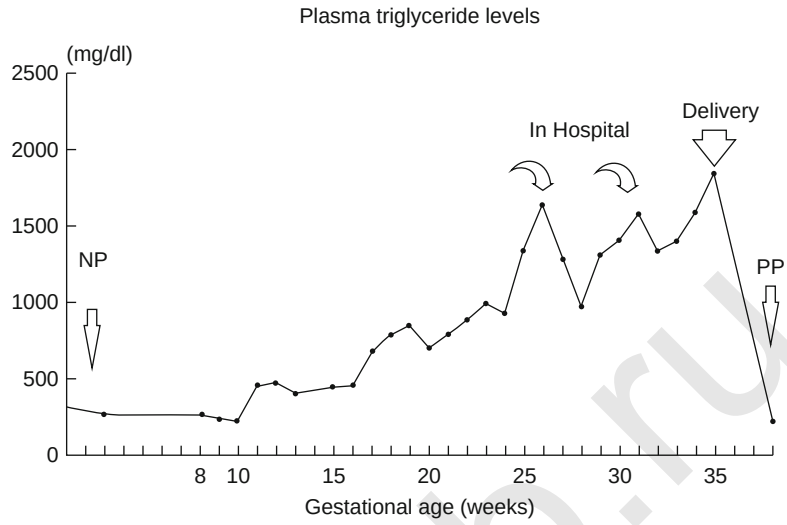

Fig. 3.2 Triglyceride levels at different gestational ages. Triglyceride levels were measured weekly beginning at 8 weeks of gestation of the patient's second pregnancy. Two separate lipid measurements during the nonpregnant (*NP*) state and one measurement 6 months postpartum (*PP*) are also included [120]

doubled during the third trimester of pregnancy [119] due to the combination of reduced LPL activity and increased hepatic lipase activity affecting both triglyceride synthesis in the liver and catabolism of triglyceride-rich particles. The elevation in triglyceride levels is even greater than that of cholesterol, and triglyceride levels usually increase two- to three-fold during the third trimester of pregnancy (Fig. 3.2) [120, 121].

Combination of a human placental lactogen-related increase in adipose tissue lipolysis and hepatic synthesis of very low-density lipoprotein results in increased production of triglyceride-rich lipoproteins [122]. These changes are thought to be adaptive for fetal-maternal requirements as triglycerides are thought to provide maternal fuel, sparing the glucose for the fetus. LPL is a key enzyme for the hydrolysis of TG from chylomicrons and VLDL particles of blood plasma [123]. They are likely to be mediated by the complex hormonal changes evolving during the second and third trimester of pregnancy. During pregnancy, there is a physiological increase in plasma levels of cholesterol and triglycerides; however, this increase is not sufficient to cause AP. These will start to rise, beginning in the third month and peak during the third trimester. Plasma triglyceride (TG) levels normally increase, often as much as threefold [124], but this is usually of little clinical consequence. The physiological increase in serum triglycerides in pregnancy will rarely exceed 300 mg/dl (3.3 mmol/l), a concentration that alone is not sufficient to cause AP. Preexisting genetic abnormalities in the lipid metabolism may be exacerbated during pregnancy and can cause gestational hyperlipidemic AP. Plasma lipid and lipoprotein concentrations are determined by complex interactions between genetic and environmental factors. This is well illustrated during pregnancy where fasting plasma triglyceride levels increase two- to fourfold by the third trimester, occurring predominantly through increased liver synthesis of triglyceride and very low-density lipoproteins (VLDL) in response to elevated estrogen levels [125]. This so-called physiological hyperlipidemia of pregnancy is thought to represent a generalized increase in substrate mobilization, both for the placenta and for the growing fetus [126, 127]. Fat depots increased during early pregnancy and later break down causing an accumulation of TGs [124]. The presence of lipoprotein receptors in the placenta together with LPL and intracellular lipase activities allows the release of fatty acids to the fetus [124].

Additionally, the clearance of VLDL and chylomicrons decreases due to a reduction of lipoprotein lipase (LPL) at the capillary endothelium [128, 129]. This appears to be due to a decrease in LPL synthesis in adipose tissue and possibly skeletal muscle, through the downregulation of LPL gene expression by estrogen [128, 130]. The direct correlation between estrogen levels and

HTG has also been observed in premenopausal women using estrogen-containing oral contraceptives [131, 132]. A similar increase in triglyceride levels has been seen in estrogen-fed rats [133] and in estrogen-fed chicks [134].

The precise mechanisms for the pathogenesis of HTG-induced AP are not established. Cameron et al. found that 38 % of pregnant women with AP had hypertriglyceridemia compared with 9 % of pregnant women without AP [135]. Havel has suggested that hydrolysis of excessive triglyceride-rich lipoproteins by high levels of pancreatic lipase releases very high concentrations of free fatty acids (FFAs) which exceed the binding capacity of plasma albumin, thus resulting in self-aggregating FFA micellar structures with detergent properties [136]. The FFA micelles injure the vascular endothelium and acinar cells of the pancreas, producing a self-perpetuating ischemic/acidic environment with resultant toxicity. Another theory favors ischemia secondary to plasma hyperviscosity due to severe chylomicronemia [137, 138]. However, these two theories are not mutually exclusive.

The development of marked HTG, specifically in pregnancy, in the absence of factors such as DM, drug, or alcohol intake, raises the possibility of partial defects in triglyceride metabolism. While several genetic factors have been implicated, the best validated has been LPL where an impairment in function has been ascribed to the presence of mutations in the LPL gene. LPL is one of two intravascular lipases whose primary roles are the clearance of the triglyceride and phospholipid components of circulating lipoproteins. This enzyme can be assayed in plasma after release from the capillary endothelium by an intravenous bolus of heparin. Mutations in the LPL gene underlying severe hyperlipidemia in pregnancy were first reported in 1994 [139], and thereafter, two additional studies have examined LPL function in women presenting with severe HTG during pregnancy [122, 140]. Of the eight subjects studied in these combined reports, only three were known to be hyperlipidemic prior to their pregnancies. Postheparin plasma LPL activity was assayed in most of these patients in the nonpregnant state and was found to vary from 12 to 100 % of normal. DNA analysis revealed six different LPL gene mutations in this patient cohort. Two subjects, however, yielded normal coding sequence at the LPL gene. In vitro assessment of the catalytic activity of the six mutant lipases revealed three to be partially active (<50 % normal) while the remaining three manifested zero activity. While pregnancy is also recognized as a secondary factor, little data are available on the magnitude of the induced HTG in carriers of LPL gene mutations, where LPL levels most often approximate 50 % of normal. The paucity of reports of severe HTG or HTG-induced AP in founder communities with high carrier frequencies (1/169) such as the French Canadians [141] indicates, however, that pathologic levels rarely ensue and suggests that 50 % of normal activity may be sufficient to prevent hyperlipidemic crises.

Interestingly, Syed et al. stated that it is HTG itself that causes AP and not hypercholesterolemia [142]. The mechanism by which HTG causes AP is not completely understood. The mechanism probably involves the release of large amounts of toxic unbound free fatty acids by pancreatic lipase that damages the endothelium in the capillaries of the pancreas. This results in sludging of red blood cells, stasis, pancreatic ischemic injury, and eventually inflammation. In addition, physical damage by cholesterol crystals might cause microvascular endothelial cell disruption [136, 143]. There are several studies that show inflammatory effects of triglyceride-rich lipoproteins. Ting et al. increased expression of leukocyte adhesion molecules and monocyte adherence in response to the inflammatory cytokine tumor necrosis factor-α (TNF-α) by treating the endothelial cells with triglyceride-rich lipoproteins [144, 145]. Dandona et al. also observed that FFA in the plasma positively correlates with NF-κ and ROS generation [146]. Locally produced fatty acids might also alter endothelial reactivity by inhibiting the actions of eNOS [147].

It is possible that estrogen, aside from producing an alteration in plasma triglyceride concentrations, has toxic effects within the pancreas itself. Pancreatic acinar cells have significant amounts of an estradiol-binding protein [148].

Estrogen increases LDL receptors [149, 150] in some situations and conceivably could promote lipid uptake into acinar cells. Sufficient excess lipid uptake leads to lipotoxicity and cellular apoptosis, a process that is best characterized in muscle cells [151]. Direct effects of estrogens on pancreatic function are supported by the observation that pancreatic amylase release in the rat is stimulated by estrogen [152]. On the other hand, it could be seen that an elevation in estrogen may increase synthesis of triglyceride [153] and depresses plasma postheparin lipolytic activities (PHLA) lowering the removal efficiency of triglyceride during pregnancy. Actually the production rates of triglyceride and total cholesterol at the end of pregnancy are markedly increased to 140 and 50 %, respectively, as compared to that of nonpregnant period [154]. Additionally, triglycerides universally increase during an episode of AP. Whether the elevated triglycerides are an epiphenomenon of the AP or the actual cause of the inflammation can be difficult to differentiate. Mild-to-moderate elevations of triglyceride are seen in up to 50 % of all-cause AP and are generally regarded an epiphenomenon rather than a cause. However, the increase caused by AP alone is transient, peaking at 72 h and declining to near-normal values in 2 weeks [155]. Generally, reported cases of hypertriglyceridemia-induced AP have included levels in excess of 1,000 mg/dl. A more recent report on AP induced by hypertriglyceridemia actually indicates that the majority of cases of AP occurred only when levels exceeded 3,000 mg/dl [156].

Patients presenting with severe HTG should be evaluated for a genetic disorder in lipid metabolism. According to Fredrickson classification of dyslipidemias, types I, IV, and V are associated with severe HTG and predispose for AP [157]. Types I and V can present with AP without an exacerbating factor, whereas type IV usually requires secondary precipitating factors (e.g., poorly controlled DM, alcohol use, estrogen and pregnancy, or medications that can increase or raise TG levels) [158]. Type I hyperlipidemia (also known as familial chylomicronemia) often presents in infancy and is caused by an autosomal recessive trait resulting in lipoprotein lipase or apo C-II deficiency. Type IV, known as familial HTG or familial combined hyperlipidemia, is autosomal dominant and presents in adulthood.

A derangement in lipoprotein lipase (LPL) has been found in association with pregnancy-induced HTG and AP. More than 30 mutations have been identified in the lipoprotein lipase gene in women with gestational AP [139, 140, 159]. More than 60 mutations of the human LPL gene have been described since the complementary DNA sequence of normal human LPL was determined by Wion in 1987 [160]. Mutations of the LPL gene (Fig. 3.1) may result in partial or more rarely complete LPL deficiency. Complete deficiency usually but not invariably presents in childhood with hyperchylomicronemia, eruptive xanthomatosis, and recurrent AP [161]. Homozygosity for a missense Ser172 → cys mutation could be responsible for a 10-fold increase in plasma triglyceride levels [120]. The report of twin sisters shows a possible cause of the AP in pregnancy – a disorder of triglyceride clearance related to defective lipoprotein lipase. LPL is a key lipolytic enzyme that may be down- and upregulated by various influences, including insulin, estrogen, and medications [128, 162]. Both patients showed a defect at amino acid residue 188 of LPL and are heterozygous for the mutation. Patient 1 had a more classic variety during the last trimester and subsequently responded well to fat restriction and conservative management. Patient 2 had a more severe and protracted course, possibly because of the use of cholestyramine resin, a drug that may have elevated rather than decreased her triglyceride levels [163, 164]. Patient 2 had multiple medical and surgical complications related to the severity of her AP. Patient 1 had mild glucose intolerance that may have exacerbated the triglyceride level. Years before developing pregnancy-induced AP, patient 1 may have had hyperlipidemia and AP as a result of the use of birth control pills. Mutation at codon 188 appears throughout the world, perhaps most often in the French Canadian population. In Quebec, the carrier rate has been estimated to be as high as 1/169, with a total of 19,600 persons affected [141, 165]. The assump-

tion is that the rarity of the clinical syndrome of hyperlipidemia and AP in pregnancy in patients with this specific genetic defect may be due to the presence of an undetected additional mutation in affected patients [140].

There is only one case report of the LPL W86R mutation causing serious exacerbation of the hyperlipidemia symptoms during pregnancy, and the first case in which the level of residual activity in a homozygous W86R mutation could be clearly documented. It is a case of a 25-year-old patient with several attacks of AP during the third trimester with the last episode of necrotizing AP. She was operated several times, and first, immediate surgery revealed diffuse peritonitis with 3 L of purulent fluid. The dead fetus was removed with the uterus, the pancreas then resected. Following this, a number of reoperations were performed due to omental abscesses and progressive intra-abdominal sepsis. Gallbladder was also removed and the abdominal wound treated in a semi-open way. She was discharged after 32 days [166].

Previous studies showed that approximately one-third of the women developing HTG-induced AP during pregnancy were nulliparous [15, 167].

3.3.4.2 Acquired Causes

Hypertriglyceridemia

HTG-induced AP occurs often in untreated or uncontrolled DM [30, 168]. In type I DM, the absence of insulin reduces the ability of LPL to reduce TG into FFA, resulting in elevated TG levels [169]. In type II DM, insulin resistance leads to enhanced production and reduced clearance of TG [170]. Diabetic ketoacidosis may pose a separate risk for HTG as evidenced by a prospective study of 100 patients presenting with diabetic ketoacidosis. Eleven percent of patients had AP, and in four cases, HTG was the only attributable cause [171]. The role of alcohol in HTG is unclear but may be attributed to alcohol competing with FFAs for oxidation, leaving more FFAs available for TG synthesis [158]. Some authors suspect that alcohol alone does not cause HTG, but more likely exacerbates an underlying genetic hyperlipidemia [168]. In addition, hypothyroidism has been documented as a cause of HTG [31, 172]. In a case report, a craniopharyngioma was implicated as it caused central hypothyroidism, leading to HTG (3,300 mg/dl) and eventual AP [31]. Medications such as estrogen [173] are known to raise the serum TG level. Accordingly, hormone therapy in women is not recommended when TG is >500 mg/dl due to heightened risk of HTG-induced AP [173].

Exogenous estrogens elevate triglycerides by increasing the production of triglyceride-carrying very low-density lipoproteins (VLDLs) by the liver and reducing the levels of LPL and hepatic lipase, thus reducing triglyceride clearance while also elevating triglycerides by augmentation of insulin resistance [174, 175]. As early as 1972, clinicians were alerted to cases of marked hyperlipidemia and AP associated with the use of birth control pills, although no genetic testing was available at that time [176]. Tamoxifen is known to cause a small, but significant decrease in high-density lipoprotein (HDL) cholesterol, unlike estrogen, which elevates HDL. In women with HTG, tamoxifen's ability to increase the triglyceride level is especially pronounced, to an extent that may induce AP [174, 177, 178]. Clomiphene citrate is a synthetic estrogen analog with a biochemical structure similar to that of tamoxifen. Clomiphene has mixed agonistic but mainly antagonistic properties [179]. The effects of clomiphene on lipid metabolism have not been as well documented as the effects of tamoxifen because it is not used continuously and not as commonly as tamoxifen. Clomiphene elevates the triglyceride level mainly in women with a predisposed risk for HTG, due to mutations in enzymes such as LPL [143, 180].

Apoprotein E (apo E), particularly apo E allele 2, has been found in association with higher triglyceride levels in pregnant patients with chylomicronemia [139]. Authors did not find apo E alleles 2 or 4 in their twin patients; both had apo E genotype 3/3. Therefore, apo E was not a primary cause of the HTG in these patients [140]. Although it is known that pregnancy results in an increase in plasma triglyceride levels [119], how this increase occurs is not totally understood. In addition, certain persons

Table 3.3 Acquired/secondary causes of hypertriglyceridemia [182]

Alcohol excess
High-carbohydrate diet
Obesity
Type 2 diabetes mellitus
Pregnancy
Chronic renal failure, nephrotic syndrome
Hypothyroidism, Cushing syndrome
Acute pancreatitis
Viral hepatitis
Biliary cirrhosis
Multiple myeloma, monoclonal gammopathy
Glycogen storage disease
Lipodystrophy
Systemic lupus erythematosus
Drugs – exogenous estrogens, tamoxifen, glucocorticoids, b-blockers, amiodarone, thiazide diuretics, ciclosporin, retinoids, bile acid binding resins, antiretrovirals (protease inhibitors), propofol, clozapine, parenteral lipid infusion

express profound elevations in triglyceride values during pregnancy [74, 181].

There are many causes of secondary hypertriglyceridemia (Table 3.3):

3.3.5 Alcohol

The pathophysiologic role of alcohol in the etiology and occurrence of acute AP is complex, but increased oxidative stress [183, 184], disruption of cytosolic calcium homeostasis [185], and changes in gene expression [186] in the pancreas seem to be involved. Yet, only 1–3 % of heavy alcohol drinkers (4–5 standard drinks of alcohol per day) develop AP after 10–20 years of follow-up [187, 188]. For many years there has been an ongoing discussion on whether the type of alcoholic beverage might influence the occurrence of AP [189]. Indeed, a potential role for type of beverage was indicated by descriptive data from Stockholm County in Sweden showing a decline in the incidence of AP alongside a decline in the sales of spirits between 1971 and 1987, despite increased sales of beer and wine [190]. In Finland, there was also a decline in the incidence of alcoholic AP between 1989 and 2007 [191]. During the same period, the percentage of people drinking spirits each week dropped from 24 % in 1988 to 19 % in 2007 [191]. However, clinical studies have generally been too small to study the association between different alcoholic beverages and the risk of AP [192–194]. In a recent population-based study from Denmark, the risk of AP was found to be associated with the amount of beer consumed [187]. However, the information on alcohol use was limited to the consumption of alcoholic beverages assessed as total number of drinks per week, not including the amount of alcohol consumed on a single occasion or overall drinking frequency. The metabolism of alcohol (ethanol) is known to induce oxidative stress, which in turn depletes cellular glutathione storage and results in lipid peroxidation and damage to pancreatic tissue [183, 195]. However, in animal models it seems that ethanol alone is not enough to induce AP [196, 197]. Beer [198] and wine [199] include polyphenols with antioxidant capabilities. In experimental studies, other constituents in spirits such as long-chain alcohols have been shown to be more potent than ethanol in inducing oxidative stress [200]. Comparing the same amounts of alcohol, spirits deplete the antioxidant capacities more readily than beer or wine [201]. Thus, there might be other constituents in spirits that induce AP, in combination with ethanol or alone. Those drinking spirits might also have lower reserves of antioxidants at baseline, which could be depleted rapidly after intake of spirits [202].

Alcohol use is associated with increased risk of AP, in a dose-dependent manner [203], but the main point is that chemical analysis (using gas chromatography/mass spectrometry) of the consumed alcohols revealed the presence of other constituents (besides ethanol and water) are potential cause of injury of the pancreas, but, to date, remain largely unexplored [189, 204]. The results reported in the study must therefore be carefully interpreted as only tentative based on semiquantitative analysis. Also data for the patterns of drinking from the Global Information System on Alcohol and Health (http://apps.who.int/globalatlas/default.asp) indicate that the more harmful the pattern of

drinking (i.e., the more heavy drinking), the higher the rates of alcohol-induced AP [205]. A recent systematic review and meta-analysis also detected the existence of a threshold at approximately four drinks daily [206].

3.3.6 Medications

AP in general population due to medications is an unusual event, although the incidence may be increasing. In a review of records from 45 German centers, only 1.4 % episodes of AP in 1993 were related to medication use [207]. Further confirming the rarity of this condition, only 0.3 % adverse drug reactions reported to the Swiss Drug Monitoring Center between 1981 and 1993 were drug-related AP [208]. The literature on drug-induced AP mostly consists of case reports and anecdotal accounts. Over 55 drugs have been implicated as etiological agents, and the list continues to grow. Proposed criteria for classifying drugs as having an association with AP include the following [209]:

- Pancreatitis develops during treatment with the drug.
- Other likely causes of pancreatitis are not present.
- Pancreatitis resolves upon discontinuing the drug.
- Pancreatitis usually recurs upon readministration of the drug.

Assignment to a particular category (definite, probable, or possible association) is often arbitrary due to inadequate and conflicting data and interpretation bias of the reviewers. Thus, the strength of the association has been interpreted differently, substantially so in some cases, by different reviewers of the subject. The pathogenesis of drug-induced AP may be due to an *allergic response* in some cases (6-mercaptopurine, aminosalicylates, sulfonamides) or to a direct *toxic effect* (diuretics, sulfonamides, steroids). AP associated with angiotensin-converting enzyme inhibitors is thought to reflect angioedema of the gland. Medications with the influence on estrogen activity are discussed in previous section of acquired causes of HTG.

Drug-induced AP in pregnancy is rare [15]. These facts would point out mifepristone or possibly gemeprost as the likely causative agents [210]. However, there have been a handful of published cases of AP complicating treatment with codeine [211–213]. A common feature of these reported cases are previous cholecystectomies [212, 213]. The patient reported here had not been cholecystectomized. Also, three cases of possible codeine-precipitated AP have been reported since 1965 to the *Swedish Drug Information System* (SWEDIS) handling reports on suspected adverse reactions to drugs used in Sweden [214]. Codeine is known to cause rapid but transient spasm of the sphincter of Oddi [212]. Laboratory studies have shown that codeine may cause a mild, transient hyperamylasemia [212]. AP following paracetamol overdose has been previously reported [212], but the doses taken in the present case are unlikely to have been causative. Gemeprost is a synthetic prostaglandin E1 (PGE_1) analog. Studies indicate that PGE_1 is a modulator of pancreatic blood flow and protein production. For instance, PGE_1 stimulated the production and secretion of alpha-amylase from minces of porcine pancreas in vitro [215] and enzyme output in dogs in vivo [216]. PGE_1 further increases mesenteric and pancreatic blood flow [216]. Thus, PGE_1 is not devoid of actions on the pancreas. Progesterone has also been shown to exert modulating action on the pancreas. In rats, progesterone stimulated pancreatic cell proliferation in vivo [217]. Progesterone receptors have also been shown to be present in human pancreatic tissue [218]. However, the effect of a progesterone receptor antagonist such as mifepristone on the pancreas has not been studied. Evidence thus exists that both PGE_1 and progesterone exert modulatory action on the pancreas, but currently no reports on AP following treatment with gemeprost or mifepristone have been published.

Diuretics can induce AP [219, 220]. Preeclampsia-associated AP can occur but is very

rare [75, 221, 222]. Preeclampsia is associated with microvascular abnormalities that may involve cerebral, placental, hepatic, renal, and splanchnic circulation. It is likely that pancreatic vasculature was also altered and caused AP that resulted in organized pancreatic necrosis. In a review from 1995 [15], none of the 43 women had preeclampsia-associated AP, whereas an older review [16] reported nine of 98 cases of preeclampsia-associated AP but five of those received diuretics and another case also reported diuretic use [16]. There is a question: is it really preeclampsia-eclampsia the cause or is therapy with diuretics the real cause of AP during pregnancy in such situations?

Additional medications associated with elevated TG include protease inhibitors [223], propofol [224], olanzapine [225], mirtazapine [226], and isotretinoin [227].

3.3.7 In Vitro Fertilization

Currently, there is only one case report of AP during in vitro fertilization (IVF) pregnancy published. A 29-year-old female with Fredrickson type V dyslipidemia and BMI 26 at 32 weeks gestation with twins was treated medically. Emergency Cesarean section was performed after 48 h due to clinical deterioration with increasing metabolic acidosis. The Cesarean section was performed with successful outcome, and postoperatively her severe HTG settled. She was discharged on postoperative day 9 on a combination of fenofibrate and Omacor [228]. Another two case reports described patients developing AP during a routine IVF stimulation cycle [229, 230]. IVF probably represents high-risk group to the number of hormones, procedures, and medications used simultaneously which could increase the probability of developing AP.

3.3.8 Postpartum Acute Pancreatitis

Evidence is abundant of gallstones and biliary sludge during pregnancy causing AP. Also, due to hormonal changes, there is increase in incidence of other causes such as hyperlipidemic/hypertriglyceridemic AP. Most of the AP resolves during medical (or surgical) therapy, but some are resolved after Cesarean section when all the gestational (mostly hormonal) changes return to pregestational state. Findings of the study by Maringhini et al. are that AP associated with pregnancy occurred in the youngest women but only during the postpartum period and was associated with gallstones but not related to pregnancy per se [231]. The association of AP with gallstones in young postpartum women is most likely due to the known alterations of bile composition, gallbladder contractility, and gallstone or gallbladder sludge formation that occurs during and after pregnancy (see Chap. 2). Small gallstones may appear during pregnancy, but most of them disappear during the early postpartum period. The appearance of gallstones during pregnancy and their postpartum disappearance may be due to the impressive modifications of bile composition and gallbladder motility that occur during pregnancy. The changes in hepatic bile that occur in the last trimester of pregnancy are secondary to high estrogen levels, while gallbladder stasis during pregnancy is due to high progesterone levels. These phenomena produce the milieu for nucleation and crystal formation that finally generates sludge and stones. Bile composition and gallbladder motility return to normal after delivery; thus, sludge and small stones may be eliminated or dissolved. The data are consistent with the hypothesis that at least some of the gallstones disappear during the postpartum period because they are ejected from the gallbladder into the bile ducts and duodenum and may cause AP. The study did not confirm direct data on the role of biliary sludge in AP in pregnancy. No women with AP had documentation of biliary sludge, but the diagnosis of biliary sludge is often difficult, and a prospective study is needed. However, authors demonstrated that gallstones are the only etiology significantly associated with postpartum-related AP. The increased RR for gallstone AP in young postpartum women is in agreement with the increased incidence of gallstones in young pregnant women [232–236]. The age-dependent risk of developing gallstones associated with pregnancy (the risk

being greatest for subjects younger than 29 years) has been shown in some Australians [234] and in Chippewa Indians [235]. Authors previously reported that the spontaneous disappearance of gallstones after delivery is significantly more frequent in older women [237]. Speculation is that a few young women eject small gallstones from the gallbladder during the postpartum period when gallbladder contraction is restored, and some of these women develop an attack of AP. In contrast, in older women with reduced gallbladder contractility, most gallstones likely remain in the gallbladder until dissolved by less lithogenic bile. Thus, AP associated with pregnancy usually occurs in young postpartum women and is usually due to gallstones [231]. Generally, AP can occur during any trimester but around 52 % of cases are found in the third trimester; it is rarely seen in the postpartum period [15].

3.3.9 Preeclampsia-Eclampsia

AP has also been reported in preeclampsia but with only several cases published [75, 221, 222, 238–242]. Preeclampsia is associated with microvascular abnormalities that may involve cerebral, placental, hepatic, renal, and splanchnic circulation. It is likely that the pancreatic vasculature was also altered and caused AP that resulted in organized pancreatic necrosis. In a review from 1995 [15], none of the 43 women had preeclampsia-associated AP, whereas an older review [16] reported nine of 98 cases of preeclampsia-associated AP but five of those received diuretics and another case also reported diuretic use [222]. Diuretics can induce AP [219]. The rise of amylase and lipase levels exceeded the expected increased values due to the slight reduction of the renal function in the preeclamptic patients and therefore indicates a concomitant injury of the pancreas [243].

3.3.10 Placental Abruption

Placental abruption is when the decidual spiral artery ruptures to cause a hematoma that separates the placenta from the uterus and is commonly associated with maternal hypertension [244]. In severe cases, blood prominently infiltrates the uterine myometrium up to the serosa, and this phenomenon is designated as uteroplacental apoplexy. Placental abruption induced by AP is very rare and was reported in 1962 by Pagliari et al. [245] and later Cheang et al. [246]. Placental abruption likely occurred in the first phase of AP, resulting from a systemic inflammatory response.

3.4 Clinical Features

AP presents essentially in the same way during pregnancy as in the nonpregnant state. However, it is difficult to diagnose AP by history and physical examination due to similarity to many acute abdominal illnesses and due to maternal changes during pregnancy.

3.4.1 History Taking

All relevant information about possible causes should be obtained. Family history about hyperlipidemias, DM, AP, etc. should be noted. It is important if these data could be noted before or during pregnancy planning to eliminate or minimize possibility of AP during pregnancy.

Since no safe level of alcohol has been established in pregnancy, it may not be socially acceptable for pregnant women to admit they consume alcohol. Assessing this risk accurately can be challenging. The T-ACE [Take (number of drinks), Annoyed, Cut down, Eye-opener] TWEAK (Tolerance, Worried, Eye-opener, Amnesia, Kut down), and AUDIT-C (AUDIT consumption) alcohol screening questionnaires show promise for use with pregnant women, but have not yet been validated as stand-alone tools in this population [247].

3.4.2 Clinical Presentation

The symptoms of AP in pregnancy could be nonspecific; the predominant symptom is upper abdominal pain which is usually midepigastric

and could radiate to the back in about 40 % of the cases [15]. Pain is commonly accompanied by midepigastric tenderness, nausea, and vomiting [248, 249]. Fever may be present [249]. Some cases may have persistent vomiting, abdominal distension, and tenderness in the whole abdomen. The duration of symptoms may vary from 1 day up to 3 weeks. In severe cases sinus tachycardia, hyperventilation, and smell of acetone of the breath can also be present [250]. If accompanied by fever, unstable respiratory and circulatory function, shock, and gastrointestinal bleeding, these are strong indications for severe AP.

AP in pregnancy is mainly related to gallbladder disorders and correlates with cholelithiasis and biliary sludge (muddy sediment, precursor to gallstone formation) as the most likely predisposing causes [15]. The symptoms of gallbladder disease can be present or can precede the clinical presentation of AP. The symptoms include abdominal pain (colicky or stabbing) which may radiate to the right flank, scapula, and shoulder. Onset of pain is rapid, with maximal intensity in 10–20 min. Pain is steady and moderate to severe. Band-like radiation of the pain to the back occurs in half of patients. Other symptoms of gallbladder disease include anorexia, nausea, vomiting, dyspepsia, low-grade fever, tachycardia, and fatty food intolerance [15]. Vomiting is a common symptom. Marcus in 1930 emphasized that persistent vomiting in pregnancy could be related to AP and that blood and enzyme studies should be done [251].

Clinical signs are the same as in nonpregnant population. Cullen's sign (Fig. 3.3) and Grey Turner's sign are rare but among most common as in general population.

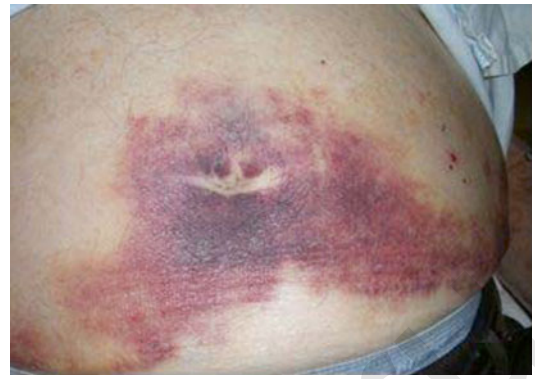

Fig. 3.3 Cullen's sign [252]

3.4.2.1 Primary Hyperparathyroidism

Truly asymptomatic PHPT in general population is rare when thorough anamnesis looks for subtle symptoms. Most frequent digestive manifestations are constipation, heartburn, nausea, and appetite loss that occur in 33, 30, 24, and 15 % of cases, respectively [253]. The diagnosis should be suspected during pregnancy if the following conditions exist: appropriate clinical signs or symptoms (especially nephrolithiasis or AP), hyperemesis beyond the first trimester, history of recurrent spontaneous abortions/stillbirths or neonatal deaths, neonatal hypocalcemia or tetany, or a total serum calcium concentration greater than 10.1 mg/dl (2.52 mmol/l) or 8.8 mg/dl (2.2 mmol/l) during the second or third trimester, respectively. Symptomatic PHPT is rarely detected in pregnancy due to the physiological changes that mask the symptoms; this includes maternal blood volume expansion, hypoalbuminemia, increased fetal calcium requirements, and increased calcium clearance. The data obtained from analysis of so far described cases indicate that in opposition to the general population, four of every five hyperparathyroid pregnant patients experience clinical manifestations of this disorder. The most frequent of them is the presence of nephrolithiasis [42, 104]. The initiation and growth of kidney calculi may be attributed to overlapping of both increased calcium load, secondary to enhanced PTH synthesis and release, and a pregnancy-induced increase in urine calcium excretion (a typical symptom of physiological pregnancy).

3.4.2.2 Acute Fatty Liver of Pregnancy

The onset of AFLP occurs typically in the third trimester or the early postpartum period and is characterized by a nonspecific prodrome of

symptoms: sudden onset of nausea, vomiting, and vague abdominal pain followed by jaundice, profound hepatic failure with encephalopathy or coma, coagulopathy, and frequent hypoglycemia. Due to the similarity of symptoms, AP during pregnancy cannot be always recognized clinically. In a series of 12 cases of AP in pregnant women with AFLP, Moldenhauer et al. [110] found the following complications: encephalopathy (50 %), respiratory failure (17 %), and acute renal failure (33 %).

3.4.2.3 Hypertriglyceridemic Pancreatitis

Though the initial presentation of HTG-induced AP is similar to AP due to other etiologies, some features should lead to the consideration of HTG-induced AP. Poorly controlled DM, alcoholism, obesity, prior AP, and personal or family history of hyperlipidemia will suggest HTG-induced AP [30, 158]. Alcoholism or DM has been reported in 72 % of HTG-induced AP episodes [30, 158]. Lactescent serum on hospital admission was found in 45 % of patients [30].

3.4.2.4 Medication-Induced Acute Pancreatitis

Drug-induced AP in general population has no distinguishing clinical features. A high index of suspicion and careful drug history are therefore essential for making the diagnosis. The time course of developing the disorder depends upon the drug involved. As an example, AP may develop within a few weeks after beginning a drug associated with an immunologically mediated adverse reaction; in this setting, the patient may also have a rash and eosinophilia. In contrast, patients taking valproic acid, pentamidine, or didanosine may not develop AP until after many months of use, presumably due to the chronic accumulation of toxic metabolic products. Proving the association with a particular drug may not always be straightforward, even in suspected cases. Thus, patients restarted on their medications should be closely monitored and the drug promptly discontinued if symptoms recur. It is known that many medications are discontinued during pregnancy by mothers themselves or by physicians when not sure about teratogenicity.

3.4.3 Physical Examination

Physical findings vary with the severity of illness; in moderate to severe AP, the patient appears acutely ill and is found lying in the "fetal position" with flexed knees, hips, and trunk. Abdominal tenderness is often found; in diffuse peritonitis muscle rigidity can be present. Bowel sounds, secondary to paralytic ileus, are usually hypoactive or absent. In severe AP the general physical examination may reveal abnormal vital signs if there are third-space fluid losses and systemic toxicity. Due to hypovolemia, tachycardia up to 150/min and low blood pressure could be found. Also, because of severe retroperitoneal inflammatory process, temperature may increase. Dyspnea, tachypnea, and shallow respirations resulting in hypoxemia may be present. Altered maternal acid-base status can adversely affect fetal acid-base status. Acute fetal hypoxia activates some compensatory mechanisms for redistribution of blood that enable fetus to achieve a constancy of oxygen consumption in the fetal cerebral circulation and in the fetal myocardium. Redistribution of blood to vital organs enables fetus to survive for moderately long period of limited oxygen supply, but during more severe or sustained hypoxemia, these responses were no longer maintained and decompensation with fetal tissue damage and even fetal death may occur [167, 254]. Some physical findings point to a specific cause of AP: jaundice in biliary origin, spider angiomas in alcoholic, or xanthomata and lipemia retinalis in hyperlipidemic AP. HTG can lead to chylomicronemia syndrome, which can manifest with eruptive xanthomata over extensor surfaces of the arms, legs, buttocks, and back (Fig. 3.4) [255–258], lipemia retinalis (Fig. 3.5) [255, 260], and hepatosplenomegaly from fatty infiltration of the liver [255, 257, 258].

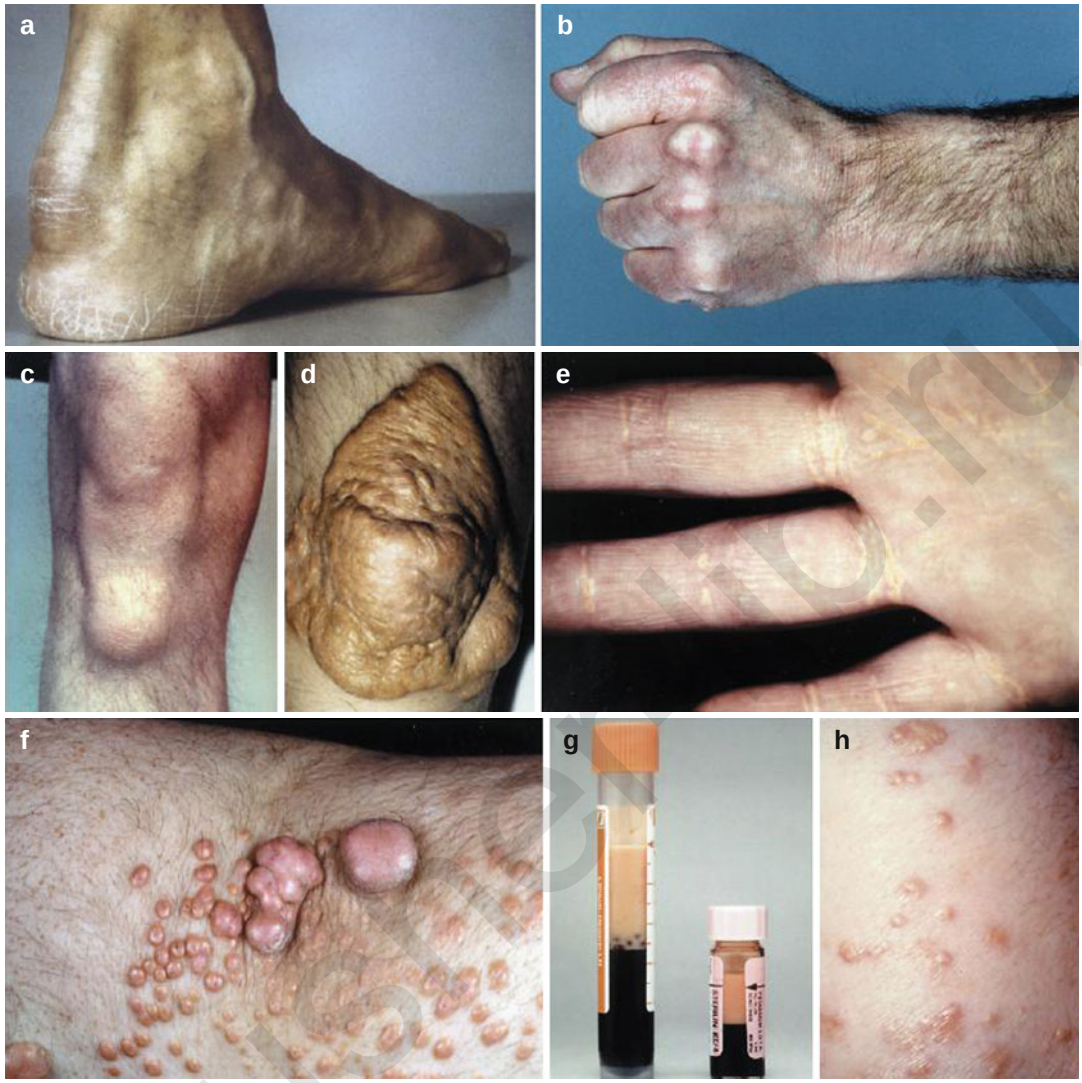

Fig. 3.4 Clinical manifestations of hyperlipidemia. (**a**) Achilles tendon xanthoma (heterozygous familial hypercholesterolemia – type IIa); (**b**) tendon xanthomata on dorsum of the hand (heterozygous familial hypercholesterolemia); (**c**) subperiosteal xanthomata (heterozygous familial hypercholesterolemia); (**d**) planar xanthoma in antecubital fossa (homozygous familial hypercholesterolemia); (**e**) striate palmar xanthomata (type III); (**f**) tuberoeruptive xanthomata on elbow and extensor surface of arm (type III); (**g**) milky plasma from patient with acute abdominal pain (severe hypertriglyceridemia); (**h**) eruptive xanthomata on extensor surface of the forearm (severe hypertriglyceridemia) [255]

3.5 Diagnosis

AP in pregnancy is diagnosed by symptoms already described, by laboratory investigations, and by imaging methods. Some important normal values in pregnant and nonpregnant women are compared in Table 3.4.

3.5.1 Laboratory Findings

Marcus in 1930 is credited with the first clinical diagnosis of AP in pregnancy with the aid of diastase and amylase studies [251]. Pregnancy-related hematological and biochemical alterations interfere with the interpretation of diagnostic

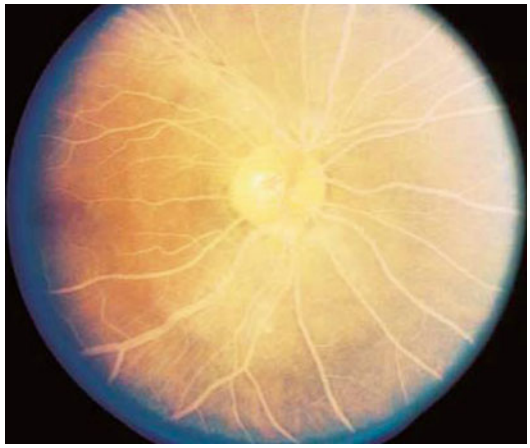

Fig. 3.5 Lipemia retinalis associated with hyperlipidemia. Rare and asymptomatic creamy white appearance of retinal vessels occurs when triglyceride value reaches more than 2,000 mg/dl (22.6 mmol/l) – the effect due to dispersion of light caused by high value of circulating chylomicrons in the blood, most commonly occurring in familial hyperchylomicronemia [259]

Table 3.4 Normal laboratory values for blood and urine in pregnant and nonpregnant women [261]

Variable	Nonpregnant women	Women in third trimester
Serum total calcium (mmol/l)	2.2–2.63	2.15–2.3, mean 2.15–2.23
Serum albumin (g/dl)	3.6–4.6	2.8–3.6
Serum ionized calcium (mmol/l)	1.13–1.32	No change
Parathyroid hormone (pg/ml)	11–80	Middle of normal range
25-hydroxyvitamin D (nmol/l)	62–200	No change
1,25-dihydroxyvitamin D (nmol/l)	37–187	Doubled
PTH-related protein (pg/ml)	0–12	Increased
Triglycerides (mmol/l)	0.4–1.7	Doubled to quadrupled
Urinary calcium (mmol/h)	<6.24	Doubled to tripled

tests and assessment of severity of AP. Laboratory investigations are the same as in nonpregnant and rely on at least a threefold elevation of serum amylase and lipase levels in the blood. The total serum amylase level rises within 6–12 h of onset of the disease, usually remains elevated for 3–5 days. However, there are several conditions (i.e., pathologic processes in salivary glands, Fallopian tubes, bowel obstruction, cholecystitis, hepatic trauma, perforative duodenal ulcer, hyperamylasemia on familial basis, etc.) that may result in the elevation of serum amylase. Serum lipase is elevated on the first day of illness and remains elevated longer than the serum amylase. In terms of diagnostic accuracy, lipase has been proven to be superior to amylase in AP [262, 263]. However, lipase is also not specific to the pancreas, having been isolated in the tongue, esophagus, stomach, duodenum, small bowel, liver, lung, and adipose tissue [264, 265]. Consequently, hyperlipasemia has been reported to appear in the event of cholecystitis, esophagitis, peptic ulcer disease, enteritis, peritonitis, and bowel obstruction and infarction [263–265]. AP could not be ruled out if normal level of serum amylase is detected. One reason is that the serum amylase may not increase when pancreas have extensive necrosis. The other reason is that amylase and biochemical parameters cannot be checked truly with the significant increase of plasma triglycerides level. So, in nonpregnant patients, a normal amylase would usually exclude the diagnosis of AP, with the exception of AP secondary to hyperlipidemia, acute exacerbation of chronic pancreatitis, and when the estimation of amylase is delayed in the course of the disease [266]. Therefore, checking the urine amylase level may be more helpful. Caution in the interpretation of serum amylase and urinary diastase determination should be exercised if morphine has been given. Morphine has been shown to cause spasm of the sphincter of Oddi with obstruction of the pancreatic drainage. In nonpregnant population with AP, no enzyme assay has a predictive role in determining the severity or etiology of AP. Once the diagnosis of AP is established, daily measurements of enzymes have no value in assessing the clinical progress of the patient or ultimate prognosis and should be discouraged. A persistently raised serum amylase activity may suggest the presence of a pancreatic pseudocyst. For the early postpartum period, there are no data available about amylase and

lipase dynamics due to the extreme rarity. An elevated serum amylase level has a diagnostic sensitivity of 81 %, and adding serum lipase increases the sensitivity to 94 %. However, amylase levels do not correlate with disease severity [267]. Typically, a serum amylase concentration greater than three times normal is seen at presentation, which peaks in the first 24 h and falls to baseline in 3–5 days. In contrast, serum lipase concentrations are elevated for up to 2 weeks, making it a more sensitive and specific diagnostic test. Karsenti et al. found that enzyme concentrations were similar in nonpregnant and pregnant women and concluded that an increase in either would be suggestive of AP in pregnancy [268].

Elevated amylase and/or lipase are the diagnostic hallmarks of AP; yet, in hypertriglyceridemia-induced AP, amylase levels may be reported as normal or even low in more than 50 % of patients. This phenomenon has been attributed to an interference of plasma lipids with the assay and/or to the presence of a circulating inhibitor of amylase in serum and urine [158, 269, 270]. In such cases, dilution or ultracentrifugation of the sample is recommended to ensure accurate analysis. Also, in general population, 16–25 % of patients with diabetic ketoacidosis may have elevated pancreatic enzymes and triglycerides, circumstance less reliable diagnosis of pancreatitis based only on biochemical parameters [171].

In addition, lipase is the pancreas-specific enzyme lasting in the blood for a long time. Despite the aforementioned, elevation of serum alanine aminotransferase levels to >3 times the upper limit of normal is a very sensitive biochemical marker of biliary AP in nonpregnant population [271, 272] and should be also suspected in pregnancy. Calculation of an amylase to creatinine clearance ratio may be helpful in pregnancy; ratio greater than 5 % suggests AP [273]. Gamma-glutamyl transpeptidase (GGTP) levels either are unchanged or fall slightly during gestation. An elevated GGTP level can help us to evaluate the history of alcohol use during pregnancy as patients might not be coming forth, due to stigmata associated with it [274].

HTG AP is conventionally thought to be triggered when triglyceride (TG) levels exceed 1,000 mg/dl (10 mmol/l) unless accompanied by lactescent serum [30, 168]. In severe HTG (serum TG level >2,000 mg/dl), there is an increased risk of aggravating preexisting AP [275, 276]. Chylomicrons are formed at these high TG levels and serum becomes lactescent (milky coloration). TG values of even 3,810 mg/dl were encountered [277].

Serum calcium level must be considered among the usual tests in patients with rare and/or nonspecific abdominal symptom, especially when AP is suspected [278]. Calcium metabolism in pregnancy is a dynamic process. Maternal serum calcium falls by about 10 % in pregnancy; however, as the serum albumin falls by 20 %, the ionized calcium remains unchanged. Making the correct diagnosis of PHPT in pregnancy is regarded crucial, because if this disorder remains unrecognized and left untreated, it may pose a significant risk to the mother and fetus, which is associated with increased perinatal and maternal morbidity and mortality [51, 279].

In a study by Tang et al. liver tests in pregnant women with biliary AP were frequently normal. The transaminase levels were less than 5× the upper normal limits in 89 % of patients and less than 3× the upper normal limits in 80 % of patients. Authors do not have a good explanation for this finding. One possibility is that increased metabolism of maternal transaminases by the placenta led to relatively normal maternal levels of liver enzymes [23].

Laboratory abnormalities consistent with AFLP include mild elevation of ALT and AST to 200–300 IU/l [108, 280], prolongation of prothrombin time and partial thromboplastin time, decreased fibrinogen, acute renal failure, severe hypoglycemia, a bilirubin level of 1–10 mg/dl, and leukocytosis. In a series of 12 cases of AP in pregnant women with AFLP, Moldenhauer et al. [110] found that elevated serum lipase was present in 91 %.

It should be noted that hyperparathyroidism may be falsely lowered due to hypoalbuminemia or suppressed by magnesium tocolysis [59].

Some authors recommend that a lipemic blood sample found at any stage during pregnancy should be considered as potentially indicative of partial LPL deficiency [159].

At present, serum CRP at 48 h is the best available laboratory marker of severity. Urinary

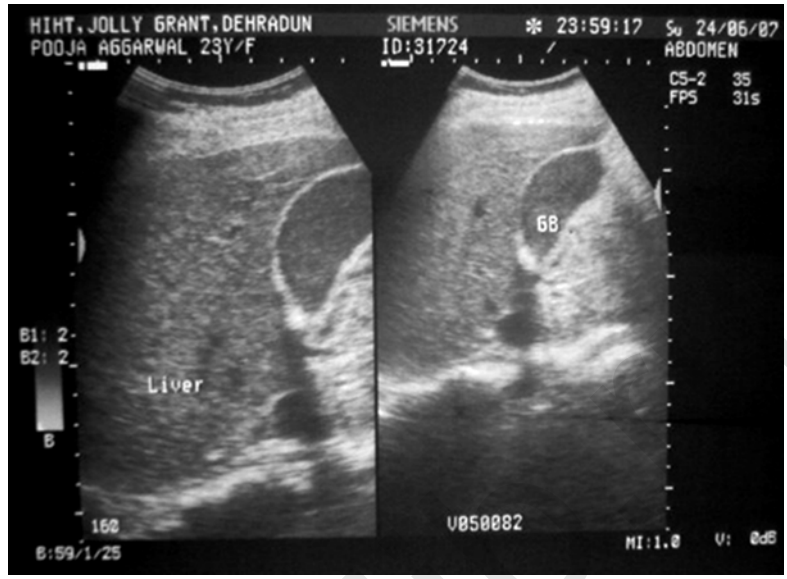

Fig. 3.6 Abdominal ultrasound of the abdomen showing gallbladder sludge in a 23-year-old nulliparous woman in 33 weeks of pregnancy [288]

trypsinogen activation peptides within 12–24 h of onset of AP are able to predict the severity but are not widely available. Serum IL-6 and IL-8 seem promising but remain experimental [266].

3.5.1.1 Confounding Laboratory Investigations in HTG of Nonpregnant Patients

Elevated TG levels can alter routine measurements of sodium, serum amylase, and LDL. Clinicians must be wary of pseudohyponatremia as the excess TG in a serum sample can displace water-containing sodium. During laboratory measurements, the sodium level appears lower than the actual value [281]. Ultracentrifugation is needed to separate the aqueous phase and measure the true sodium level [281]. HTG levels >500 mg/dl may cause a falsely normal amylase level, likely from HTG interference with calorimetric reading of the assay or presence of an interfering inhibitor. This problem can be partially overcome by assaying serial sample dilutions [282] or measuring *serum lipase or amylase to creatinine ratio*, neither of which is affected by HTG [158, 283]. There are no official recommendations on lipase utility in HTG-induced AP; however, serum lipase was found to have higher specificity and sensitivity for AP compared to amylase in a report by Treacy et al. [284]. Friedewald calculations used to determine LDL from triglyceride levels lose accuracy with high TG levels [285]. A commonly accepted upper limit is 400–500 mg/dl [286]. Lipid analysis requires direct measurement through centrifugation or immunoprecipitation.

3.5.1.2 Ranson Criteria

Ranson scoring system is calculated in several case reports but is not validated in pregnancy. With a Ranson prognostic index at 7, as calculated in one patient with AP due to preeclampsia-eclampsia, there was a high risk of death. However, recovery was prompt and uneventful [221]. Another patient with Ranson score 3 had two exploratory laparotomies and survived after complicated course [287].

3.5.2 Imaging Methods

Imaging in pregnancy remains a controversial issue with concern of the effect of radiation on the developing fetus. Abdominal ultrasound (US) with no radiation to the fetus is the initial imaging technique of choice to identify or exclude biliary etiology, the finding on which further therapy depends (Fig. 3.6). However, it is insensitive for the detection of common bile duct

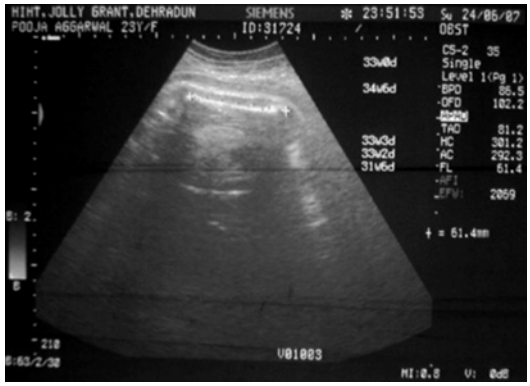

Fig. 3.7 Sonography of the same patient as in Fig. 3.6 showing femur length of 61.4 mm corresponding to 33 weeks of gestation with oligohydramnios [288]

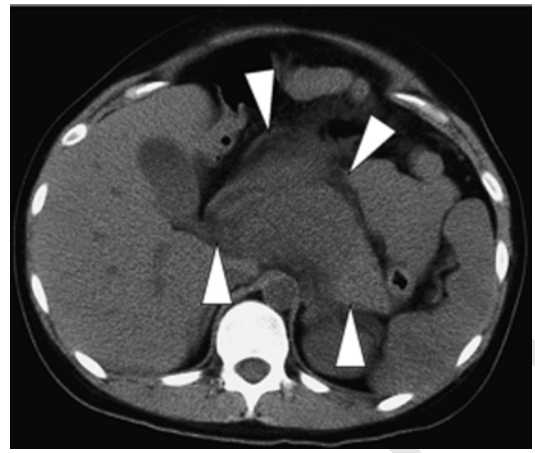

Fig. 3.8 Computed tomogram on admission of a 25-year-old primigravida at 35 weeks of gestation shows marked swelling of the pancreas (*arrowheads*) and effusion around the pancreas [289]

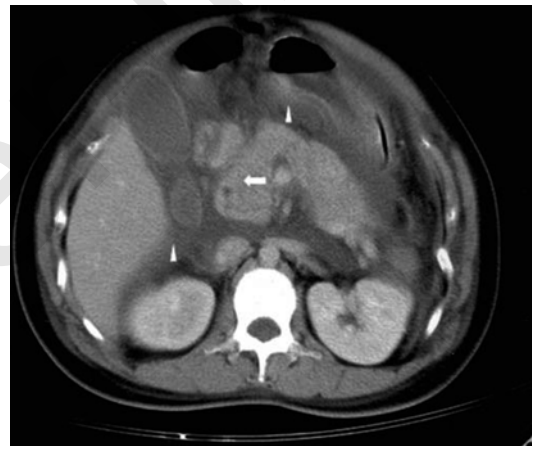

Fig. 3.9 Abdominal CT of a 28-year-old female in the 34th week of pregnancy with swelling of the pancreas and blurring of the mesenteric fat plane (*arrow*). Reactive paralytic ileus, fluid accumulation at bilateral anterior pararenal space, lesser sac, and extraperitoneal space are noted (*arrowheads*) [287]

stones or sludge and the morphological changes of the pancreas. It is not accurate for detection of dilated pancreatic ducts but is good for pseudocysts and focal accumulations larger than 2–3 cm. US is limited by operator skill, patient obesity, and bowel dilation especially found in patients with peritonitis. Additional abdominal US role is for estimation of fetal vitality by measuring direct (femur) or indirect parameters (oligohydramnios) (Fig. 3.7).

Computed tomography (CT) should be avoided, especially during the first trimester, because of radiation exposure to the fetus, but has to be performed when benefits outweighed the risk. Imaging diagnostic modalities are used not only for the diagnosis but also to provide information about the severity in AP (Figs. 3.8, 3.9, 3.10, and 3.11) [290]. In a series of 12 cases of AP in pregnant women with AFLP, Moldenhauer et al. [110] found that imaging techniques (ultrasound and computed tomography) were accurate in only 58 %. In addition, if thyroid ultrasound is equivocal, a helical CT scan is helpful in mediastinal parathyroid adenoma localization, especially during pregnancy when radioisotope techniques are contraindicated.

When a common bile duct stone is suspected, endoscopic ultrasound (EUS) has a high positive predictive value nearing 100 %, even for small stones ≤2 mm or sludge [291, 292]. EUS is considered the best imaging study to evaluate the common bile duct but requires expensive equipment, intravenous sedation, and technical expertise. It is superior to magnetic resonance cholangiopancreatography (MRCP), an imaging method providing multiplanar large field of view images of the biliopancreaticoductal system.

There are some concerns about the safety of MRCP in the first trimester of pregnancy because radiofrequency pulses result in energy deposition and could potentially result in tissue heating

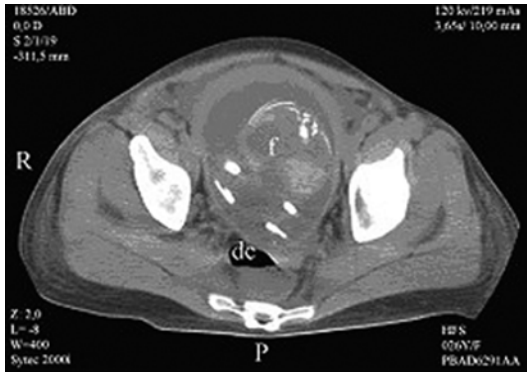

Fig. 3.10 Pregnant uterus (*f* fetus, *dc* Douglas collection) [111]

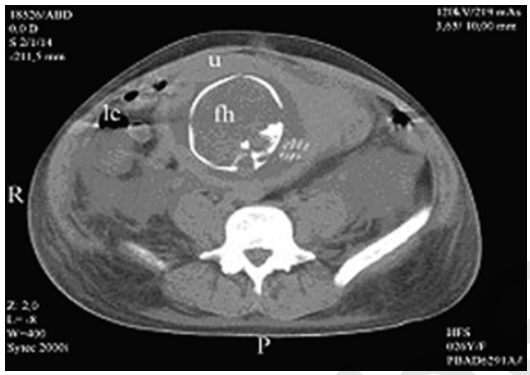

Fig. 3.11 Pregnant uterus (*u* uterus, *fh* fetal head, *lc* liquid collection) [111]

[293]. MR procedures are indicated in pregnancy if other nonionizing forms of diagnostic imaging studies are inadequate or if the examination provides information that would otherwise require exposure to ionizing radiation with excellent soft tissue contrast (Fig. 3.12) [295].

Endoscopic retrograde cholangiopancreatography (ERCP) as a diagnostic tool lost its value because of the risk of radiation and the availability of safer procedures (i.e., EUS or MRCP). ERCP should be used only as a therapeutic option in selected cases with confirmed bile duct stones. In cases of severe acute biliary pancreatitis (SABP) with or without cholangitis, early ERCP, preferably within 24 h, is recommended [296]. Decompression of the common bile duct and removal of gallstones with subsequent papillotomy could prevent complications and reduce

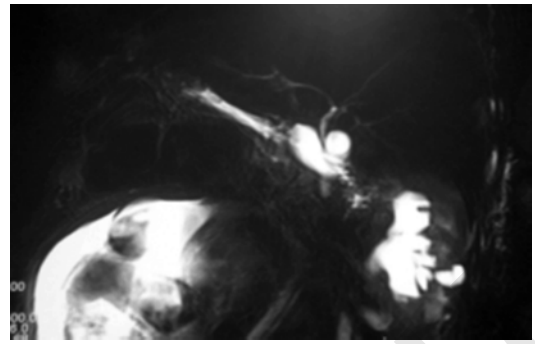

Fig. 3.12 Magnetic resonance cholangiopancreatography showing normal common bile duct and pregnancy in coronal section [294]

mortality in SABP. Before proceeding to therapeutic ERCP, a less-invasive diagnostic method such as MRCP or EUS should be performed. In pregnancy it is necessary to minimize radiation exposure during ERCP, the procedure should be carried out only by a very experienced endoscopic and radiological team, and the fetus should be shielded all the time [297, 298]. With the advent of ERCP and MRCP, the need for intraoperative cholangiogram is minimal, although there have been no reports investigating the safety of IOC during pregnancy [254]. Laparoscopic US scan appears to be alternative to retained common bile duct stones [254].

3.6 Differential Diagnosis

Differential diagnosis contains the same diseases present in nonpregnant population with the addition of some specific diseases and states present in pregnancy. Interestingly, even a case of ruptured ectopic pregnancy mimicking AP is described with elevated serum amylase and lipase levels [299]. This is due to the fact that a variety of organs and secretions contain amylase activity, including the pancreas, salivary glands, Fallopian tubes and ovarian cyst fluids, testes, thyroid, tonsils, breast milk, sweat, tears, and some malignant neoplasms [300]. Therefore, hyperamylasemia has been reported to occur in mumps, parotitis, perforated peptic ulcer, perforated appendicitis, intestinal obstruction, mesenteric infarction,

pulmonary embolism, pneumonia, myocardial infarction, lung cancer, breast cancer, lymphoma, and several tubo-ovarian disorders [264, 301–303]. The discovery that structures containing epithelium of Müllerian and mesonephric duct origin could produce amylase was made over 50 years ago [304]. In keeping with this, hyperamylasemia has been documented in association with several tubo-ovarian pathologies, including ruptured ectopic pregnancy, salpingitis, pelvic inflammatory disease, ovarian papillary serous cystadenocarcinoma, ovarian adenosquamous carcinoma, ovarian endometrioid carcinoma, mucinous tumors, and surface papillary carcinoma [305–309]. In all published cases of hyperamylasemia associated with tubo-ovarian disease in which isoenzyme analysis was performed, the predominant amylase has been shown to be either electrophoretically identical to s-type amylase or an acidic variant thereof [310–313]. However, predominantly p-type hyperamylasemia has up to this case been reported previously with tubo-ovarian disorders. In addition, according to Saruc et al. hemolysis of extravasated blood might have been the reason of the elevated pancreatic enzyme activity [314]. Ruptured ectopic pregnancy in rare situations can present with significantly elevated amylase and lipase levels mimicking the diagnosis. The problem is if hemorrhagic AP is suspected and conservative approach indicated, prolonged hemorrhage from ectopic pregnancy can lead to hemorrhagic shock [299].

In terms of diagnostic accuracy, lipase has been proven to be superior to amylase in AP [262, 315]. However, lipase is also not specific to the pancreas, having been isolated in the tongue, esophagus, stomach, duodenum, small bowel, liver, lung, and adipose tissue [264, 265]. Consequently, hyperlipasemia has been reported to appear in the event of cholecystitis, esophagitis, peptic ulcer disease, enteritis, peritonitis, and bowel obstruction and infarction [263–265]. Currently, there are only two published cases of hyperlipasemia occurring with tubo-ovarian disorders. One is aforementioned and another is Sinha et al. who presented a case of lipase activity elevation secondary to ruptured ovarian cyst [316].

3.7 Treatment

When a diagnosis of AP in pregnancy is made, assessment of severity based on clinical signs, blood tests, urinalysis, and imaging tests should be performed to determine the appropriate treatment for each patient. The treatment of AP is not standardized and is mainly supportive, and severe AP is still a significant clinical problem for all physicians. The treatment goals are to avoid organ failure and infectious complications which also influence on the fetal development. With the advances of diagnostic techniques and therapeutic methods, maternal and fetal outcomes have significantly improved over the last decades.

3.7.1 Conservative Treatment

3.7.1.1 Supportive Measures

It is important to stress that treatment includes the treatment of the AP itself and also specific treatment of the cause of AP. The initial management of AP during pregnancy is similar to management in nonpregnant patients. Treatment consists of fluid restoration, oxygen, analgesics, antiemetics, and monitoring of vital signs. An adequate volume of intravenous fluid should be administered promptly to correct the volume deficit and maintain basal fluid requirement [290, 317, 318]. Fluid resuscitation should be done carefully by closely monitoring the patient's vital signs. Important additional measures during pregnancy include fetal monitoring, attention to the choice of medications, and positioning of the mother to avoid inferior vena cava obstruction.

Mild AP (MAP) treated conservatively usually resolves within 7 days. Ten percent of patients have severe course, and they are best managed in an intensive care unit (ICU). The third-space fluid sequestration is the most serious hemodynamic disorder leading to hypovolemia and organ hypoperfusion resulting in multiple organ failure. In volume-depleted patients, the essential treatment modality is initial infusion of 500–1,000 ml of fluid per hour [319]. Monitoring of hydration, cardiovascular, renal, and respiratory functions is important for early detection of volume overload

and electrolyte disturbances [320]. In cases with severe AP (SAP), ICU should be considered, and intensive care is recommended to prevent both organ failures and infectious complications. Hemodynamic stabilization and respiratory support are the major parts of intensive care in the early period of SAP. Parenteral nutrition is considered to be safe and necessary in pregnancy [24]. Currently, there are still different opinions on the use of total parenteral nutrition (TPN) or enteral nutrition (EN). Pezzilli et al. showed that enteral feeding in SAP is better than TPN, because EN may help to maintain the immune function of the gastrointestinal mucosa, protect the mucosal barrier, and improve the blood supply to the small intestine [290].

Many pharmacological agents (somatostatin, octreotide, N-acetylcysteine, gabexate mesylate, lexipafant, and probiotics) have been investigated in AP, but because most of them have failed to show a positive effect, they should be avoided in pregnancy. The use of Stilamin (Somatostatin) may be effective to improve pathophysiology of the pancreas, especially in the early stage of AP. Applying Stilamin (Somatostatin) to inhibit both exocrine and endocrine portions of the pancreas is a very important part of nonsurgical treatment. However, it has not yet been proved whether somatostatin should be applied in pregnancy because of its potential effect on the fetus. In study by Li et al. Stilamin (Somatostatin) was administered in ten cases with good outcomes without malformations and abnormal newborn [78]. Treatment strategy cases with SAP is as follows: when the benefits of the drug may outweigh its risks with the permission of the patient and the agreement and signing of her family member, Stilamin (Somatostatin) is used in the early stage of SAP. Stilamin (Somatostatin) should be infused continuously with intravenous syringe infusion pumps with a low dose (150–250 μg/h) for 24–72 h and then reduced or withdrawn timely when the condition improves with hemodynamic stabilization. Despite the encouraging results, the data are limited, and somatostatin is not recommended for routine use.

Cessation of oral feeding has been thought to suppress the exocrine function of the pancreas and to prevent further pancreatic autodigestion. Bowel rest is associated with increased infectious complications, and TPN and EN have an important role in the management of AP. Keeping the patients *nil by mouth* with the use of TPN has been for years a traditional treatment of AP but carries a significant risk of infections and metabolic distress. EN is physiological, helps the gut flora maintain the gut mucosal immunity, and reduced translocation of bacteria, while simultaneously avoiding all the risks of TPN. Parenteral nutrition in pregnancy is considered safe and necessary when adequate oral nutrition is not possible, although the frequency of complications from centrally inserted catheters is higher than in nonpregnant patients [321]. Mild cases of AP do not need nutritional support, as the clinical course is usually uncomplicated and a low-fat diet can be started within 3–5 days. Treatment of SAP should include enteral feeding by nasojejunal tube and, if needed, should be supplemented by parenteral nutrition [322].

3.7.1.2 Antibiotics

Prophylactic use of antibiotics is very controversial and the choice of antibiotic in pregnancy is difficult. There are concerns with regard to the antibiotic being transplacentally transferred to the fetus with a risk of teratogenicity. Antibiotics have no role in the treatment of mild AP, normal common bile duct size, and no evidence for cholangitis, while the control of infection in the treatment of SAP plays an important role [290, 317, 318]. The use of prophylactic broad-spectrum antibiotics could reduce infection rates in necrotizing form of SAP [290]. The use of prophylactic antibiotics in severe AP remains controversial. The available evidence demonstrates that antibiotic prophylaxis might have a protective effect against non-pancreatic infections but failed to show a benefit on reduction of mortality, infected necrosis, and need for surgical intervention [296, 323, 324]. But the choice of antibiotic in pregnancy is difficult, and literatures show that penicillins and cephalosporins are preferred. There is no benefit in the prophylactic use of antibiotics in AP complicated by CT-proven pancreatic necrosis in the general population [323, 325]. In a meta-analysis, only imipenem significantly reduced the risk of pancreatic infection [325].

The use of imipenem/cilastatin is indicated in necrotizing AP, but dose adjustment in pregnancy should be considered even though there are currently no studies proposing the optimal dose [326]. Imipenem (N-formimidoyl thienamycin) is classified as category C although limited animal studies have shown no teratogenic risk or adverse fetal effects; data in humans are not available [327]. The pharmacokinetics of imipenem will change during pregnancy with a larger volume of distribution and faster total clearance from plasma [328]. The dose adjustment during pregnancy should be considered. Metronidazole passes freely across the placenta. However, studies from the 1990s do not show any association with an increased risk of teratogenic effects with metronidazole [329, 330]. Quinolones have been classified as category C because adverse effects have been noted in some animal studies. Due to the lack of evidence on beneficial effect of antibiotics, an even more conservative approach is recommended in pregnancy. Regardless of initial drug regimen, therapy should be modified to reflect the organisms recovered in blood cultures and the clinical status of the patient.

3.7.1.3 Continuous Renal Replacement Therapy

Continuous renal replacement therapy (CRRT), including a variety of blood purification techniques, which can remove water, nitrogenous wastes, and even inflammatory mediators, slowly and steadily, has been widely used in patients with critical conditions such as severe AP. CRRT is associated with significant improvement in pulmonary gas exchange, hemodynamic instability, azotemia control, fluid overload, and nutritional support in patients with MODS and acute renal failure [331]. Yekebas et al. [332] investigated the impact of different modalities on sepsis-induced alterations in the course of experimental AP, finding that CVVH (continuous veno-venous hemofiltration) can prevent sepsis and improve survival. Wang et al. [333] applied continuous high-volume hemofiltration in the treatment of patients with severe AP complicated with MODS and achieved satisfactory results. However, CVVH does not allow large molecules to pass through the hemofilter. Ronco et al. [334] proposed a *peak concentration hypothesis* of MODS and found that CVVH can be combined with plasma filtration absorption techniques to remove the excess circulating inflammatory mediators. HP (hemoperfusion) is another blood purification modality which can absorb pathogenic molecules in the blood flow circuit by sorbent materials installed in the hemoperfusion cartridge. Unlike CVVH, HP is more effective for removing middle and large molecules and toxins bound to proteins. For this reason, HP is wildly applied in drug overdose or intoxication cases [335]. Saotome et al. [336] reported a case of severe AP induced by alcohol abuse using CTR-001 direct HP cartridge to perform cytokine apheresis and demonstrated that this treatment can effectively reduce the serum levels of pro-inflammatory cytokines during severe AP. A pilot study performed by Kobe et al. [337] using direct HP (CYT-860) in patients with hypercytokinemia reported significant decrease in blood level of cytokines and improvement of PaO_2/FiO_2. Besides, a prospective, pilot, before-and-after self-crossover clinical trial carried out by Mao et al. [338] investigated the effect of coupled plasma filtration adsorption (CPFA) on the immune function of patients with MODS, finding that CPFA (using the resin cartridge HA-330I) was better than high-volume hemofiltration (HVHF) in increasing the ratios of anti-inflammatory to pro-inflammatory mediators, improving antigen presentation ability, and restoring leukocyte responsiveness. In only pregnant patient with AP, authors combined CVVH and broad-spectrum HP, assuming that HP can effectively remove excess endogenous and exogenous pathogenic molecules. The treatment was successful. After the first 3 days of treatment, the patient's general condition significantly improved and her laboratory parameters virtually normalized [339]. Several studies suggest that toxic free fatty acids derived from plasma triglycerides induce local inflammation, leading to AP [144, 145]. HP may be more effective in clearing these fat-soluble factors because of its specific design. After receiving HP and CVVH treatments, the

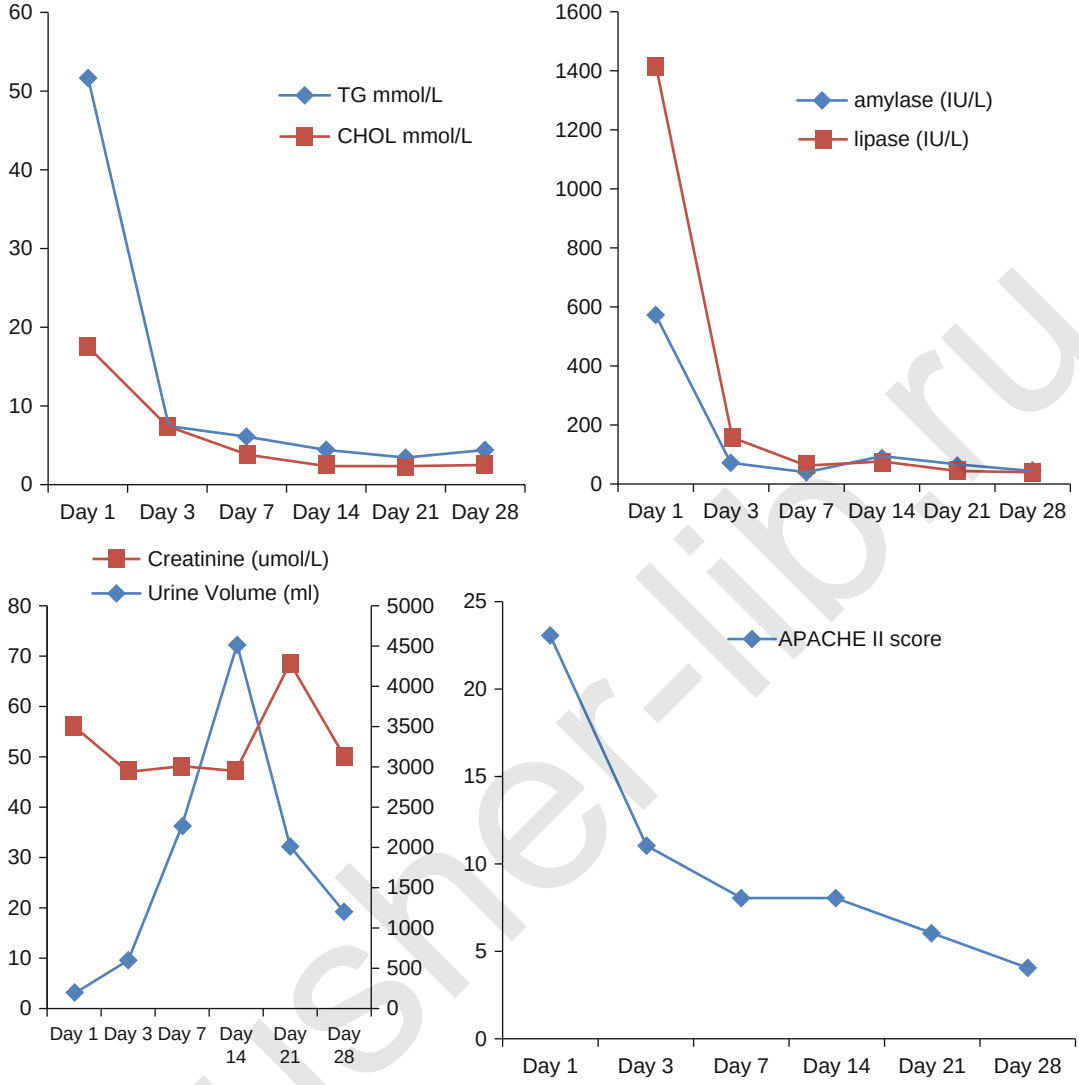

Fig. 3.13 The changing tendency of triglyceride (*TG*), cholesterol (*CHOL*), amylase, lipase, renal

TG, CHOL, amylase, and lipase levels decreased dramatically (Fig. 3.13), explaining rapid recovery [339]. Moreover, the patient developed no side effects such as coagulopathy, hypotension, thrombocytopenia, or hypocalcemia.

Function, and APACHE II score during the treatment. CVVH and HP were initiated on day 1 and discontinued HP on day 3. CVVH was stopped on day 7. Normal range: TG 0.29–1.83 mmol/l, CHOL 2.8–5.7 mmol/l, amylase 25–125 IU/l, lipase 13–60 IU/l [339]

3.7.1.4 Intensive Care Unit Referral

In the general population, indicators for admission to ICU are [340]:

- Need for fluid resuscitation
- BMI >30 kg/m^2
- Pleural effusions
- CRP >150 mg/dl at 48 h
- Necrosis of over 30 % of the pancreas
- Ranson criteria ≥3

Organ failure may occur in 50 % of patients. Early admission and management of critically ill obstetric patients in the ICU decreases maternal mortality and morbidity [341].

3.7.1.5 Hyperlipidemic/ Hypertriglyceridemic Pancreatitis

While a moderate increase in plasma lipids in pregnancy is seen normally, severe HTG, predominantly chylomicrons and VLDL, is rarely encountered. This can however be a serious health problem if undetected as the predisposition to AP poses a significant risk of mortality for both mother and fetus [258]. Multiple treatment modalities have been suggested in the management of HTG-induced AP, but no clear consensus or accepted guidelines have been established [283].

The goals of management of pregnant patients with HTG-induced AP should include decreasing the serum triglyceride concentration and pancreatic activity while supplying maternal and fetal nutritional needs. Preconceptional control of TG levels may prevent or shorten the course of AP. Achieving these goals may be quite challenging. Therapies like plasma exchange, use of gemfibrozil, and extracorporeal lipid elimination may be effective in controlling triglyceridemia but do not meet the nutritional requirements of the mother and child [342, 343].

Avoidance of oral diet and intravenous administration of 5 % dextrose along with insulin often lead to a dramatic reduction of serum triglycerides [344]. A favorable effect of intravenous hyperalimentation (IVH) with nothing by mouth on AP with hyperlipidemia and pregnancy was referred by Weinberg et al. in 1982 [345]. The patient's symptoms and triglyceride levels were only controlled after initiation of lipid-free total parenteral nutrition; however, the fetus developed intrauterine fetal growth retardation, while in a case by Ihimoyan et al. the patient delivered a healthy neonate with no compromise on fetal growth [346]. However, intravenous 5 % dextrose does not supply enough calories and could not be used for the extended duration required for enteric rest.

Dietary modification with a minimal fat oral diet should theoretically reduce chylomicron levels and decrease serum triglyceride concentration. However, it paradoxically increases the synthesis of very low-density lipoproteins which leads to enhanced production of triglycerides by the liver elevating the serum triglyceride levels [345]. The growing fetus requires essential fatty acids and amino acids for development and maturity of vital organs like the brain and lungs. TPN is an effective means of providing the necessary calories and essential amino acids for the growing fetus while controlling the maternal triglyceride concentrations and preventing the induction of AP. TPN with up to 10 % of calories of fat does not significantly increase maternal serum triglycerides. This is because of the systemic delivery of lipids which bypasses the liver where production of triglyceride-rich lipoproteins occurs. It also enables the supply of other nutritional supplements that are required by the fetus. The first reported case of TPN use in gestational HTG-induced AP was described by Weinberg et al. [345]. The patient's symptoms and triglyceride levels were only controlled after initiation of lipid-free total parenteral nutrition; however, the fetus developed intrauterine fetal growth retardation. Parenteral nutrition in pregnancy should be managed preferably by an experienced clinical nutrition support staff. Other case of TPN resulted in the delivery of healthy neonate [346]. The major complications are related to central venous catheter placement and include pneumothorax, hemorrhage, and rarely death [347]. There has been a trend toward the use of peripherally inserted central catheters (PICC) because of lower rate of major complications and relative ease of insertion compared to central venous catheters [347]. PICCs should always be considered particularly in high-risk populations like pregnant women. Several studies however have shown a higher rate of minor complications like thrombophlebitis in patients with PICCs [321, 348]. PICC insertion is highly operator dependent, and lowest complication rates have been seen in the most experienced centers [349].

Additionally, lipid-lowering medications or plasma exchange has also been described in the literature as alternative therapies [277, 350, 351].

Here is one example of clinical course during lipid-lowering diet of hyperlipidemic AP during first and second pregnancy of the same patient (Figs. 3.14 and 3.15).

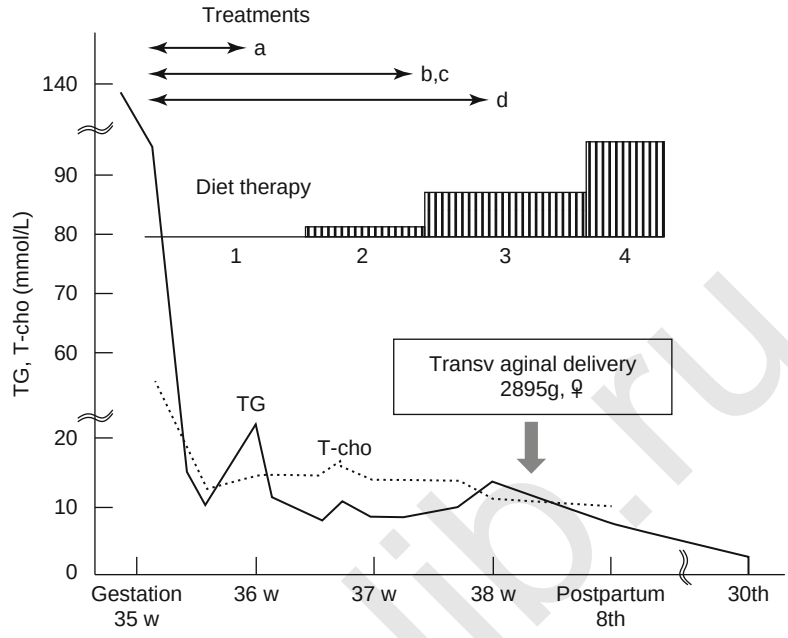

Fig. 3.14 Clinical course of the first pregnancy with type V hyperlipidemia (complicated with AP). Treatments were dietary therapy ((*1*), fasting for 11 d; (*2*), fat-restricted diet including 2.0 g of fat for 6 d; (*3*), fat-restricted diet including 10.0 g of fat; and (*4*), fat-restricted diet including 20.0 g of fat) and (*a*) a protease inhibitor (ulinastatin), (*b*) antibiotics (piperacillin, sulbactam/cefoperazone), (*c*) H_2-blocker (famotidine), and (*d*) anticoagulation therapy (heparin) from admission. *T-cho* total cholesterol, *TG* triacylglycerol [289]

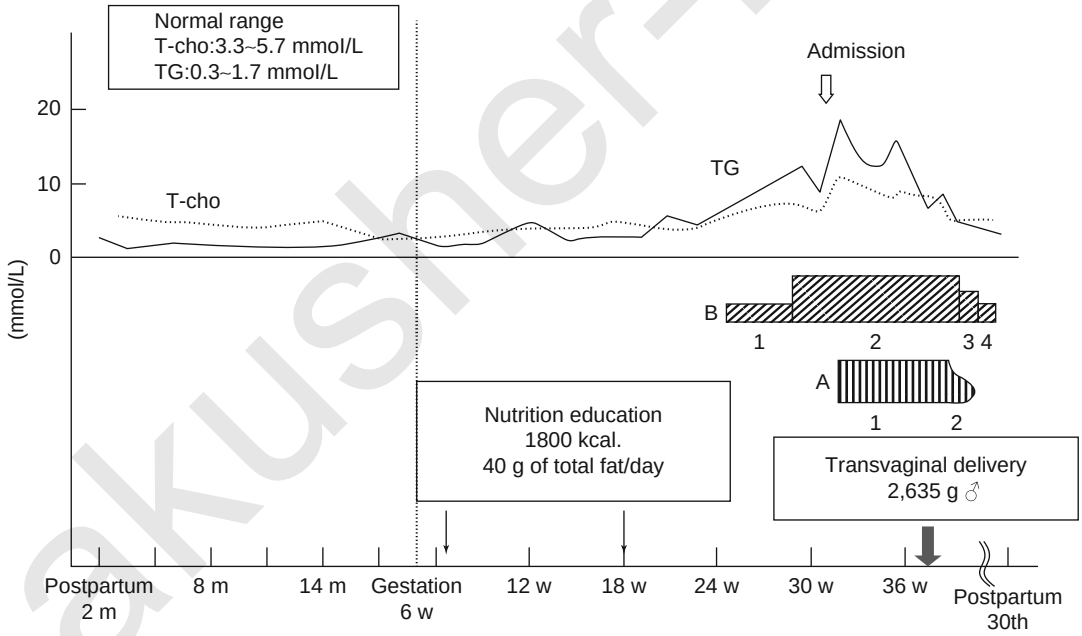

Fig. 3.15 Clinical course of the second pregnancy with type V hyperlipidemia of the same patient (without AP). Treatments were (*A*) dietary therapy ((*1*), fat-restricted diet including 20 g of fat daily; (*2*), fat-restricted diet including 15 g of fat daily) and (*B*) u-3 fatty acids ((*1*), 0.9 g; (*2*), 2.7 g; (*3*), 1.8 g; (*4*), 0.9 g). *T-cho* total cholesterol, *TG* triacylglycerol [289]

Insulin

Insulin activates LPL, an enzyme that accelerates chylomicron degradation into glycerol and FFAs. Insulin has also been shown to increase messenger RNA levels of LPL in animal adipose cells in vitro [352]. A few case series have demonstrated successful management with insulin monotherapy in the setting of HTG-induced AP [353–355].

Insulin (with administration of glucose) is safe and effective in the treatment of HTG-induced AP, even in patients without DM [353, 354]. Intravenous insulin may be more effective than subcutaneous insulin in severe cases given the potential limitations of absorption with the subcutaneous route. Intravenous insulin may be given as a continuous infusion starting with 0.1–0.3 U/kg per hour with titration as required.

Heparin

LPL is a ubiquitous, endothelially bound lipolytic enzyme. Intravenous heparin uncouples the enzyme from its endothelial anchor, thus stimulating the release of endothelial LPL into the circulation [356]. It has been used without insulin to successfully manage HTG [351, 357, 358]. A heparin dose of 10,000 U/day seems to be safe, as evidenced by a normal APTT [351]. Despite the success of intravenous heparin in combination with insulin in HTG management, heparin has come under greater scrutiny. Intravenous heparin does cause an initial rise in circulating LPL levels but is quickly followed by increased hepatic degradation [359]. This degradation contributes to further depletion in plasma stores of LPL and may ultimately potentiate the subsequent accumulation of circulating chylomicrons [360]. A further potential hazard is the risk of transformation into hemorrhagic AP. Heparin has been used to lower triglyceride levels. There are reports in the literature in which heparin therapy for AP has been seen to be both therapeutic and safe [158, 351]. Although heparin is an option to control triglyceride levels, women with AP are at risk for life-threatening hemorrhage within the pancreas, and therefore heparin could conceivably worsen the ultimate outcome.

Extracorporeal Elimination of Triglyceride-Rich Lipoproteins

Plasma apheresis for severe HTG was first reported in 1978 [361]. There are several controversial aspects to plasma apheresis including technical controversies as to whether plasma exchange is more efficacious than double membrane filtration. In clinical practice, appropriate and timely access to plasma apheresis is rare, and the evidence supporting its utility in HTG-induced AP has been confined to isolated case reports [283]. Plasmapheresis is successful in lowering TG levels. However, in the absence of a comparison with standard treatment (heparin or insulin infusion and lipid-lowering agents), the effect of plasmapheresis on lowering the morbidity and length of stay of patients with HTG-induced severe AP is uncertain and warrants further investigation into its efficacy. Another problem is the small number of patients for making strong prospective studies [142].

In the follow-on phase, as the triglyceride levels usually rapidly decrease within 48 h of the onset of AP, an accurate diagnosis outlining the etiology of the HTG and prevention of further attacks takes priority. Treatment modalities include dietary intervention initially, followed by drug therapy that includes a spectrum of pharmacological agents such as the fibric acid derivatives, omega-3 fatty acids, and nicotinic acid derivatives, insulin, and/or heparin treatment. When the etiology is LPL deficiency, pharmacological therapy is relatively ineffective. In this setting, the role of dietary restriction is central.

First reports of long-term extracorporeal elimination of triglyceride-rich lipoproteins by three modes of treatment (plasma exchange, immunospecific apheresis, and a combination of both treatments) were by Swoboda et al. [342, 362]. The loss of immunoglobulins remained acceptable.

Drug Therapy

Fibrates

Fibrates effectively lower triglyceride levels by 40–60 % and raise HDL-C levels [363, 364]. The triglyceride-lowering effects of fibrates have been attributed to enhanced catabolism of triglyceride-rich particles and reduced secretion of VLDL [363]. Nicotinic acid lowers triglyceride levels by 30–50 % [364] by reducing VLDL secretion, but flushing and gastric upset are prominent side effects [137]. Omega-3 fatty acids, studied in a prospective, double-blind, placebo-controlled trial, have proved capable of lowering high triglycerides (5.5–22.5 mmol/l, 500–2,000 mg/dl) by 45 % [365]. Fenofibrate 200 mg and niacin 500 mg daily and omega-3

fatty acids are relatively ineffective in patients with primary (genetic) HTG.

All fibric acid derivatives are renally excreted and can consequently display a prolonged plasma half-life of several days in severe renal impairment cases. Since all fibric acid derivatives have a high degree of protein binding (>95 %), none are removed by hemodialysis [366]. Gemfibrozil is the most frequently prescribed lipid-lowering agent for patients with renal insufficiency, as it is least dependent on renal excretion [367]. Gemfibrozil has however been reported to cause rhabdomyolysis in patients with compromised renal function. Although most incidences of rhabdomyolysis occur in patients taking both gemfibrozil and HMG-CoA reductase inhibitor [368, 369], rhabdomyolysis induced by gemfibrozil alone has also been reported [370]. The pathophysiologic mechanism of gemfibrozil toxicity remains unknown [367, 370], despite its relatively frequent occurrence.

Statins

Although statins have been identified as potential teratogens on the basis of theoretical considerations and small case series, the available evidence is far from conclusive. In fact, epidemiological data collected to date suggest that statins are not major teratogens. The actual risk for an exposed pregnancy seems to be small, if present at all, and does not by itself warrant termination of pregnancy. Nevertheless, given the scarcity of available data, it is still advisable to avoid use of these drugs in patients who are planning pregnancy in order to reduce the risks as much as possible [371, 372]. Statins are used for lowering cholesterol in general population but there are also cases of statin-induced AP (see Sect. 3.3).

Prophylactic Plasma Apheresis

Despite legitimate safety concerns regarding the use of fibrates, nicotinic acid, and omega-3 fatty acids in pregnancy, case reports of patients being prescribed these drugs suggest that they may be safe from both the maternal and fetal perspective [373]. As always, a careful risk-benefit analysis needs to be made when considering these therapeutic agents. Other treatment options for unresponsive patients include insulin/heparin therapy and plasma apheresis [374]. "Prophylactic" plasma apheresis has been proposed as a preventive treatment for severe uncontrolled HTG resistant to diet and drug therapy, and Piolot et al. have reported a reduced incidence of AP in such patients treated with prophylactic plasma apheresis at 4-week intervals [375].

Because pregnancy might lead to the exacerbation of hypertriglyceridemia in patients with familial hyperlipidemia, delivery is advocated because it is estimated to lower lipid levels by 15–20 % within 24 h and return them to prepregnant levels by 6 weeks postpartum [129, 342, 376, 377]. Others believe that there is no improvement in maternal outcome and that fetal and maternal health may be jeopardized by complicated delivery. In preterm pregnancies, delivery is recommended only if maternal or fetal condition deteriorates taking into account history of episodes of AP, gestational age, and the presence of persistent disease. The mode of delivery should be determined by obstetric factors [378].

Dietary Approach

The patient will be required to work closely with the dietician who must focus on a low-fat diet; this is primarily to cut off the production of chylomicrons [379]. Severe HTG can be exacerbated during pregnancy, imposing an even greater need for strict adherence to a low-fat diet, usually ≤20 g/day and sometimes as low as ≤10 g/day. Total caloric intake should be adequate, and what little fat is ingested should contain omega-3 and omega-6 fatty acids [289]. Medium-chain triglyceride-rich foods, such as coconut oil, can be used for cooking, as they are absorbed directly into the portal vein without becoming incorporated into the chylomicron triglyceride. The success of this therapy depends on the individual's acceptance of the fat restriction, including both unsaturated and saturated fat.

Antioxidant therapy has been used by some experts in the management of HTG in patients with recurrent AP due to familial LPL deficiency [380]. This antioxidant cocktail significantly reduced the recurrence of AP in these individuals. It is thought that they neutralize free radicals resulting from chylomicronemia-related microvascular ischemia

and thereby prevent the potential damage to pancreatic acinar cells and the resulting AP. A suggested pharmacological dose utilizes Antox® version 1.2 that contains antioxidants such as α-tocopherol, β-carotene, vitamin C, organic selenium, and methionine. The dose is two tablets three times a day.

3.7.1.6 Pancreatitis Secondary to Hyperparathyroidism

Hypercalcemia is the underlying cause of many of the maternal and fetal risks associated with hyperparathyroidism, and management normalizes the calcium level, decreasing these complications. Rajala et al. theorized that high-dose magnesium might be a therapeutic alternative for hyperparathyroidism in pregnancy [59].

In the reported cases, the hypercalcemia was managed with medical intervention, usually with magnesium infusion [44, 64]. When magnesium proves ineffective, other agents such as phosphate-of-soda enemas, oral phosphates, calcitonin, and loop diuretics have been used with varied success [43, 59]. In the past mithramycin was used but is currently contraindicated secondary to teratogenic effects [57]. Corticosteroids have also been used to decrease the absorption by the gastrointestinal tract but have shown minimal effect when the hypercalcemia is secondary to hyperparathyroidism [57]. Patient in one case report had undetectable levels of parathyroid hormone while receiving magnesium therapy, serum calcium never normalized, and serum vitamin D-1,25 was elevated. It is possible that a compensatory increase in serum vitamin D-1,25 in response to the decrease in the parathyroid hormone level caused by the magnesium increased calcium absorption from the gastrointestinal tract. Therefore, for some patients, because of persistent hypercalcemia, magnesium sulfate might not be a viable treatment option for hyperparathyroidism during pregnancy [44].

3.7.2 Surgical Treatment

3.7.2.1 Anesthetic Considerations

Before surgical treatment, anesthetic considerations are important in pregnant population. The choice of anesthesia for Cesarean delivery is not clearly defined. Hemodynamic stability may be better with general anesthesia and may be of benefit in the presence of sepsis and use of anticoagulants such as heparin. General anesthesia was chosen to allow greater hemodynamic control and facilitate management of the acid-base status especially in patients receiving epoprostenol for CVVH. Postoperative ventilatory support on ICU permits resolution of the acidosis.

3.7.2.2 Surgical Principles

Surgical treatment has two aspects, which include operative intervention for the AP itself and surgical management of associated local (biliary tract disease) or distant (PHPT, HTG, etc.) cause of the AP during attack or once acute inflammation subsides.

Since the first study published in 1963 [381] (see Chap. 2), the dilemma, whether or not to treat pregnant patients with gallstones conservatively, still exists. Risk of conservative treatment includes risk to the fetus due to recurrent episodes, complications of gallstones, and risk of malnutrition caused by lack of oral intake. Conversely, surgical treatment carries risk to the fetus from surgery and anesthesia and risk specific to laparoscopic surgery. Laparoscopic cholecystectomy (once considered contraindicated during pregnancy) [382] is currently the best treatment for the patients who failed to respond to conservative management or because of recurrent episodes [315, 383]. Benefits of laparoscopy during pregnancy appear similar to those nonpregnant patients including less postoperative pain, less postoperative ileus, significantly reduced hospitalization, and decreased narcotic use and quick return to a regular diet and faster recovery. Other advantages of laparoscopy include less manipulation of the uterus and detection of other pathology that may be present and because of early mobility reduced risk of postoperative deep vein thrombosis [254]. Cholecystectomy is considered safe at all stages of pregnancy and may be performed in any trimester of pregnancy without any increased risk to the mother or fetus [315, 383]. Historical recommendations to delay surgery until the second trimester or gestational age

limit of 26–28 weeks of pregnancy have been refuted. Laparoscopy in pregnancy was connected with the fear of damage to the gravid uterus upon Veress or trocar insertion; technical difficulty in performing the surgery with the presence of an enlarged, gravid uterus; and the concern of fetal acidemia due to decreased uterine blood flow because of increased intra-abdominal pressure from insufflation and possible fetal carbon dioxide absorption [13]. Also, maternal venous return secondary to increased intraperitoneal pressure from CO_2 insufflation could be present. The use of a uterine manipulator is contraindicated in pregnancy. At the beginning of 2011, *The Society of American Gastrointestinal and Endoscopic Surgeons* (SAGES) updated its guidelines for laparoscopy during pregnancy [383]. A report from 1999 suggests that the risk of fetal wasting and teratogenicity from gastrointestinal operation during pregnancy is minimal [384]. However, some precautions should be followed: the use of an open technique for the insertion of the umbilical port, avoiding high intraperitoneal pressures, using of left lateral position to minimize aortocaval compression, avoiding rapid changes in the position of the patient, and using electrocautery cautiously and away from the uterus [254].

Early cholecystectomy should be performed in patients with mild biliary AP, while patients with SABP should undergo this procedure within 4–6 weeks after hospital discharge [320].

Early surgery for necrotizing AP is not recommended, and it should be delayed as long as possible [25, 385]. Antibiotics are not indicated. The data suggest that remission could be achieved in most patients (78.9 %) with the conservative treatment. Therefore, the indications for surgery [25, 290, 317, 318, 340, 385] and antibiotics are as follows:

- Pancreatic necrosis and infection (3–4 weeks after the onset of symptoms)
- Large intra-abdominal exudates
- Clinical deterioration (Fig. 3.16)

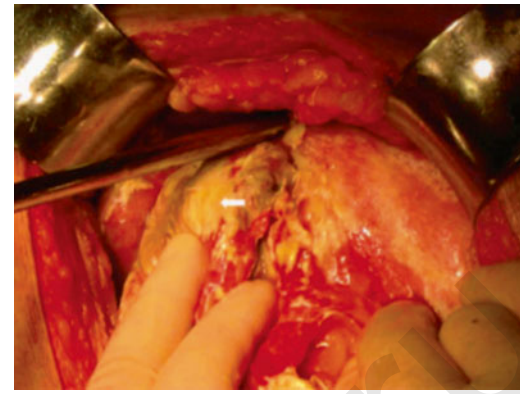

Fig. 3.16 Prominent pus coating over the omentum, intestine, and colon, peripancreatic fatty necrosis, and excessive solid mass of swollen inflamed pancreas are noted. An area of impending perforation (*arrow*) over the transverse colon is also visible [287]

Minimal invasive surgical techniques are new in the management of AP with only a few relatively small series reported to date [386].

Percutaneous drainage, endoscopic drainage, or surgical procedures can be selected in accordance with the conditions of individual cases. Some reports show that the decompression and percutaneous drainage help avoid or delay surgery in most patients with SAP [25, 318, 385]. For patients with pancreatic abscess, drainage is recommended [317, 387]. Necrosectomy should be performed as late as possible and it can be also performed in the Cesarean section.

Pancreatic Pseudocysts

In nonpregnant patients, pancreatic pseudocysts are most frequently associated with alcoholic AP. The recommended management is to observe asymptomatic pseudocysts and those present for less than 6 weeks, as these have a 30–40 % rate of spontaneous resolution [388]. Internal drainage is preferred for symptomatic cysts >5 cm in diameter or those present for over 6 weeks, as these have a 3 % chance of resolution and a 57 % risk of rupture, infection, hemorrhage, or obstruction [389]. Internal drainage can be accomplished by anastomosis to the duodenum, a Roux-en-Y limb of the jejunum, or the posterior wall of the stomach. When the pseudocyst is infected, located greater than 1 cm from the bowel, or has

a cyst wall insufficiently thick to permit anastomosis, percutaneous drainage can be considered despite a recurrence rate of 20–70 % [389, 390] and the potential risks of infection [391] and fistulization [390].

Endoscopy is used to avert surgery in high-risk cases [392]. An indwelling transgastric or transduodenal pigtail catheter may be placed or a more permanent internal fistula created by cautery between the cyst and the adjacent viscus. This last procedure, while reportedly effective, carries a significant risk of bleeding and depends on the skill of the endoscopist. Endoscopic transpapillary stenting is another alternative for patients with a partial pancreatic duct disruption and a communicating pseudocyst [388]. Limited information is available to guide the management of pancreatic pseudocysts in pregnancy. Many case reports of pancreatic pseudocysts occurring during pregnancy are limited by the lack of ultrasound measurements. Recommendation is that uncomplicated pseudocysts should be surgically managed in the postpartum period [393, 394].

Table 3.5 compiles the available information about presentation, etiology, management, and outcomes in these cases since 1980, when ultrasound, amylase, and lipase became widely available [395].

Pancreatic pseudocysts complicate 6.9 % of cases of AP and are almost never found in association with gallstone AP in pregnancy [396]. Six of the eight women of known gestation were primiparous. Alcohol was the etiology in less than a quarter of the cases. Gallstones, by far the most common cause of AP during pregnancy [15], accounted for only one case. Hyperlipidemia accounted for almost half of the cases. One patient was found to have Type I familial hyperlipoproteinemia [74] and another type V [257]. Two other cases were not fully diagnosed [397, 398]. Although their values are suggestive of type V hyperlipoproteinemia, it would be unwise to presume the diagnosis because type I may masquerade as type V in times of stress [257]. It can be concluded that non-gallstone AP in pregnancy has been shown to be significantly more prone to pseudocyst formation [24].

The natural history of pancreatic pseudocysts appears similar to that in nongravid patients because pseudocysts less than 5 cm shrank or resolved while those greater than 5 cm remained the same size or enlarged. In three cases, intervention was performed antepartum: two patients underwent percutaneous drainage and one was stented endoscopically. Percutaneous drainage of one 6 cm cyst had an unspecified result [35]; another, of a 13 cm cyst at 24 weeks gestation, showed initial relief of symptoms and reduction in cyst size with daily aspirations. However, in the latter case, the cyst subsequently collapsed around the drain, the cyst reaccumulated, and the patient had a preterm delivery [399]. One patient had a cystogastric stent placed with ERCP at 17 weeks gestation. In this case, the cyst shrank from 7 to 2 cm after the stent placement but grew rapidly to 4 cm once the stent fell out. A transpapillary stent was then placed at 35 weeks gestation, which stabilized the cyst until delivery at term [392]. Two cases of successful vaginal delivery were reported in women with 8 and 4 cm pseudocysts [392, 400], but concern over the risks of Valsalva during labor seems warranted in light of one report of a pancreatic pseudocyst rupturing during vaginal delivery, causing hypotension and shock and necessitating intensive care [257]. With the exception of this case and Tang et al.'s [395] patient's splenectomy, all cases of morbidity reported in Table 3.5 resulted from AP or its underlying cause, rather than from the pseudocyst. Cystic neoplasms are even less common than pancreatic pseudocysts but can occur during pregnancy [401–403] and may mimic inflammatory fluid collections. Especially notable is papillary cystic neoplasm, which occurs predominantly in young women and whose growth may be enhanced by progesterone [402]. Factors to help differentiate inflammatory from neoplastic fluid collections include serum amylase level, which is elevated in 50–75 % of pseudocysts [404] and 5 % of pancreatic neoplasms[390]; cyst amylase level, which is normal in neoplasm and elevated in inflammatory fluid collections; ultrasonography demonstrating multiple cysts or internal septa that suggest neoplasm rather than inflammation [404]; and a history of AP

Table 3.5 Characteristics of pancreatic pseudocysts in pregnancy [395]

Author	Age/gravida, para/EGA	EGA when cyst was found	Size and location	Etiology	History of cyst	Management	Delivery	Morbidity and mortality
Nies	26 years old/ gravida 2, para 0/34 weeks	PP	6 cm, tail	Lipid	Remained the same size	Conservative	Vaginal PT	Pleural effusion versus pneumonia; ICU
Glueck	gravida 1, para 0/39 weeks	PP	N/A	Lipid	N/A	Conservative	Vaginal T	Ruptured cyst, shock, ICU
Chen	28 years old/ gravida 2, para 1/31 weeks	31 weeks	4 cm, tail	Lipid	Shrunk to 2 cm spontaneously	Conservative	N/A	None
Bar-David	28 years old/ gravida 1, para 0/17 weeks	29 weeks	N/A	Lipid	Infected pancreatic pseudocyst noted at 29 weeks disappeared by 37 weeks	Conservative	Vaginal T	Septic shock, pneumonia with mechanical ventilation, TPN, ICU
Stowell	37 years old/ gravida 3, para 2/31 weeks	31 weeks	5 cm, head; 8 cm, tail	Alcohol	Cyst in head resolved; tail cyst remained the same size	Conservative; PP cystgastrostomy	Vaginal T	TPN for 5 weeks; FGR
Ryan	35 years old/6 weeks	Present before pregnancy	6 cm, tail	Idiopathic (alcohol?)	Grew to 7 cm; shrunk to 2 cm after stent; grew to 4 cm when stent fell out; stent replaced and cyst stable until 2 months PP	Cystogastric stent placed by ERCP at 17 weeks; transpapillary stent placed at 35 weeks; PP pancreatectomy	Vaginal T	None
Beattie	20 years old/ gravida 1, para 0/24 weeks	27 weeks	13 cm, posterior to stomach	Anatomic	1 l of fluid aspirated, then daily aspirations	Percutaneous drainage at 24 weeks; PP hepatico-jejunostomy	C/S PT	Cyst collapsed around drain
Eddy	24 years old/ gravida 3, para 0/26 weeks	26 weeks	6 cm, tail	GS	Grew to 15 cm	Conservative; PP pancreatectomy	C/S T	TPN for 3 weeks; splenectomy
Swisher	N/A	N/A	6 cm	Non-GS (alcohol or idiopathic)	N/A	Percutaneous drainage	N/A	N/A
Hess	25 years old/ gravida 1, para 0/31 weeks	PP	N/A	Hyperparathyroidism	N/A	Conservative	Induced Vaginal PT	Initial mental status changes, hypocalcemia after neck surgery renal failure

G gravity, *P* parity, *EGA* estimated gestational age, *N/A* information not available, *GS* gallstone pancreatitis, *PP* postpartum, *C/S* cesarean section, *T* term, *PT* preterm, *TPN* total parenteral nutrition, *ICU* transfer to intensive care unit, *FGR* fetal growth restriction

or antecedent factors suggesting an inflammatory cause such as gallstones, hyperlipidemia, or alcoholism. There is only one case published of mucinous cystadenoma of the pancreas in pregnancy causing AP [77]. The presence of estrogen and progesterone receptors in the stroma of these cysts may cause accelerated cystic growth during pregnancy [405].

Primary Hyperparathyroidism

PHPT in pregnancy represents a significant risk for maternal and fetal complications that cannot be predicted by duration of symptoms or serum calcium levels. Persistency of symptoms and mainly calcium levels above 11 mg/dl are considered indications for surgical treatment, regardless of the trimester of pregnancy. Truong et al. favor this approach, underlying the need to weigh the benefits and risks of the surgical procedure [406]. Successful surgical management of PHPT eliminates the risk of PHPT deterioration postpartum and the risk of neonatal tetany. Surgery during the third trimester has been reported to increase the risk for preterm labor [406] along with other severe complications, although the occurrence of these complications could be due to the long-standing hypercalcemic status of both the mother and the fetus [406, 407]. Surgical treatment should be considered early, and a minimally invasive approach with ultrasound is best suited to mitigating the risk to the mother and fetus. Equally important, Tc-99 m sestamibi imaging may be used safely for localization of the parathyroids after negative cervical explorations. Although the treatment of choice in PHPT is the surgical intervention performed preferably during the second trimester of pregnancy, the patient declined this option of treatment because of the fear of potential complications to the fetus [105, 408]. Some authors claim that parathyroidectomy in pregnancy is associated with a slightly increased risk of a spontaneous abortion [105, 408]. Others did not have any maternal or fetal complications after surgery [407].

Medical therapy in pregnancy for symptomatic PHPT has been discouraged, due to safety issues of drug therapy and the suboptimal control of serum calcium which leads to a high fetal loss rate [42]. However, in symptom-free patients or those with no radiologically identifiable parathyroid adenoma or those with mild hypercalcemia diagnosed in third trimester may be managed medically, postponing the operation until after delivery. If conservative management is considered intensive, maternal and fetal surveillance should be initiated. Medical therapy primarily involves stabilizing the patient with hydration; limiting calcium intake; correcting electrolyte imbalance; and administration of magnesium sulfate, oral phosphate, and calciuretic diuretics [39, 80]. If the patient with the indication for operative treatment chooses medical therapy for PHPT, calcitonin is administered. It is considered the safest conservative treatment option in patients with hypercalcemia in pregnancy [42]. The safety of calcitonin during gestation probably results from its negligible passage through the placenta [409, 410]. The choice of this agent was also supported by suggested but not fully supported beneficial effects of calcitonin in the management of AP observed in nonpregnant patients [411]. Although presently no parameters are known that may predict the outcome of PHPT, in order to limit the risk of serious complications, most recommend maintaining total plasma calcium <3.0 mmol/l [412]. Exceeding this level is considered an indication for calcitonin administration. Interestingly, although calcitonin treatment may be associated with the development of tachyphylaxis [413], only tendency to tachyphylaxis was observed in the third trimester, and it disappeared after introduction of oral phosphates. This fact may be explained by administration of this agent only if plasma calcium levels exceeded the established threshold. Moreover, there was no nausea, vomiting, diarrhea, flushing, injection site reactions, and any other side effects associated with calcitonin treatment [413]. Although some animal studies suggested low birth weight in offspring of dams treated during pregnancy with high doses of calcitonin [411], this was not a published case, and infant's birth mass was within normal limits. Interestingly, Horjus et al. have shown the benefits of combined administration of calcitonin and cinacalcet in pregnancy and puerperium [412]. In one case the only symptom

experienced by the neonate after delivery was transient hypocalcemia, which disappeared shortly after the beginning of intravenous calcium administration. The presence of transient mild hypocalcemia probably resulted from increased calcium levels in fetal plasma, inhibiting parathyroid PTH synthesis and release during the pregnancy [409, 410, 414]. Interestingly, neonatal hypocalcemia was absent in the patient's subsequent pregnancy, taking place after parathyroidectomy, which supports the recommendations that surgery should be considered the treatment of choice in young hyperparathyroid pregnant women or desiring pregnancy [105, 408]. The effectiveness of surgical intervention in the prevention of fetal and neonatal complications clearly indicates that PHPT, if successfully treated, cannot be regarded as a contraindication for consecutive pregnancies.

Rajala et al. theorized that high-dose magnesium might be a therapeutic alternative for hyperparathyroidism in pregnancy [59]. It is possible that a compensatory increase in serum vitamin D-1,25 in response to the decrease in the PTH level caused by the magnesium increased calcium absorption from the gastrointestinal tract. Therefore, for some patients, because of persistent hypercalcemia, magnesium sulfate might not be a viable treatment option for hyperparathyroidism during pregnancy [44].

Identification and removal of a hyperfunctioning parathyroid tumor, including most mediastinal tumors, can usually be accomplished by cervical exploration [415]. Occasionally, because of their deep location in the chest, median sternotomy is necessary. In a series of 38 patients from the Mayo Clinic who underwent median sternotomy for removal of a parathyroid adenoma, 21 % had postoperative chest complications [416, 417].

Six of nine (67 %) reported cases up to 1996 were diagnosed during the third trimester of pregnancy, of which four underwent neck exploration after delivery. The three cases diagnosed before the third trimester underwent surgery during the second trimester. Parathyroid adenoma was the underlying disease in eight cases; one case was caused by a parathyroid carcinoma [43].

3.7.3 Therapeutic Delivery

Because pregnancy might lead to the exacerbation of hypertriglyceridemia in patients with familial hyperlipidemia, delivery is advocated because it is estimated to lower lipid levels by 15–20 % within 24 h and return them to prepregnant levels by 6 weeks postpartum [129, 342, 376, 377]. Both cholesterol and triglyceride concentrations decreased significantly within 24 h of delivery, and this was reflected in all lipoproteins. However, while triglyceride levels continued to decrease rapidly returning to nonpregnant levels during the puerperium, cholesterol in low-density lipoprotein remained elevated for at least 6–7 weeks postpartum [121]. Others believe that there is no improvement in maternal outcome and that fetal and maternal health may be jeopardized by complicated delivery. Early delivery may allow more aggressive treatment of the mother, including the use of lipid-lowering agents or plasmapheresis. Delivery also makes it easier to resuscitate the mother and may prevent fetal distress if AP deteriorates rapidly. Hypotension during Cesarean section, however, can exacerbate AP due to hypoxia and should be avoided. Also, some lipid-lowering medications, such as statins, which are contraindicated in pregnancy (FDA Class X), can be introduced after delivery.

In preterm pregnancies, delivery is recommended only if maternal or fetal condition deteriorates taking into account history of episodes of AP, gestational age, and the presence of persistent disease. The mode of delivery should be determined by obstetric factors.

In AP due to gallstones or of unknown cause, rapid resolution has been described after intrauterine death of the fetus [21] and after vaginal delivery with a live birth [418]. In AP associated with hyperlipidemia, the effect of delivery on the decline of plasma triglyceride levels can be immediate and dramatic [419]. However, the morbidity from AP does not always fall proportionally. Rapid improvement [419] and worsening of hyperlipidemic AP after delivery [397] have both been described, and AP can progress to maternal death [258].

Stimulation of fetal lung maturation in the critical period for delivery is important. Standard therapy includes corticosteroids. In experimental animals, administration of 17 beta-estradiol accelerates fetal lung maturation and stimulates surfactant production: the hormone increases the amount of surfactant in fetal lung lavage, increases the rate of phosphatidylcholine synthesis, depletes fetal lung glycogen, and accelerates morphological maturation of the fetal lung. Both estrogens and glucocorticoids stimulate fetal lung choline-phosphate cytidylyltransferase in a number of in vivo and in vitro systems, and there is increasing evidence that this enzyme may be of particular importance in the regulation of phosphatidylcholine synthesis. Estrogen appears to increase the catalytic activity rather than the amount of choline-phosphate cytidylyltransferase. This action of estrogen is mediated by phospholipids [420].

3.7.4 Obstetric Treatment

Recommendation is to inhibit uterine contractions to reduce premature labor [78]. If the disease was improved, we would terminate the pregnancy to ensure the safety of the mother and fetus. Indications for termination of pregnancy included (1) obvious signs of miscarriage or premature birth, (2) fetal distress or intrauterine deaths, and (3) if the fetus can survive after birth, usually chosen Cesarean section timely; if the fetus is dead, make an induction of labor [78].

Mode of delivery in patients with associated pancreatic pseudocysts should be determined on a case-by-case basis [395]. While a case of pseudocyst rupture during Valsalva efforts during delivery is reported, there is a paucity of data to guide delivery recommendations.

3.8 Prognosis

3.8.1 General Considerations

The outcome and prognosis depend, as in general population, on the severity of the AP, cause of AP, and fetal outcome partly depending on the trimester of occurrence of AP. In one series of 53 patients with AP during pregnancy published in the medical literature before 1951, the vast majority of diagnoses were made during surgery and/or on autopsy. In only three patients was the diagnosis made based on clinical grounds [421]. In 1973 Wilkinson reviewed 98 cases of AP during pregnancy, 30 patients died (37 %), significantly higher than that in nonpregnant patients then: 12–33 % [16]. In the same study, the perinatal mortality was high -37 % [16]. Joupilla et al. in 1974 have quoted a maternal mortality rate of 5–15 % [422]. Maternal and perinatal mortality due to AP during pregnancy is variously reported to vary from 20 to 50 %, and most occur during the third trimester [15, 16, 20]. A more recent reviews found a maternal mortality rate of less than 1 % for AP during pregnancy of all etiologies [23, 24, 73, 78]. Swisher et al. (30 pregnant women) and Ramin et al. (43 pregnant patients) reported no maternal deaths [15].

There was a 72 % relapse rate during the same pregnancy [35]. Non-gallstone AP as a whole had worse outcomes than simple gallstone AP. One of the explanations for better maternal and fetal outcomes is higher trend of cholecystectomy in pregnant women who developed AP or symptomatic cholelithiasis/cholecystitis especially in early trimesters [23, 423]. This supports the high relapse of biliary colic and its complications during pregnancy [424]. Also, in earlier studies, the recurrent AP risks were reported to be 50–70 % during the same pregnancy [25, 35]. Traumatic, hyperlipidemic, and alcohol-induced AP had particularly poor outcomes [24].

Aging is associated with increased severity of AP characterized by augmented and prolonged pancreatic inflammation and the presence of multiple extra-pancreatic sequels including thrombosis [425]. Incidence rates for AP in general population in England with admission to hospital rose in both men and women from 1963 to 1998, particularly among younger age groups. This probably reflects, at least in part, an increase in alcoholic AP. Mortality after admission has not declined since the 1970s. This presumably reflects the fact that no major innovations in the treatment of AP have been introduced. AP

remains a disease with a poor prognosis during the acute phase [426].

Fetal mortality rates quoted in the literature have improved in the last 20 years, as earlier studies reflected fetal deaths after preterm delivery which has reduced as a result of improved neonatal care [15]. One study found that 74 % of patients suffering AP delivered full-term healthy infants with 10.5 % of fetal mortality rate noted overall. A more recent study found a perinatal mortality rate of 3.6 % [24]. It is, however, important to note that these publications do not distinguish between the various causes of AP during pregnancy. In an 11-year retrospective study from 1995 describing 43 pregnant women with AP, there was no maternal mortality, but there were six preterm deliveries, and only two of these six infants survived [15]. ERCP had not been incorporated into the standard management at that time. Recently, the percentage of fatal outcomes of AP in general population has been less than 5 % [427], and, currently, data show no maternal mortality and 19 % of preterm labor but with fetal mortality of 5 % (single-center experience over 10 years with 21 patients with 34 attacks of AP) [25].

Patients who developed AP in the first trimester had the lowest percentage probability to reach term pregnancy (60 %), highest risk of fetal loss (20 %), and preterm delivery (16 %) [23, 27]. Maternal and perinatal mortality due to AP during pregnancy is variously reported to vary from 20 to 50 % and most occur during the third trimester [15, 16, 20]. It should be kept in mind that preterm labor may occur in as many as 60 % of patients who have AP in late pregnancy; therefore, gestational age is a primary determinant of perinatal outcome. In the past decades, high perinatal mortality rate, up to 50 % [16], secondary to AP resulted from neonatal deaths after preterm delivery but with early recognition and better supportive treatment of AP and improvements in neonatal intensive and supportive care play important role in premature babies' survival. More recent publications report no maternal mortality and 0.57–4.7 % fetal mortality [25, 254]. The mechanisms of demise include, also, placental abruption and profound metabolic disturbance, including acidosis. Serious maternal pulmonary complications are often associated with AP. The destruction of pulmonary surfactant by degradation of lecithin accompanied with an increase of serum PLA2 results in increased capillary permeability of the lung and the elevation of surface tension. This leads to pulmonary edema which is considered an important etiopathogenic factor of acute respiratory insufficiency [428]. It is not known whether this mechanism is responsible for perinatal morbidity and mortality. All this highlights the importance of regular fetal monitoring and consideration of delivery if the maternal disease is deteriorating. AP complicated by DIC usually occurs in the third trimester and is particularly associated with poor fetal and maternal outcomes [23]. Post-ERCP AP does not adversely affect pregnancy-related outcomes [23, 423]. Hepatobiliary diseases can result in maternal and fetal physiological dysfunction, leading to adverse pregnancy outcomes, such as prematurity and low birth weight [423]. Thus, it is particularly important to identify hepatobiliary disease early during pregnancy and to intervene appropriately as early as possible.

Another point for discussion is AP in the postpartum period. It is known that estrogen is one of the initiators of different causes of acute pancreatitis and that some of them are cured with Cesarean section as additional measure not only to save the newborn. Opinion is that postpartum period should be analyzed separately. One of the examples is that biliary sludge and gallstones form in up to 31 and 3 % of pregnant women, respectively, with the sludge frequently resolving postpartum [237, 429, 430]. Langmade and Edmondson in 1951 observed a 73 % recurrence rate in the puerperium [421].

3.8.2 Primary Hyperparathyroidism

3.8.2.1 Maternal Outcome

Increased risk for mother complications apart from AP is also present including nephrolithiasis, weakness, lethargy, muscle cramps, and bone disease [57]. If the mother is treated medically to term (or if spontaneous or elective abortion occurs), the mother should be monitored for hyperparathyroid crisis postpartum. It consists of nausea, vomiting, weakness, and central nervous

system retardation which could progress to uremia, coma, and death [57]. Sudden worsening of hypercalcemia can result from the loss of the placenta (active placental calcium transport may be somewhat protective) and dehydration [57]. Up to 1998 and from the 13 patients, maternal mortality was 15 % [66]. Mortality seems to be related to delayed resection of parathyroid tumor [66].

3.8.2.2 Fetal Outcome

Studies suggest that the fetal mortality rate when PHPT without AP is present can be reduced by a factor of four if operative cure is achieved [42, 431]. Hyperparathyroidism during pregnancy poses fetal risks of intrauterine demise, second-trimester loss, neonatal demise, and generalized tetany after delivery [57]. Up to 1998 and from the 13 patients, fetal mortality was 23 % [66]. Mortality seems to be related to delayed resection of parathyroid tumor [66]. PHPT results in high concentrations of fetal serum calcium that acts to suppress the parathyroid glands. Fetal calcitonin concentrations are high to encourage bone mineralization. At birth, however, the neonate is suddenly deprived of this source of calcium. It is incapable of mobilizing calcium from the bone owing to the low concentrations of parathyroid hormone and high concentrations of calcitonin. *Acute neonatal hypocalcaemia* results in neonatal tetany and convulsions, usually at 5–14 days of age. If the infant is breast-fed, tetany can be delayed by 1 month or more [415, 432]. Up to 1970, 17 children born of nine mothers have been reported to exhibit this phenomenon since the first description by Friderichsen in 1939 [433–437].

3.8.3 Acute Fatty Liver of Pregnancy

Report from 1980 demonstrated a very high maternal and perinatal mortality of 75 and 85 %, respectively [107]. More recent reports, however, indicate that with prompt diagnosis and treatment, the maternal and perinatal mortality rates have greatly decreased to approximately 18 and 23 %, respectively [438, 439]. In a series of 12 cases of AP in pregnant women with AFLP, Moldenhauer et al. found the following complications: encephalopathy (50 %), respiratory failure (17 %), and acute renal failure (33 %) [110].

3.8.4 Hypertriglyceridemia

3.8.4.1 Maternal Outcome

Interestingly, beyond the apparent significance of a TG threshold level to initiate AP (approximately 1,000 mg/dl), the severity of HTG-induced AP does not seem to correlate directly with TG level. In a series of 43 patients with HTG-induced AP, there was no relationship between TG level and severity of disease course or complications [440]. HTG-induced AP in pregnancy is a serious complication, and earlier studies noted that it is associated with a significant risk of death for both mothers (21 %) and fetuses (20 %) [376]. However, in 15 cases of gestational hyperlipidemic AP, no maternal death was reported [74, 346]. Though severity and complication rates with HTG-induced AP have been reported as higher in comparison to AP from other etiologies, mortality rates have not been found to differ. In a study of the clinical course of HTG-induced AP, the disease course of HTG-induced AP (19 patients) was compared to biliary AP (19 patients). Patients with HTG-induced AP had significantly more prior episodes of AP (possibly due to HTG) and more complications such as pancreatic necrosis, abscess formation, sepsis, or renal insufficiency, though there were no deaths in either group [441].

3.8.4.2 Fetal Outcome

Previously reported high perinatal mortality rates secondary to AP are due to neonatal deaths after preterm delivery. In recent series, perinatal mortality rates were improved with 74 % of infants delivered at term [15], or even preterm babies (five cases) delivered by Cesarean section could be saved due to better perinatal care [167], but studies still confirm of high premature delivery with even 100 % [78]. Pancreatic hemorrhage following pancreatic necrosis was also reported during pregnancy [442].

Outcomes for the mother and fetus in 1970 were similar with 21 % mortality rate for the mother and 20 % mortality rate for the fetus [376].

3.8.5 Medications

The prognosis of drug-induced AP in general population is generally excellent. In one report of 22 cases, for example, 19 were associated with interstitial AP; none of the patients with pancreatic necrosis on abdominal CT or ultrasound had over 33 % of the pancreas involved, and none died [207]. Mortality has also been rare in other reviews, although there are reports of a few deaths directly related to drug-induced AP.

3.8.6 Alcohol

3.8.6.1 Maternal Outcome

Patients with alcoholic AP were more likely to have recurrence of AP during pregnancy (75 % vs. 29 %) compared to cases where alcohol was not a factor [24]. Pseudocysts were almost exclusively associated with non-gallstone AP [24].

3.8.6.2 Fetal Outcome

Alcoholic AP was associated with significantly higher rates of preterm delivery and recurrence than all-cause AP. Patients with alcoholic AP were more likely to have preterm delivery (67 % vs. 26 %) compared to cases where alcohol was not a factor [24].

3.8.7 Preeclampsia-Eclampsia

Hojo et al. reported five maternal deaths and four cases of intrauterine fetal demise, all before 1973 [67, 75, 221, 222]. Only one case was with maternal death when deterioration was rapid, but amylase and lipase were not taken during the course of the disease and also authors did not perform the abdominal CT scan [238].

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Nontraumatic Gastroduodenal Perforations

4

4.1 Perforated Peptic Ulcers

4.1.1 Peptic Ulcer in Pregnancy with General Considerations

I have never seen undue activity of a peptic ulcer during pregnancy, but I am very familiar with the opposite state of affairs where ulcer symptoms disappear during pregnancy.

Grey Turner

4.1.1.1 History

The first known peptic ulcer was found recently in China in a corpse 2,200 years ago [1] with increasing frequency since then. But there is this gap of 2,000 years since the Greeks started Western medicine and conceived that abdominal pain could be due to an ulcer inside the stomach lining akin to ulcers they were familiar with on the rest of the body. The testing of this hypothesis could, of course, come only from necropsies from about the fifteenth century, when ulcers, first gastric, then in the eighteenth century duodenal, were recorded and became more common and, then later, less frequent in most age groups [2].

4.1.1.2 Incidence

There are approximately 500,000 new cases and 4.5 million people suffering from these diseases each year in the United States [3].

Lower Incidence in Women

It has long been observed that the ratio between men and women who develop duodenal ulcer is 1.9:1 in the United States, whereas in Europe and Asia, this ratio is 2.2:1 [4–7] and 3.1:1 [8], respectively. Incidence in pregnancy is fortunately extremely low due to several factors.

Declining Incidence

With time, there has been a dramatic fall in the prevalence of peptic ulcer disease (PUD) in developed countries. There is an approximately 30–40 % fall in hospitalizations for PUD complications between 1993 and 2006 with a larger reduction in duodenal ulcers (−37.2 %) than gastric ulcers (−19.6 %) [9]. Similar percentage is found in other studies from other countries over the past three decades [9–11]. Duodenal ulcer is more common than gastric ulcer, although the largest decreases in ulcer incidence have been seen in duodenal ulcer [12]. Despite a declining incidence overall of PUD, the incidence of PUD complicated by either bleeding or perforation has remained constant or in fact even increased. Although the data are inconsistent in different countries, data from Finland and the Netherlands suggest that the rate of ulcer complications and the need for emergent ulcer surgery may have increased slightly over the past 30 years [10, 11].

Lower Fertility Rate in Women with Peptic Ulcer

One of the causes of rarity of the disease in pregnancy is that patients with duodenal ulcer, regardless of sex, have a 25 % lower fertility rate compared to the general population (at least in the era before methods of assisted reproduction) [13]. Lower reproduction rate is associated with

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peptic ulcers of all types. The results revealed that peptic ulcer reduces the reproductive ability of the individual in the sense that the number of children born to affected probands as well as affected parents is smaller than to unaffected individuals. The finding was supported by the observation that the number of children of patients with peptic ulcer was not influenced (i.e., further reduced) by a positive family history of peptic ulcer. By contrast, detailed analysis revealed that childlessness was more frequent in affected probands with a positive family history of peptic ulcer than in affected probands with a negative family history: 26 % compared to 16 %, respectively. A positive family history has thus been shown to participate in the higher rate of childless marriages for subjects suffering from peptic ulcer. At the same time, it has no bearing on the number of children who are born. The number is, however, reduced compared to the average for the general population, as a result of the probands disease.

Incidence in Pregnancy

Cappell and Sidhom reported that of 29,317 pregnant patients, 56 pregnant women who were hospitalized (0.19 %) were found to have severe upper gastrointestinal complaints [14]. Only 2 of 20 of the women undergoing esophagogastroduodenoscopy (EGD) were identified as having PUD (specifically for duodenal ulcers). Tests to evaluate suspected PUD (e.g., upper gastrointestinal series or EGD) that are routine in the general population have been conservatively performed on pregnant women [15, 16]. At the Central Middlesex Hospital, London, during the 11-year period (1951–1961), there were 22,994 confinements; there were duodenal ulcer in two, gastric ulcer in two, and peptic ulceration and hemorrhage in two (with additional dyspepsia in three and gastritis in three) patients [17]. In England and Wales [18], for the years 1951–1960, of 1,193 deaths associated with pregnancy but not due to it, 0.58 % were due to peptic ulceration; while of 8,429 deaths from all causes in women aged 20–49, 0.3 % were due to PUD [19]. Duodenal ulcers in early pregnancy are extremely rare (see Sect. 4.1.1.3). In a 15-year period, there were five cases published [20, 21]. On the contrary, there is higher incidence of maternal dyspepsia during pregnancy in comparison to general population. Dyspepsia is among the most common gastrointestinal diagnoses and is estimated to occur in 14–20 % of adults [22, 23]. Dyspepsia is a very common symptom in pregnancy, particularly in the second part, when 21 % of pregnant women complain of heartburn daily, 52 % at least once a month, and as many as 80 % in the third trimester [24, 25].

4.1.1.3 Pathophysiology

Dyspeptic symptoms usually disappear about the end of the 3rd month of pregnancy, but they may persist till term. The estrogen level and the greatly elevated histaminase concentration afford part of the explanation why symptoms, and especially complications, from peptic ulcer are so rare during pregnancy. Occasionally, more severe indigestion occurs with considerable resemblance to ulcer. Sandweiss et al. in 1939 reported 52 pregnancies in 25 women who were known to have peptic ulcer. In all but one case, the ulcer symptoms disappeared during pregnancy [26]. Clark in 1953 investigated dyspeptic symptoms during 313 pregnancies in 118 women diagnosed as suffering from peptic ulcer before pregnancy. He found that there was a remission of ulcer symptoms in 88 % of the pregnancies. More than half of these women claimed to have been completely symptom-free during the whole pregnancy; the remainder had minor symptoms which they regarded as unconnected with the ulcer. In the remaining 12 %, symptoms persisted which were indistinguishable from those of ulcer, and 1/3 of these were admitted to hospital for treatment of "indigestion." In no case did hemorrhage or perforation occur during the pregnancy [27].

The benefits derived from pregnancy in women with PUD are apparently short-lived. In Clark's series, there was recurrence in almost every case within 2 years postpartum [27].

Gastric Position Changes

Hurst and Stewart in 1929 stated that there was no doubt that pregnancy exerts a favorable influence on the symptoms of an ulcer and in some cases appears to lead to actual healing apart from any specific treatment. This they attributed to the

mechanical effects of support of the stomach by the rising uterus. This is supposed to relieve the strain on the lesser curvature and improve the local circulation, which promotes healing of any ulcer [28]. Both in James's case [29] as well as Mulsow and Brown's case [30], the major accidents took place at a time when the stomach could not have been lifted much higher in the later weeks of pregnancy. Therefore, the mechanical theory by Hurst and Stewart is questionable.

Hypochlorhydria

Balint in 1927 [31] first suggested a general tendency toward increased alkalinity in tissue fluids during pregnancy, and other observers have confirmed that with increased alkalinity, there is found a hypo- or even achlorhydria, especially in the first 6 months of pregnancy; thereafter, the acid values began to rise toward normality and might even reach supernormal figures in the puerperium in certain cases [32–37]. The earliest observations on gastric acidity in pregnancy were made in 1925 by Nakai, who showed that there was a striking diminution in both the free and the total acid content of gastric juice in response to a test meal [32]. This was confirmed by Artz [36], who drew attention to the fact that the lowest secretion of free acid coincides with the period of pregnancy when nausea and vomiting are common. Murray et al. noted with the maximal histamine test that maximal secretion was decreased in the first 30 weeks of pregnancy [38]. This decreased secretion could be due to several factors. Plasma diamine oxidase (histaminase) levels are markedly increased in pregnancy [39], and there is evidence from the 1960s that this substance is related to gastric secretion and may inhibit it [40, 41]. Another important observation is that regurgitation of duodenal contents especially bile is present in only 3 % of pregnant patients despite common nausea and vomiting during (early) pregnancy [33, 42]. Authors share opinion that duodenal regurgitation is not the cause of hypochlorhydria.

Hormonal Influence

Crohn (1927) and others noted that peptic ulcers tend to break down in the puerperium. Winkelstein (1940) thought that the agent responsible for the breakdown might possibly be prolactin, the lactogenic hormone of the anterior pituitary. During gestation, the formation of prolactin is inhibited by the high blood levels of ovarian and placental hormones. He made experimental studies on animals with chemically produced peptic ulcers by treating them with the ovarian hormone theelin. The response was good and the ulcers healed within 10 days. Abrahamson et al. in 1942 treated peptic ulcers in human beings with theelin and, while getting a slightly better immediate response as compared with a number of controls treated on routine lines, found the long-term results no better [43].

One study confirmed previous observation that following ovariectomy, the gastroduodenal mucosa is less sensitive to ulcerogenic stimuli [44]. The reduction by ovariectomy of cysteamine- and indomethacin-induced ulcers of the stomach and the duodenum might relate to the decrease of plasma 17a-estradiol levels, since mucosal damage induced by cysteamine was increased by exogenous administration of the hormone into intact female rats. In contrast, administration of progesterone protected the gastroduodenal mucosa against ulcerogenic treatment with cysteamine or indomethacin. This last finding is in agreement with recent data showing that an increase of endogenous progesterone levels by early pregnancy or the administration of exogenous progesterone decreases the vulnerability of gastroduodenal mucosa to cysteamine [45]. Interestingly, progesterone acts as a protective factor also in male rats.

The maximal levels of chorionic gonadotropins also correspond to the period of decreased gastric secretion. The increased level of estrogen may be a factor, for Truelove has shown that stilbestrol does have a beneficial effect on duodenal ulcers [46]. Others confirmed these results [47, 48]. The equal sex incidence of peptic ulceration in children, the decreased incidence in women during the childbearing years, and the marked increase in incidence at the time of menopause [49] all suggest that the female sex hormones have some relationship to peptic ulceration and that the alterations in the hormones during pregnancy may give rise to an increased resistance to peptic ulceration. Duodenal ulceration and its

complications in the presence of high blood levels of both estrogens and progestagens must be due to factors other than changes in acid output. Interestingly enough, Kahlson et al. have shown protection against gastric ulceration during pregnancy in rats in the presence of raised acid output [50]. The resistance against digestion is provided by many factors, most of which are still poorly understood, including mucus, rapid epithelial turnover and migration, secretion of proteolytic ferments in the inactive form in the basal part of the gastric glands, and gastric urease, and it may be that estrogens exert a beneficial influence on duodenal ulceration by altering the secretion of mucus.

Izak [51] and Gryboski [52] noted that plasma pepsinogen rises in the last trimester of pregnancy, reaching a maximum on the first postpartum day. Murray et al. [38] examined the gastric secretion of pregnant women, both in the basal state and after the administration of 0.04 mg of histamine acid phosphate per kilogram of body weight. He noted decreased secretory response during pregnancy, mainly during the first 30 weeks. Two possible explanations for diminished hydrochloric acid secretion have been offered. The first is the antisecretory effect of plasma histaminase, which increases in pregnancy, sometimes as much as 1,000-fold [53]. Barnes [39] showed that plasma histaminase begins to rise about 7 weeks after the last normal menstrual period and that the peak is reached in the 26th–28th weeks of gestation. Preparations of histaminase administered to dogs with Heidenhain pouches were shown to diminish histamine-stimulated secretion [54]. Furthermore, the administration of histaminase inhibitors appears to augment both basal and gastric secretory response to a meal [40].

Way in 1945 attempted to explain the rarity of peptic ulcer and complications in pregnancy by correlating the hypochlorhydria found in these patients with the increased secretion of the anterior-pituitary-like hormones in the urine. He concluded that the greater the secretion of these latter, the more marked the hypochlorhydria. This endocrine explanation appears to be the most likely reason for the rarity of peptic ulcer activity during pregnancy [42]. Same theory was postulated by Horwich in 1958 [55]. Hormonal changes characterized by significant increases in levels of 17-hydroxysteroids and 17-ketosteroids have also been implicated as a possible factor in peptic ulcer in late pregnancy [56]. These and other observations suggest that estrogens may protect against peptic ulceration. This concept is supported back in 1960 by the beneficial effect, demonstrated in when stilbestrol was used in the treatment of men with duodenal ulcer [46].

It has also been suggested that female gestational hormones (particularly progesterone) decrease the rate of ulcer formation by increasing gastric mucus synthesis. An increase in plasma histamine in pregnancy (caused by placental histaminase synthesis) increases metabolism of maternal histamine, thereby reducing gastric acid secretion during pregnancy [39].

Changes in Nutritional and Lifestyle Habits

Avoidance of ulcerogenic factors such as cigarette smoking, alcohol, and drugs including NSAIDs (nonsteroidal anti-inflammatory drugs) all probably contribute to the reduced incidence of PUD in pregnancy.

4.1.1.4 Risk Factors

All known risk factors for peptic ulcers in general population are also risk factors in the pregnant population.

Helicobacter pylori Infection

H. pylori infection and NSAID use account for most cases of PUD. The rate of *H. pylori* infection for duodenal ulcers in the United States is less than 75 % for patients who do not use NSAIDs. Excluding patients who used NSAIDs, 61 % of duodenal ulcers and 63 % of gastric ulcers were positive for *H. pylori* in one study. These rates were lower in whites than in nonwhites. Prevalence of *H. pylori* infection in complicated ulcers (i.e., bleeding, perforation) is significantly lower than that found in uncomplicated ulcer disease. Several studies reported that *H. pylori* infection is not associated with an increase in dyspepsia, hyperemesis gravidarum, or maternal or neonatal morbidity [57–60].

Medications

NSAID use is a common cause of PUD. These drugs disrupt the mucosal permeability barrier, rendering the mucosa vulnerable to injury. Around 30 % of adults taking NSAIDs have adverse GI effects. Factors associated with an increased risk of duodenal ulcers in the setting of NSAID use include history of previous PUD, advanced age, female sex, high doses or combinations of NSAIDs, long-term NSAID use, concomitant use of anticoagulants, and severe comorbid illnesses. Although the idea was initially controversial, most evidence now supports the assertion that *H. pylori* and NSAIDs are synergistic with respect to the development of PUD. A meta-analysis found that *H. pylori* eradication in NSAID-naive users before the initiation of NSAIDs was associated with a decrease in PUD [61].

Corticosteroids alone do not increase the risk for PUD; however, they can potentiate ulcer risk in patients who use NSAIDs concurrently.

The risk of upper GI tract bleeding may be increased in users of the diuretic *spironolactone* [62] or *serotonin reuptake inhibitors* with moderate to high affinity for serotonin transporter [63].

Lifestyle Factors

Evidence that *tobacco* use is a risk factor for duodenal ulcers is not conclusive. Support for a pathogenic role for smoking comes from the finding that smoking may accelerate gastric emptying and decrease pancreatic bicarbonate production. However, studies have produced contradictory findings. In one prospective study of more than 47,000 men with duodenal ulcers, smoking did not emerge as a risk factor [64]. However, smoking in the setting of *H. pylori* infection may increase the risk of relapse of PUD [65]. Smoking is harmful to the gastroduodenal mucosa, and *H. pylori* infiltration is denser in the gastric antrum of smokers [66].

Ethanol is known to cause gastric mucosal irritation and nonspecific gastritis. Evidence that consumption of alcohol is a risk factor for duodenal ulcer is inconclusive. A prospective study of more than 47,000 men with duodenal ulcer did not find an association between alcohol intake and duodenal ulcer [64].

Little evidence suggests that *caffeine* intake is associated with an increased risk of duodenal ulcers.

Severe Physiological Stress

Stressful conditions that may cause PUD include burns, CNS trauma, surgery, and severe medical illness. Serious systemic illness, sepsis, hypotension, respiratory failure, and multiple traumatic injuries increase the risk for secondary (stress) ulceration. Cushing ulcers are associated with a brain tumor or injury and typically are single, deep ulcers that are prone to perforation. They are associated with high gastric acid output and are located in the duodenum or stomach. Extensive burns are associated with Curling ulcers. Severe illness and a decreased gastric pH are related to an increased risk of gastric ulceration and hemorrhage.

Hypersecretory States (Uncommon)

The following are among hypersecretory states that may, uncommonly, cause PUD:

- Gastrinoma (Zollinger-Ellison syndrome) or multiple endocrine neoplasia type I
- Antral G-cell hyperplasia
- Systemic mastocytosis
- Basophilic leukemias
- Cystic fibrosis
- Short bowel syndrome
- Hyperparathyroidism

Physiological Factors

In up to one-third of patients with duodenal ulcers, basal acid output (BAO) and maximal acid output (MAO) are increased. In one study, increased BAO was associated with an odds ratio [OR] of up to 3.5, and increased MAO was associated with an OR of up to 7 for the development of duodenal ulcers. Individuals at especially high risk are those with a BAO >15 mEq/h. The increased BAO may reflect the fact that in a significant proportion of patients with duodenal ulcers, the parietal cell mass is increased to nearly twice that of the reference range [67].

In addition to the increased gastric and duodenal acidity observed in some patients with duodenal ulcers, accelerated gastric emptying is often

present. This acceleration leads to a high acid load delivered to the first part of the duodenum, where 95 % of all duodenal ulcers are located. Acidification of the duodenum leads to gastric metaplasia, which indicates replacement of duodenal villous cells with cells that share morphological and secretory characteristics of the gastric epithelium. Gastric metaplasia may create an environment that is well suited to colonization by *H. pylori*.

Genetics

More than 20 % of patients have a *family history of duodenal ulcers*, compared with only 5–10 % in the control groups. In addition, weak associations have been observed between duodenal ulcers and *blood type O*. Furthermore, patients who do not secrete ABO antigens in their saliva and gastric juices are known to be at higher risk. The reason for these apparent genetic associations is unclear.

A rare genetic association exists between *familial hyperpepsinogenemia type I* (a genetic phenotype leading to enhanced secretion of pepsin) and duodenal ulcers. However, *H. pylori* can increase pepsin secretion, and a retrospective analysis of the sera of one family studied before the discovery of *H. pylori* revealed that their high pepsin levels were more likely related to *H. pylori* infection.

Fasting (In General Population)

Most of the studies showed that the frequency of PUD is increased during Ramadan [68–71]. Donderici et al. reported that peptic ulcer complications are more frequent during Ramadan compared to periods before and after Ramadan [72]. There are no studies in the pregnant population. Of three studies, two reported an increase (only in patients with predisposing factors especially dyspepsia) [72, 73], and one reported no change [74] in the frequency of duodenal ulcer perforation during Ramadan in general population. It is interesting that during Ramadan fasting, incidence of male dominance of duodenal ulcer perforation significantly decreases. This observation is found in two studies [72, 73]. Up to date, there are no such studies in pregnant population.

Table 4.1 Some of the less common causes of peptic ulcer disease in general population

Hepatic cirrhosis
Chronic obstructive pulmonary disease
Allergic gastritis and eosinophilic gastritis
Cytomegalovirus infection
Graft versus host disease
Uremic gastropathy
Henoch-Schönlein gastritis
Corrosive gastropathy
Celiac disease
Bile gastropathy
Autoimmune disease
Crohn's disease
Other granulomatous gastritides (e.g., sarcoidosis, histiocytosis X, tuberculosis)
Phlegmonous gastritis and emphysematous gastritis
Other infections (Epstein-Barr virus, HIV, *Helicobacter heilmannii*, herpes simplex, influenza, syphilis, *Candida albicans*, histoplasmosis, mucormycosis, and anisakiasis)
Chemotherapeutic agents, such as 5-fluorouracil (5-FU), methotrexate (MTX), and cyclophosphamide
Local radiation resulting in mucosal damage, which may lead to the development of duodenal ulcers
Use of crack cocaine, which causes localized vasoconstriction, resulting in reduced blood flow and possibly leading to mucosal damage

Additional Risk Factors

Other risk factors may be associated with PUD and are listed in Table 4.1.

4.1.1.5 Clinical Presentation

Peptic ulcer is rare and difficult to diagnose during pregnancy. Obstetric patients as a rule are not questioned closely with respect to past gastrointestinal symptoms. Epigastric distress, heartburn, nausea, and vomiting are frequent complaints during normal pregnancy and, therefore, often overlooked. These symptoms are also associated with hyperemesis gravidarum and hiatal hernia, both more prevalent than peptic ulcer in pregnancy. On the contrary to peptic ulcer itself, dyspepsia is among the most common gastrointestinal diagnoses and is estimated to occur in 14–20 % of adults [22, 23]. Dyspepsia is a very common symptom in pregnancy, particularly in the second part, when 21 % of pregnant women complain of heartburn daily, 52 % at least once a month, and as many as 80 % in the third trimester [24, 25].

Cardinal symptoms of PUD are upper abdominal pain, nausea, and vomiting. The pain is often epigastric and worse at night. In the presence of a gravid uterus (and especially when labor ensues), it can be quite difficult for patients to localize pain. Unlike gastroesophageal reflux disease, the pain is not exacerbated by recumbence or associated with regurgitation. Although nausea and vomiting occurs in 50–80 % of normal pregnancies, it is uncommon for these symptoms to persist beyond 20-week gestation. Nausea and vomiting of pregnancy is classically most intense in the morning while PUD symptoms are worse nocturnally and postprandially during the day. PUD symptoms also get worse with increasing gestation and are therefore usually most severe in the third trimester. Occasionally, PUD may present with hematemesis. Uncomplicated PUD produces minimal physical signs.

The symptoms of peptic ulceration are improved during pregnancy in many women. Relief occurs early in pregnancy, but unfortunately, the symptoms frequently recur following delivery [28, 29].

4.1.1.6 Diagnosis

Diagnostic modalities are the same for pregnant and general population. The most common diagnostic tool of nonemergent presentation is esophagogastroduodenoscopy because it can obtain samples for histopathological examination as well as *H. pylori* presence. The procedure is safe in pregnancy if no sedative medications are used which can lead to fetal hypoxia [75, 76]. *American Society for Gastrointestinal Endoscopy* (ASGE) guidelines state two indications for EGD:

- Significant or continued GI bleeding
- Severe or refractory nausea and vomiting or abdominal pain

Therefore, if only uncomplicated ulcer is suspected, there is no need for endoscopy during pregnancy or it should be postponed to the second trimester [77].

4.1.1.7 Therapy

Pharmacological treatment is the same in pregnant and general population (see Sect. 4.1.2.5). All classes of medications are safe for the fetus, and no increase in incidence of fetal anomalies was found on large samples [78]. No severe side effects were observed in any of the mothers or their newborns. No malfunctions or malformations were observed in the newborns. Follow-up of the children between 2 and 12 years showed normal development in all children [79]. Recent studies confirmed that higher rate of congenital anomalies was not found in the offspring of mothers with PUD [78]. One study showed that severe chronic dyspepsia in early pregnancy and drug treatment for this was not associated with a higher risk of congenital malformations except possibly isolated rectal/anal atresia/stenosis [80].

4.1.1.8 Prognosis

Perforated gastroduodenal ulcers in pregnancy, as in nonpregnant condition, should be divided into benign peptic ulcers, malignant ulcers/perforated carcinomas, and specific forms such as Zollinger-Ellison syndrome. The division is necessary because therapeutic principles and prognosis between these groups are different.

Nationwide, population-based study revealed that maternal PUD was independently associated with a 1.18-, 1.20-, and 1.25-fold increased risk of having babies with low birth weight, preterm delivery, and small for gestational age, respectively, after adjusting for family income and maternal, paternal, and infant characteristics. With the comparison of the PUD women without treatment with the unaffected mothers, gestational PUD was found to have an adverse impact on pregnancy outcomes. However, in further examining women with treated PUD, authors were unable to identify improved effects of PUD medication on the risks of adverse neonate outcomes [81]. It remains unclear what factors elevate the risk of adverse birth outcomes among patients with PUD. The possible role of diet and nutrient absorption deserve more examination. In animal models, maternal starvation decreased the extent of metabolic substrate produced by the mother and provided to the fetus, retarding fetal intrauterine growth [82]. Glucose, transmitted from the mother to fetus, is the main energy substrate for intrauterine growth [83].

Whereas glucose is produced by maternal metabolism, dietary restriction or maternal hypoglycemia decreases availability of metabolic fuel

and consequently slows fetal growth [84, 85]. Likewise, low micronutrient intake during pregnancy is associated with adverse neonatal outcomes such as preterm delivery [82]. In response to symptoms of anorexia, abdominal distention, epigastric pain, and postprandial vomiting, mothers with PUD during pregnancy may restrict their dietary intake to avoid the discomfort. The risk of constrained fetal growth and adverse birth outcomes might be elevated accordingly. Stress might also contribute to the link between gestational PUD and adverse pregnancy outcomes. Stress is strongly associated with PUD because threats to homeostasis prompt an adaptive or allostatic response [86]. Maternal vasoconstriction, resulting from the release of catecholamines in exposure to stress, might also obstruct the transmission of oxygen and vital nutrients to the fetus [87]. Fetal central nervous system and particularly glucocorticoid brain receptor development might subsequently be affected [88, 89]. Previous literature indeed demonstrated a significant relationship between maternal prenatal stress and infants with low birth weights and decreased gestational age at birth [89]. Thus, women with PUD might be those who perceive or experience more stressful circumstances. The further exposure of their fetuses to stress and elevated levels of adrenal hormones might consequently elevate the risk of negative birth outcomes. Furthermore, Chen et al. identified increased risk of adverse pregnancy outcomes among mothers with PUD who took no medication for it during pregnancy [81]. Meanwhile, no significant difference in outcomes was observed for those who did take medication during pregnancy. PUD medications, such as H_2 blockers or proton pump inhibitors [90–92], are probably safe during pregnancy according to current clinical data but with the possibility that the lack of insignificant difference is due to the relatively small sample size. The trend toward slightly increased though insignificant risk of low birth weight and preterm birth might reflect more severe PUD symptoms among women who were prescribed PUD medication.

4.1.1.9 Specific Considerations

Zollinger-Ellison Syndrome

Zollinger-Ellison syndrome (ZES), described in 1955, is an ulcerative disease of the upper gastrointestinal tract that includes high levels of gastrin and gastric acid. There is little information on the management of pregnancy in patients with pancreatic endocrine tumors such as ZES. This has occurred because the syndromes are uncommon (i.e., ten cases/million population/year); until last decades, these patients frequently died soon after the diagnosis, which was often established only late in the disease course and the hormonal syndrome often caused severe metabolic or nutritional deficiencies that may have interfered with pregnancy [93–95]. However, at present, because of earlier diagnosis and the increased ability to medically control the hormonal symptoms, especially in patients with ZES with potent gastric acid antisecretory drugs, these patients are living longer [93, 95–97] and women with the disorder more frequently become pregnant. The tendency of the tumor to grow slowly enables the physician to focus on symptomatic treatment. Gastrin levels do not change significantly during pregnancy and thus are useful for the diagnosis and follow-up of this syndrome [98]. There is a controversy whether pregnancy offers protection against ZES. Some have reported the absence of symptoms of ZES during pregnancy [99, 100], while Ezeh et al. [101] reported a case of exacerbation during pregnancy that required i.v. omeprazole treatment. The patient by Mayer et al. had been treated operatively and had low gastrin levels requiring high doses of omeprazole. This fact might strengthen the theory that pregnancy does not offer protection against ZES [102].

The management of pregnant patients with an asymptomatic pancreatic endocrine tumor syndrome such as ZES presents a number of unique problems. ZES is the most common symptomatic malignant pancreatic endocrine tumor [93]. Similar to the other pancreatic endocrine tumors, these patients have two different treatment problems [93]. First, symptoms caused by the ectopic hormonal release must be controlled, and, second,

treatment must be directed against the tumor, which in all the syndromes, except insulinoma, is malignant in 30–90 % of cases [93]. In ZES the ectopically released gastrin causes gastric acid hypersecretion that, if untreated, results in severe ulcer disease, malabsorption, and frequently severe gastroesophageal reflux disease [93–95]. The gastrinoma is malignant in 60–90 % of cases [93–95], and 34 % of patients have liver metastases [93]; however, in most patients the tumor grows relatively slowly [97]. Because of the slow rate of progression of most gastrinomas, the primary problem during pregnancy in patients with ZES is controlling the severe gastric acid secretion. This problem is complicated by the large volume of gastric acid secretion, necessitating daily gastric acid antisecretory drug treatment [93, 96]; the requirement for high doses of these drugs in many patients [96]; and the unknown safety profiles of any of the gastric antisecretory drugs during pregnancy, especially in high doses.

It is possible for patients with ZES to have pregnancies that are not complicated by gastric acid hypersecretion. If the ZES is diagnosed before pregnancy, curative resection with parietal cell vagotomy may obviate the need for gastric antisecretory drugs. If metastases are present or the diagnosis of ZES is made after conception, ranitidine in the lowest possible dose should be used to control acid secretion. If acid secretion in uncontrolled, the dose may be increased or omeprazole may be used [103].

Antacids are generally ineffective in the management of ZES and thus are not a realistic option. The histamine H_2 receptor antagonists and H^+-K^+ adenosine triphosphatase inhibitors can control gastric hypersecretion in all patients with ZES [96]; however, high doses of these drugs are frequently required [93, 96]. In various studies of patients with ZES, the mean dose of cimetidine required was 3.6 g, for ranitidine it was 1.2 g, and for famotidine it was 0.25 g, all of which were more than four times the doses required for the treatment of idiopathic PUD [93, 96]. Similarly, the median dose of omeprazole or lansoprazole required is 60 mg, which is also higher than the 20 or 30 mg, respectively, used in routine idiopathic PUD [96]. The safety of these drugs in pregnancy is the central issue in trying to decide the proper approach to the management of the acid hypersecretion in these patients during pregnancy. Studies have shown that the high doses used in ZES cimetidine can cause antiandrogen side effects in some patients [104]. Ranitidine, however, has not been shown to possess these antiandrogenic effects in pregnant rats or in patients with ZES even at high doses [105]. There are case reports describing the safe use of cimetidine and ranitidine in pregnant patients with gastroesophageal reflux disease, hyperemesis gravidarum, Mallory-Weiss tears, and active PUD [106–108]. Detailed strategy of treating patients with ZES prior to and during pregnancy could be found in the article by Stewart et al. [103].

Helicobacter pylori

H. pylori infects the human stomach, causing gastritis, peptic ulcer, and gastric cancer. *H. pylori* infection has also been related to extragastric disorders. During pregnancy, preferential induction of Th_2-type cytokines downregulates Th_1-type responses, allowing fetal survival. The results suggest that *H. pylori* infection can induce activation of resident uterine immune cells and/or recruitment of cells at the endometrial level. It can be hypothesized that the local Th_1-type response induced by *H. pylori* infection could alter the systemic Th_1-/Th_2-type cytokine balance at sites under particular physiopathological conditions of active tissue and/or vascular formation, such as pregnancy. This is the first evidence in an animal model of the possible influence of *H. pylori* infection on pregnancy. Further work is required on its mechanism and its relevance for humans [109]. Transmission of *H. pylori* infection from the mother to infant was not detected by culture in animal study, suggesting that decreased baby weight may be due to decreased milk supply or altered nutrition from the mother [110].

Physiological and epidemiological evidence suggests that *H. pylori* may interfere with iron metabolism, lowering it [111–114]. In the study

by Weyermann et al., the reduction of hemoglobin levels during pregnancy in the presence of *H. pylori* infection seemed to be slightly higher among women with iron therapy during pregnancy compared with women without [115]. Even though the difference between both groups was not statistically significant, this pattern would be consistent with the hypothesis of a possible increase in bacterial density by iron therapy, which might in turn reduce the benefit from iron therapy, because microbiologic and ferrokinetic studies suggested that outer membrane receptors of *H. pylori* in vitro are able to capture iron from human lactoferrin and use it for growth [116]. However, this hypothesis must be confirmed.

Women who were infected with *H. pylori* were generally shorter than women who were not infected. Moreover, women who gave birth to babies with intrauterine growth retardation were also shorter than women who gave birth to normal-sized babies. Many studies have shown that close contact and overcrowding among family members promotes the transmission of *H. pylori* infection [117–119]. Therefore, the possibility exists that an infected mother may more often transmit *H. pylori* to her infant and thereby continues a vicious cycle of growth restriction. The possible mechanisms by which *H. pylori* may affect fetal growth are speculative. However, it is conceivable that *H. pylori* may be linked with an increase in symptoms including dyspepsia [120], nausea [121], or vomiting [122, 123], because of underlying undiagnosed PUD, which in turn may affect maternal appetite and therefore restrict the growth of the fetus, although this was not determined in this study. Another possible mechanism linking intrauterine growth retardation with *H. pylori* infection may be the effect of chronic *H. pylori* infection upon the vascular system. Acute atherosclerotic changes have been noted in placental and uterine spiral arteries in cases with intrauterine growth retardation [124]. Previous studies have suggested that *H. pylori* infection may increase platelet aggregation and fibrinogen, as well as having an effect on lipid peroxidase [125–128]. Therefore, chronic *H. pylori* infection might induce vascular disease, which in turn may affect the placenta and thereby cause intrauterine growth retardation. Therefore, direct link between perforated peptic ulcer and abnormal pregnancy and/or fetal consequences could not be proved because acute/chronic *H. pylori* infection and other potential confounders could have the same or even more influence on negative pregnancy outcomes.

It has been shown in mice that *H. pylori-infected* mice show a decrease in implantation rates and their offspring are of low birth weight [109]. Infection with *H. pylori* cytotoxin-associated gene (CagA)-positive strains has been shown to cause a severe inflammatory response and significant neutrophil infiltration in the gastric mucosa [129]. There is statistically significant relationship between CagA-positive strains of *H. pylori* and early pregnancy loss (EPL) which might be explicable on the basis of general inflammatory reaction to infection. Concentrations of IL-1β, IL-8, and TNF-α were all significantly higher in *H. pylori*-positive gastric mucosa samples [130]. These cytokines may cause systemic inflammation that could affect the integrity of the fetoplacental unit and threaten the welfare of the fetus [131]. It was shown that poor oral hygiene is associated with a history of miscarriage [131], possibly due to systemic inflammatory response to oral bacterial infection. It may be assumed that a parallel mechanism underpins the ELL in women infected with CagE-positive *H. pylori* strains.

In infertile human males, *H. pylori* infection was shown to be associated with low sperm quality compared to uninfected patients [132]. The pathogenicity of an *H. pylori* isolate depends on strain-specific factors [133]. The Cag pathogenicity island, for which CagA is the marker, has been associated with both duodenal ulcer and gastric cancer [134], and infection with CagA-positive strain is generally associated with a higher level of inflammatory mediators compared to CagA-negative strains. In CagA-positive male patients, a significant reduction in sperm motility was observed along with increased apoptosis and necrosis [132] with two hypotheses explaining this finding: inflammatory reaction to infection and the immune reaction between *H. pylori* and the sperm antigen [135].

Peptic Ulcer Disease Complicated by Gastric Outlet Obstruction

Several such cases are described [136, 137]. Ideally, the operation during pregnancy should be avoided due to surgical stress and possible postoperative nutritional deficiencies to the mother and fetus. Gastric outlet obstruction should be treated with endoscopic balloon dilatation with additional procedures such as endoscopic needle-knife radial incisions [138]. Duration of the therapeutic effect depends on the underlying cause of the gastric outlet obstruction, but most studies report therapeutic effect in months which is enough to postpone the definitive treatment by operation after delivery [139]. If malignancy is confirmed, surgery is indicated by oncologic principles in pregnancy.

4.1.2 Perforated Peptic Ulcer

> *I cannot remember a perforated gastric or duodenal ulcer during pregnancy.*
>
> *Sir Gordon-Taylor*

> *Every doctor, faced with a perforated duodenal ulcer of the stomach or intestine, must consider opening the abdomen, sewing up the hole, and averting a possible or actual inflammation by careful cleansing of the abdominal cavity.*
>
> *Johann von Mikulicz-Radecki, 1884*

4.1.2.1 History

For thousands of years, healthy people have had acute abdominal pain, nausea, vomiting, and diarrhea followed by death in a few hours or days. Often these symptoms were contributed to poisoning, and people have been sent to prison for this [140]. King Charles I's daughter, Henriette Anne, died suddenly in 1670 (at age 26) after a day of abdominal pain and tenderness. Since poisoning was suspected, autopsy was performed revealing peritonitis and a small hole in the anterior wall of the stomach. However, the doctors had never heard of a perforated peptic ulcer (PPU) and attributed the hole in the stomach to the knife of the dissector [141]. Necropsies were first allowed since 1500 and became more common between 1600 and 1800 [141, 142]. As a consequence, more often perforation of the stomach was observed. Johann Mikulicz-Radecki (1850–1905), often referred to as the first surgeon who closed a perforated peptic ulcer (PPU) by simple closure in 1884, said: "Every doctor, faced with a perforated duodenal ulcer of the stomach or intestine, must consider opening the abdomen, sewing up the hole, and averting a possible or actual inflammation by careful cleansing of the abdominal cavity" [143]. Robert Daniel Mussey (Fig. 4.1) was one of the first, in 1927, who reported two cases of peptic ulceration in 370 operations during pregnancy at the Mayo Clinic in a period of 10 years [145]. It is not known whether these two operations were made in elective or emergent settings.

Fig. 4.1 Robert Daniel Mussey (1884–1958) is a physician in a family of six generations of physicians (*cropped picture*) [144]. He guided the development of an obstetrics/gynecology department at the Mayo Clinic and was Professor of Obstetrics and Gynecology there until he retired in 1950

4.1.2.2 Considerations in General Population

Remarkable changes have occurred in the sex and age incidence of PUD in North-West Europe. The fluctuations over the previous 150 years were studied by Jennings in 1940 [146]. He examined the incidence of perforations, which provide perhaps the most uniform index of the incidence of ulcers for the total period. His interpretation suggested that during this period, there had been

three observable syndromes: perforations of acute gastric ulcers in young women, perforations of duodenal ulcers in young and middle-aged men, and perforations of gastric ulcers in older men [146].

Perforations began to be noted with increasing frequency at the beginning of the nineteenth century. Half of all perforations were then in young women in their twenties, and these reached a peak in the latter half of the century. They seemed to be *acute gastric ulcers*, which caused death from perforations near the cardia or from hemorrhage [146, 147]. By the end of the century, this condition had begun to disappear. But even in 1905, the Registrar General was able to write: *Gastric ulcer does not appear frequently as a cause of death until the attainment of the reproductive period, when the female rate greatly exceeds the male, while at later ages the male rate is in excess* [148].

The common perforations of today made an appearance only at the beginning of the twentieth century; these are *juxtapyloric ulcers* occurring mainly in young and middle-aged men [149]. Studies up to 1955 show a continuing trend of increase in perforations of peptic ulcers in men [150]. The incidence of perforation during the 1940s in the two sexes was much greater in men, varying from 25:1 [43, 151–155].

In the 1950s, however, there were signs that the volume of peptic ulcer had at last reached a peak and was beginning to fall. A halt in mortality from *gastric ulcer* was noted in the early 1950s, and it then seemed possible to ascribe this to better treatment [156]. Subsequently the death rate has continued to fall, and sickness statistics show the same trends. The decline is found in sickness rates reported from general practice, from the Army, and from insurance certificates [157–159].

Trends for duodenal ulcer are similar but follow about 5 years behind. In the mid-1950s, death rates reached a plateau and then began to fall. This fall can also be seen from the census of clinically diagnosed peptic ulcers in York and from the duration and the number of spells of sickness absence [160]. As yet it does not appear in statistics of the last decade from general practice and from the Army, both of which showed stable rates [157–159]. All these trends together suggest that we are observing a recession of the PUD. This has affected the age groups unequally. Since the war, mortality from gastric and duodenal ulcers has declined in young men and women, although up to 1962, it was still rising at ages over 65 (Fig. 4.2a–d). One possible explanation is that the fluctuations in peptic ulcer rates represent a *cohort phenomenon* and that each generation has carried its own particular risk of bearing ulcers throughout adult life. In order to examine this hypothesis, the experience of each generation or cohort must be followed separately through its life cycle.

Because of the success of medical therapy in the management of PUD, surgery has a very limited role, and elective peptic ulcer surgery has been virtually abandoned. The number of elective operations for PUD dropped more than 70 % in the 1980s; 80 % of these procedures were emergent operations [162]. The lifetime prevalence of perforated peptic ulcer (PPU) has been estimated at 5 % [163]. Currently, mortality and morbidity following PPU are substantial, and mortality rates as high as 25–30 % have been reported [164–167]. Several prognostic factors and scoring systems for PPU have been examined [166, 168–172]. The mortality incidence doubles for every 6-h period from the time of perforation to the time of surgery; after 24 h the mortality rate is maintained at the high rate of over 60 %. Sepsis is frequent and a leading cause of death in patients with PPU, and some of the reported prognostic factors are associated with the sepsis syndrome [173, 174]. The authors of the first surgical procedures for PPU were as follows:

- 1892 resection: Heusner
- 1894 oversaw: Dean
- 1937 omental patch: Graham
- 1990 laparoscopy: Mouret

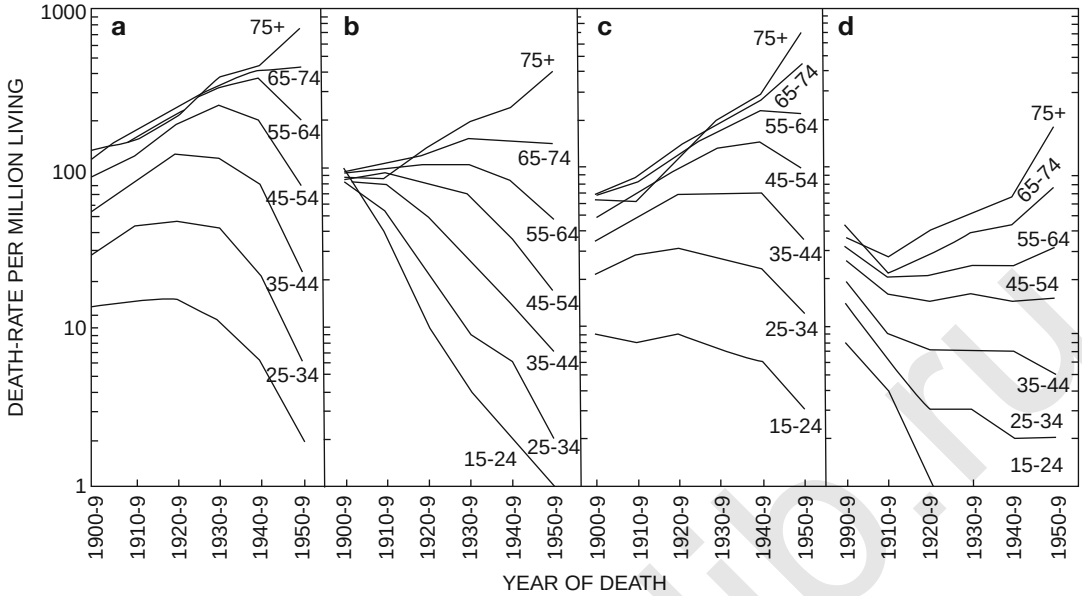

Fig. 4.2 Deaths from peptic ulcer by age and sex and year of death. (**a**) Gastric ulcer: males. (**b**) Gastric ulcer: females. (**c**) Duodenal ulcer: males. (**d**) Duodenal ulcer: females; mean rates for 10-year periods were calculated from the Annual Reviews of the Registrar General. Populations include non-civilians. Correction factors for the pre-1940 data to allow for the change in death certification (males 1.034, females 1.042) have not been used. Log graphs [161]

4.1.2.3 Perforated Peptic Ulcer in Pregnant Population

History

In pregnant population, Chabannes [175] in 1903 first drew attention to this subject, followed by Szenes [176]. This point is further buttressed by the seminal work of Hooker in 1933, in which only one case of duodenal ulcer was recorded following 1,564 puerperal deaths from 348,310 pregnancies [177]. Sandweiss et al. have subsequently reviewed the topic and found nine PPUs [178]. Howkins in 1950 quoted Professor Grey Turner's statement that *he has never seen undue activity of a peptic ulcer during pregnancy, but is very familiar with the opposite state of affairs where ulcer symptoms disappear during pregnancy*; also Sir Gordon-Taylor's statement that *he cannot remember a perforated gastric or duodenal ulcer during pregnancy* [179] and it must be extremely rare to meet with this complication. Scott in 1945, discussing the differential diagnosis of acute abdominal lesions in pregnancy, does not even mention ulcer perforation as a possibility [180].

Incidence

Sandweiss et al. found only one case of perforated duodenal ulcer in 70,310 pregnancies in Detroit in the period 1928–1937 and also one case of perforated gastric ulcer in 348,310 pregnancies over a period of 3 years in New York. Both patients died [178]. The low incidence of peptic ulceration in pregnancy has been demonstrated in a number of series from 1939 to 1955; a compilation of four of these has shown that among 233,650 deliveries, only 11 patients had peptic ulcers [28, 181–183], and among 1,564 maternal deaths in 348,310 pregnancies, only one death was due to peptic ulceration [184]. In early reports perforation was more frequent than bleeding during pregnancy [178]. Reports have found 13 cases of PPUs (nine duodenal and four gastric) during pregnancy and the first week after delivery [185]. Nine of the 13 mothers died, and the four cases in which the mother survived were reported from this country up to 1961 by James [29], Horwich [55], Ross [186], and Burkitt [187]. Only 24 cases of PPUs have been described

up to 1966 [19, 29, 55, 154, 178, 186–193]. Up to 1971, 31 perforations (and 32 cases of hemorrhage) proved from peptic ulcer which occurred during pregnancy have been reported [194]. In the last 20 years, there are several more cases published [195, 196].

Risk Factors

Risk factors for PPU are the same as for the peptic ulcer itself. Fasting can be a risk factor [197]. Even a case of perforated gastric ulcer was described after adjustable gastric banding. The case does not define localization, macroscopic appearance, and whether the ulcer was peptic or related to silicone ring and local ischemia (marginal ulcer) [198].

Ulcer Type

Summary of case reports show that most cases during pregnancy are located in the first part of the duodenum on the anterior surface which is a common presentation in young nonpregnant population (Table 4.2).

Clinical Presentation

Clinical presentation is similar to nonpregnant population: acute, severe abdominal pain, and sometimes with vomiting. It is difficult to see abdominal distension in advanced pregnancy.

Perforated Peptic Ulcer in the Puerperium

PPU rarely occurs in the puerperium. Anderson first described such a case in 1942, when a 29-year-old woman developed abdominal pain a few hours after a normal delivery and died in septic shock due to perforated duodenal ulcer [154]. The relative rarity of perforated duodenal ulcer in pregnancy and puerperium often causes delay in both diagnosis and surgical intervention [201]; this is made worse considering that the usual signs of perforation may be diminished or subtle in the puerperium [186, 202].

Table 4.2 Important data of published studies of perforated peptic ulcers during pregnancy (without puerperium)

Study	Age	Pregnancy (weeks)	Ulcer type	Duration (hours)	Operation	Mother/birth	Child
James, 1948 [29]	24	36	Duodenum, anterior	10		Live, vaginal	After 4 days, live
Burkitt, 1961 [187]	38	31	Duodenum	10	Partial gastrectomy	Live, vaginal	Less than 24 h, one twin alive
Horwich, [55]	30	31	Duodenum, anterior	60	Sutures		Before operation, dead
Lindell and Tera, 1962 [188]	26	9 months	Pylorus, greater curvature, 1 cm			Live, vaginal	Less than 24 h, live
Winchester and Bancroft, 1966 [193]		34	Duodenum		Roscoe Graham	Live, vaginal	37th week, live
Gali et al., 2011 [197]	16	28	Duodenum, anterior		Roscoe Graham	Live, vaginal	After 3 days, died
Goh and Sidhu, 1995 [195]			Duodenum				
Hsu et al., 2011 [196]	23	20		96		Live, vaginal	Live
Segal, 1959 [199]	29	6	Pylorus, anterior	18	Sutures	Live, lost for follow-up after 24 weeks of pregnancy	
Essilfie et al., 2011 [200]	27	38	Duodenum, anterior		Roscoe Graham	Live, vaginal	38th week, live

The symptoms may commonly be attributed to obstetric-related causes, and therefore, a high index of suspicion is necessary. However, earlier diagnosis may be enabled with the conventional plain abdominal X-rays and ultrasound scan [203].

In the last 40 years, there are only several cases published. There is approximately equal number of these perforations developed after Cesarean section and vaginal delivery. The important figure is that after Cesarean section, these perforations occur during the first several days of puerperium [177, 204–207]. In the immediate postoperative period, abdominal symptoms may be interpreted as constitutional symptoms emanating from pregnancy or surgery [202]. Often a presumptive diagnosis of paralytic ileus is made and in some instances that of puerperal sepsis, which could result in a relaxed approach in dealing with such symptoms.

After vaginal delivery, there are also several cases with half of patients being older (41 and 42 years old [201, 208]) and two were younger (28 and 29 years) [154, 186]. In this group perforated ulcer also developed during first days after delivery.

There are two reports of gastric perforation [209, 210] and one perforation of duodenal ulcer in the puerperium, but most of the medical data were not available (Table 4.3) [211].

There are several diagnostic problems in puerperium. Nonspecific abdominal pain is experienced by 98 and 92 % of primiparous and multiparous women, respectively, in the puerperium [212]. Another fact is that about 60 % of all post-laparotomy patients will have evidence of pneumoperitoneum and this will take 1–24 days to be absorbed [213]. This is important for patients with abdominal pain after Cesarean section making the diagnosis more difficult. In such cases water-soluble contrast swallow will show a free peritoneal leak.

4.1.2.4 Diagnosis

The only role radiology would have in the pregnant patient with PUD is confirmation of perforation. The usual approach to the diagnosis of pneumoperitoneum is to perform an abdominal

Table 4.3 Published studies of perforated peptic ulcers during puerperium

Study	Age	Days after delivery	Ulcer type	Duration (hours)	Operation	Mother/birth	Child
Anderson, 1942 [154]	29	4 h	Duodenum			Died, vaginal	Live
Ross, 1958 [186]	28	1	Duodenum, anterior	60		Live, vaginal	Live
McGarvey et al., 1952 [208]	41	2	Duodenum				
Parry, 1974 [211]			Duodenum				
Munro and Jones, 1975 [201]	42	4	Prepyloric	70	Sutures	Vaginal	
Kaczmarek, 1970 [205]						C-section	
Opitz, 1971 [209]			Gastric				
Gaĭstruk et al., 1980 [210]			Gastric				
Uchikova et al., 2004 [204]			Duodenum			C-section	
Engemise et al., 2009 [177]	29		Duodenum, anterior	50	Omental patch	Live/C-section	Live
Alabi-Isama et al., 2009 [206]							
Sule and Omo-Aghoja, 2010 [207]	25	3	Duodenum, anterior	7 days	Omental patch	Live/C-section	Live

series, but this would involve irradiation of the fetus in the pregnant patient. In a series of 100 patients with known pneumoperitoneum, Woodring and Heiser showed that the upright lateral chest radiograph confirmed pneumoperitoneum in 98 % of the cases. This was more sensitive than the upright posteroanterior chest radiograph, which showed the pneumoperitoneum in only 80 % of the cases [214]. The performance of a lateral chest radiograph excludes the fetus from the direct beam; if negative for the presence of free intraperitoneal air, this would support more conservative management. In the presence of strong clinical suspicion for intra-abdominal disease, the decision to perform further imaging, such as abdominal CT, versus surgical exploration will have to be made on an individual basis.

4.1.2.5 Treatment

The treatment of PPU consists of surgical intervention and perioperative pharmacological gastric acid suppression.

Surgical Treatment

In the first half of the twentieth century, there were cases of PPU in pregnancy treated conservatively. Only 24 cases of PPUs have been described up to 1966 [19, 29, 55, 154, 178, 186–192]. In that series 16 patients were treated medically (nasogastric suction, nil by mouth, and antibiotics) with 16 maternal and 11 infant deaths. As in nonpregnant population, conservative therapy of PPU is not an acceptable option. Omental patch repair with *H. pylori* eradication (if present) is the standard of care for sealing duodenal perforations and preventing reperforations. Postoperative complications such as intra-abdominal abscess [207] should be drained as soon as possible. If the adjustable gastric band is the cause of marginal or peptic ulcer, it should be removed during emergency operation [198].

Perioperative Gastric Acid Suppression

Histamine$_2$ Receptor Antagonists (H$_2$RA)

The H$_2$RAs are the most commonly used and safest medications for the pregnant woman with heartburn not responding to lifestyle modification and nonabsorbable medication. All four drugs (cimetidine, ranitidine, famotidine, and nizatidine) are FDA (Food and Drug Administration)-approved category B drugs for pregnancy.

Cimetidine and ranitidine. Cimetidine and ranitidine have had considerable use in pregnancy over the last 30 years with an excellent safety profile. Only ranitidine's efficacy has been specifically studied during pregnancy for heartburn [215]. No adverse pregnancy outcomes or drug reactions were noted. Cimetidine has a weak antiandrogenic effect in animals, as evidenced by a reduction of the size of testes, prostate glands, and seminal vesicles [216]. Ranitidine has no antiandrogenic activity in animals [105]. Neither H$_2$RA has reports of human sexual defects in infants. To date, the safety of cimetidine and ranitidine has been assessed in over 2,000 pregnancies in database studies not sponsored by the manufacturers. In the surveillance study of 229,101 pregnancies in the Michigan Medicaid recipients between 1985 and 1992, similar rate of major birth defects was detected (4.3 % with cimetidine, 4.5 % with ranitidine, and 4.3 % in women taking no medications during their pregnancies) [217]. In a 1996 prospective cohort study, 178 women exposed during pregnancy to H$_2$RAs were matched with 178 women with no exposure with similar maternal age, smoking, and alcohol history [91]. Among these subjects, 71 % took ranitidine, 16 % cimetidine, 8 % famotidine, and 5 % nizatidine. The outcomes of both groups were similar in terms of live births, spontaneous or elective abortions, gestational age at delivery, birth weight, or major malformation. The latter rate was 2.1 % in subjects exposed to H$_2$RAs versus 3.0 % in the nonexposed cohorts. The Swedish Medical Birth Registry in 1998 reported on 553 babies delivered by 547 women using various acid-suppressing medications in early pregnancy [218]. Seventeen infants had congenital defects (3.1 %) compared with the expected rate of 3.9 % in the Registry among women not taking any medications. Of the 17 infants, ten had been exposed to PPIs, six to H$_2$RAs, and one to both classes of drugs. Two birth defects (5.7 %) in 35 infants exposed to cimetidine and six defects (3.8 %) in 156 infants

exposed to ranitidine were reported. Overall, the odds ratio for malformations after H_2RAs was 0.46 in contrast to 0.91 for infants exposed to PPIs, early during pregnancy. Finally, two databases, one from England and another from Italy, were combined in a study published in 1999, which compared the incidence of congenital malformations in infants and women receiving cimetidine, ranitidine, or omeprazole during the first trimester of pregnancy with unexposed control women [92]. The relative risk of malformation (adjusted for maternal age and prematurity) was similar among all three drugs: cimetidine 1.3, ranitidine 1.5, and omeprazole 0.9. In summary, cimetidine and ranitidine have not been associated with an increased risk of congenital malformations. Ranitidine is the only H_2RA with documented efficacy in pregnancy. Some authorities have recommended that cimetidine not be used during pregnancy because of possible feminization as observed in some animals and nonpregnant humans [219].

Famotidine and nizatidine. There are much less reported safety data with these latter H_2RAs than cimetidine and ranitidine. Animal studies with famotidine revealed no fetal toxicity or teratogenicity [220]. However, pregnant rabbits with the equivalent of 300 times the recommended human dose of nizatidine encountered abortions, low fetal weights, and fewer live fetuses [221]. On the contrary, rat studies found no adverse effects on the fetal pups [222]. In the Michigan Medicaid Surveillance Study, 6.1 % of fetuses exposed to famotidine during the first trimester of pregnancy developed major birth defects compared with the expected prevalence of one. The small size was too small to draw firm conclusions, however. With nizatidine there is only a single case report of a woman delivering a healthy baby after taking the drug during 14–16 weeks of gestation [217]. Although few reports are available, famotidine appears safe during pregnancy. Although nizatidine was previously classified as category C, the FDA recently reclassified it as a category B drug. However, the conflicting animal data are troublesome and suggest that other H_2RAs may be safer during pregnancy. Proton pump inhibitors are the most effective drug therapy for symptom control and healing of esophagitis. The PPIs have not been as extensively used in pregnancy as the H_2RAs, or is their efficacy proven in pregnancy, and the data about total safety are more limited. Omeprazole is categorized as a class C drug by the FDA because of fetal toxicity. The other PPIs are categorized as class B drugs. However, unlike the nonpregnant heartburn patient, PPIs should only be used during pregnancy in women with well-defined complicated GERD, not responding to lifestyle changes, antacids, and H_2RAs.

Proton Pump Inhibitors (PPIs)

Omeprazole. Omeprazole, the first of the PPIs, is classified as a class C drug in pregnancy because at doses similar to those used in humans, omeprazole produced dose-related embryonic and fetal mortality in pregnant rats and rabbits [223]. No teratogenicity was observed. The FDA has received reports of at least 12 birth defects in pregnant women exposed to omeprazole, including anencephaly and hydroencephaly [217]. However, other case reports and small case series have found no infant congenital malformations in mothers taking 20–60 mg omeprazole/day, even in the first trimester of pregnancy [79, 224]. A meta-analysis from 2002 assessed the risks of congenital fetal malformations in women using PPIs in the first trimester of pregnancy [225]. Five studies met the inclusion criteria, all were cohort studies ascertaining pregnancy outcomes with either registry linkage [92, 218, 226] or by direct interview with the mother [225, 227]. A total of 593 infants were exposed to PPIs, most (534) received omeprazole. The summary relative risk for all major malformations among any PPI exposure was 1.18, a nonsignificant relative risk. For the four studies where data for only omeprazole could be extracted (Fig. 4.3), the summary relative risk was 1.05, also indicating a nonsignificant relative risk for malformations. Although the weight of evidence suggests omeprazole is safe in pregnancy, the FDA has not changed its class C rating. With the advent of newer PPIs, especially esomeprazole, omeprazole is currently infrequently prescribed. However, the drug is now over the counter at a 20 mg dose and cheaper than prescription PPIs.

Lansoprazole. Animal studies using doses of lansoprazole up to 40 times the recommended human dose have found no evidence of impaired fertility or fetal toxicity [229].

Human data on the safety of lansoprazole in pregnancy are more limited. In one nonobservational cohort study [224], six pregnant patients taking lansoprazole during the first trimester delivered seven healthy newborns. Lansoprazole was the only acid-suppressing drug exposed in 13 infants reported to the Swedish Medical Birth Registry [218]. Two birth defects were observed: one atrial septal defect and one undescended testes. In a Danish study published in 1999, 38 patients had taken PPIs during the first trimester of pregnancy (35 omeprazole, 3 lansoprazole) [226]. The prevalence of major birth defects, low birth weight, and prematurity were no different than in pregnant controls not receiving any medications. In a study published this year, 295 pregnancies exposed to omeprazole, 62 to lansoprazole, and 53 to pantoprazole were compared with 868 pregnant controls for the development of congenital abnormalities [230]. As with other studies, the rate of congenital abnormalities did not differ between the exposed and control groups: omeprazole 3.6 %, lansoprazole 3.9 %, and pantoprazole 2.1 % versus controls 3.8 %. No differences were found when exposure was limited to the first trimester. The lack of teratogenicity in animals is reassuring, accounting for the FDA class C risk category for lansoprazole use during pregnancy. However, the data on safety in human pregnancies are limited, and avoidance of this PPI and all PPIs, especially during the first trimester, is the safest course. If lansoprazole is required or if inadvertent exposure occurs early in gestation, the fetal risk seems to be low. Based on product information from the individual manufacturers, the newer PPIs (rabeprazole, pantoprazole, and esomeprazole) have been shown safe in various animal studies. No reports describing the use of these newer PPIs during human pregnancies are available [217].

Gastric Acid Suppression During Lactation

All systemic antireflux medications are excreted in breast milk and could harm the infant. Therapeutic options must be explained and discussed with women who require treatment but who want to breast-feed. Drug safety during lactation has been assessed in animal studies and human case reports (Table 4.4).

Table 4.4 Safety of antiulcer/GERD medications during lactation

Medications	Safety	Comments
Antacids	Yes	Not concentrated in breast milk
Sucralfate	Yes	Minimal, if any, excretion in breast milk
Cimetidine	Yes	Compatible with breastfeeding (*American Academy of Pediatrics*)
Ranitidine	Yes	Excreted in breast milk in concentrations similar to cimetidine
Famotidine	Yes	Lowest concentrations in breast milk of all H_2RAs
Nizatidine	No	Growth depression in pups of lactating rats
PPIs	No	Growth depression in pups of lactating rats

GERD gastroesophageal reflux disease, *H_2RA* histamine$_2$ receptor antagonist, *PPI* proton pump inhibitor

Antacids

Aluminum and magnesium hydroxide antacids are not concentrated in breast milk and, thus, are safe during lactation. Neither Gaviscon nor sucralfate has been studied during lactation but is presumed safe because of limited maternal absorption.

Histamine$_2$ Receptor Antagonists

All H_2RAs are excreted in human breast milk. Cimetidine and ranitidine reach concentrations in breast milk 4–7 times the doses present in maternal serum [231]. In contrast, famotidine only reaches a mean milk to plasma concentration of 1.78, 6 h after ingestions [232]. Small amounts of nizatidine are excreted into human breast milk [233]. In the only animal studies assessing H_2RA safety during lactation, pups reared by lactating rats ingesting nizatidine experienced growth retardation [234]. The effects of H_2RAs in breast milk on the nursing human infant are unknown. In 1994, the *American Academy of Pediatrics* classified cimetidine as compatible with breastfeeding [235]. Others also suggest that ranitidine

and famotidine are safe and the latter H_2RA may be preferred because of the lower concentration in human breast milk. Nizatidine should be avoided in the breastfeeding mother because of the single animal study [234].

Proton Pump Inhibitors

Little is known about PPI excretion in breast milk or infant safety in lactating women. PPIs probably are excreted in human milk, because of their relatively low molecular weight. This was confirmed in the only report of PPI use during breastfeeding [236]. During the day, the patient fed her infant son just before taking omeprazole at 8:00 am, refraining from nursing for 4 h, and then expressed and discarded her breast milk at noon. At 3 weeks postpartum, blood and milk samples were obtained at 8:00 am and then every 30 min for 4 h. Breast milk levels of omeprazole began to rise at 9:30 am and peaked at 11:00 am at 58 mm, considerably lower value than simultaneous maternal level of 950 mm. The infant was doing well at 1 year. However, rats administered with omeprazole at 35–345 times and rabeprazole at a dose of 195 times the recommended human dose during late pregnancy and lactation had decreased body weight gain of their pups [223]. Therefore, PPIs are not recommended for use by lactating mothers. Women can either take PPIs and discontinue nursing or use medications (i.e., H_2RA) from another class.

4.1.2.6 Prognosis

The diagnosis is often made late in pregnancy with quite devastating consequences. In the series of 24 cases described up to 1966, 16 patients were treated medically with 16 maternal (maternal mortality 100 %) and 11 infant deaths (fetal mortality of 69 %), while 8 patients received surgical treatment (seven simple closures and one partial gastrectomy) without maternal and two infant deaths (of the two infants who died, one was a twin; the other twin survived), making fetal mortality 29 % [19, 29, 55, 154, 178, 186–193]. It is questionable how Paul et al. in 1976 found only six (including their case) cases of maternal survival following perforation of a peptic ulcer and, of these, only four [237] (including their case) were associated with survival of both the mother (maternal mortality 33 %) and infant [238]. Early surgical diagnosis and treatment followed by vaginal delivery of the fetus offer the best hope for survival of the mother and child.

Table 4.2 shows ten cases during pregnancy (without puerperium) with maternal data of eight mothers. All survived and the survival rate today is approaching 100 %. Table 4.3 shows 12 cases of PPU during puerperium, but the data about maternal and fetal outcome are lacking; therefore, conclusions about prognosis cannot be made but probably are the same as during pregnancy. Clinicians are not reluctant to indicate necessary imaging methods during puerperium as in general population because there is no fear of radiation exposure to the fetus.

4.2 Perforated Malignant Ulcer/Carcinoma

Perforated gastric carcinoma is an extremely rare condition due to the rarity of the gastric cancer in pregnant population. The characteristics of gastric cancer in young (pregnant) women are discussed for easier understanding and diagnosis of such condition during pregnancy.

4.2.1 Gastric Cancer in Pregnancy

4.2.1.1 Incidence

Whereas gastric cancer is prevalent in the elderly, the incidence of gastric cancer associated with pregnancy is comparatively low, 0.026–0.1 % of all pregnancies [239–242]. There are few reports of pregnancy-associated gastric cancer from countries other than Japan. It was first reported by Fujimura and Fukunda in 1916 [243]. Jaspers et al. reviewed a total of 31 cases of pregnancy-associated gastric cancer in reports that were published in academic journals from 1969 to 1999 [244]. Theirs was the only major study in Western countries, and subsequent reports have been sporadic [245–252]. On the other hand, owing in part to the relatively high incidence of gastric cancer in Japan, more than 100 cases have been reported in this country up to 1987 [240].

The largest study from Japan accumulated 137 patients adding to Ueo et al. [240] another 37 cases of pregnancy-associated gastric cancer that had been newly reported in Japan from 1988 to 2007: these consisted of two cases in 1968–1977, six cases in 1978–1987, and 29 cases in 1987–2007 [253–271].

Krukenberg (Metastatic) Tumor

The association of Krukenberg tumor and pregnancy is extremely rare. For over a century and its first description in 1896 by Krukenberg [272], few cases have been reported in world literature [273]. Yaushiji on a series of 112 Krukenberg tumor reported only three cases during pregnancy, so an incidence of 2.6 % [274]. The rarity of this disease is due to the rarity of gastric cancer in young women. Only 0.4–0.5 % of gastric cancers occurs in women aged less than 30 years [275]. Incidence in future decades cannot be estimated. On one hand, with increasing fertility of women over 30 years, one could expect an increased incidence of this disease over the next decades, but on the other, the incidence of (advanced) gastric cancer is declining.

4.2.1.2 Pathology

Pathology according to the largest review on the topic shows that diffuse type is more common (86.9 %) than the intestinal type (13.1 %) [276]. While in older patients the majority of carcinomas are of the intestinal, usually well-differentiated type, the tumors in young patients are mainly poorly differentiated carcinomas of the diffuse type with signet ring cells and peritoneal metastasis.

4.2.1.3 Pathophysiology

Gastric adenocarcinoma occurs infrequently in patients under 40 years of age. The literature on gastric cancer in the young adults has described almost similar findings: the female dominance with a male to female ratio of 1:1.5 [277], more aggressive histological features, the advanced disease stage at presentation, and the poorer prognosis [278]. These characteristics were even more pronounced in the pregnancy-associated cases [242, 279]. Being more common in females, the association of gastric cancer and pregnancy could be purely a natural coincidence, but on the other hand, it has been postulated that the immunosuppression during pregnancy is conducive for tumor growth and the biological and hormonal circumstances further enhances tumor progression [279, 280]. Furukawa et al. demonstrated experimentally a suppressive effect of sex hormones on spreading of stomach cancer in rat models [280]. Placenta secretes histaminase which degrades histamine function; hence, the patient shows no deterioration of symptoms caused by the cancerous ulcer. As it is known, blood circulation increases during pregnancy; pregnant women are particularly susceptible to the rapid growth and spread of cancer.

4.2.1.4 Clinical Presentation

Krukenberg Tumor

A maternal and fetal virilization can be observed [281]. This virilization, nonspecific to Krukenberg, is due to luteinized ovarian stroma reaction, stimulated by the placental production of steroids and human chorionic gonadotropin. The pelvic mass was found in 49.3 % of cases in the series of Yaushiji [274]. Its management during pregnancy is difficult. Indeed, the incidence of malignant tumors is only about 1–6 % of adnexal masses associated with the pregnancy. The differential diagnosis with luteomas or other benign adnexal pathology, where the management is radically different, is not always easy.

4.2.1.5 Diagnosis

Hormonal and immunosuppressive effects of pregnancy could explain why most cases of gastric cancer associated with pregnancy are usually advanced by the time that they are diagnosed. Misdiagnosis is another contributing factor as the symptoms are frequently masked by factors related to the normal pregnancy. In one case initial symptoms of gastritis were mingled and masked by the hyperemesis gravidarum. Even on admission, the acute abdomen was thought to be pregnancy related. Similar to other reported cases, symptoms were attributed to the pregnancy and not evaluated further until delivery or complications developed [242, 279]. Detection can

be further delayed as therapeutic approaches will usually be restricted by the physical and psychological clinical events surrounding the pregnancy.

Diagnostic modality for definitive diagnosis as in nonpregnant patients is esophagogastroduodenoscopy (EGD). Indications for the repeated EGD are the same as in nonpregnant patients. It is confirmed by the fact that a patient with an exacerbation of peptic ulcer presented with gastric carcinoma during pregnancy [282].

In pregnant patient MRI is preferred to CT scan due to the ionizing radiation. Although not specific, the presence of solid components showing hypo-intensity on T2-weighted images in an ovarian mass appears to be a characteristic finding of Krukenberg tumors (Figs. 4.3 and 4.4), especially if the tumors are bilateral, have sharp margin, thin-walled, and have an oval configuration [283, 284]. Except primary tumor, the metastatic form can be found, which can sometimes, as when Krukenberg tumor is present, mislead the clinician to the diagnosis of primary ovarian tumor during pregnancy. Therefore, the definitive diagnosis is histological, marked by areas of mucoid degeneration and by the presence of signet ring cells.

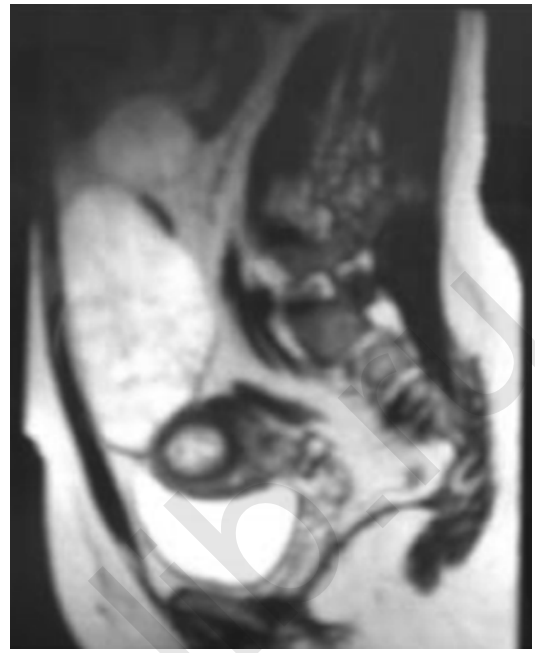

Fig. 4.3 Sagittal T2-weighted MR image revealing a gravid uterus with two ovarian masses [228]

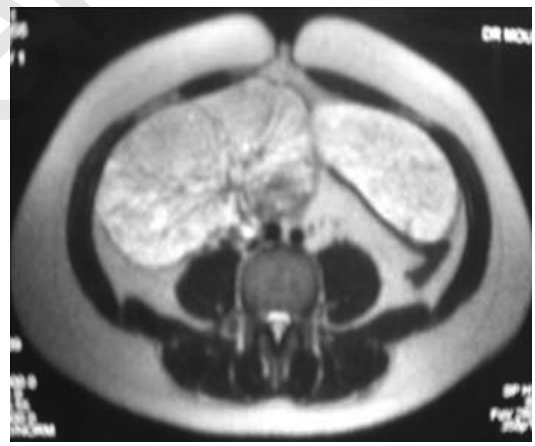

Fig. 4.4 Axial T2-weighted MR image revealing bilateral Krukenberg tumors. Both are well encapsulated and have oval form [228]

4.2.1.6 Treatment

Primary Gastric Tumor

Because of this as well as the fact that the peritoneal cavity will already be contaminated by cancer cells, surgery should be as palliative as possible. In view of the poor outcome, a simple closure of the perforation or omentopexy is the usual procedure.

Metastatic Tumor

Indication for the palliative or curative surgery is the same as in general population. Concerning Krukenberg tumor, aggressive surgery can improve the prognosis; but its management depends essentially on the finding at laparotomy [285–287]. If no other metastatic disease except involvement of both ovaries is found (Fig. 4.5), bilateral oophorectomy with or without hysterectomy can be performed. The decision on the termination of pregnancy depends on the trimester of pregnancy and patient's decision about current pregnancy. If the diagnosis of primary gastric carcinoma is known before the operation, definitive operation can be done in the same act. If primary tumor is not known, the diagnostic workup should be done and the indications for the operation made according the stage of the primary gastric carcinoma.

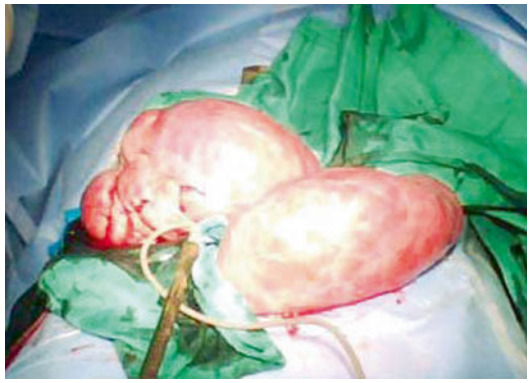

Fig. 4.5 Bilateral Krukenberg tumor at 10-week pregnancy without other metastatic disease found at laparotomy [228]

Cesarean Section

With regard to the fetus, an induced delivery or early Cesarean section will simplify management of the mother provided the fetus has reached viability. Otherwise an abortion is not known to be therapeutic, and an early pregnancy can be left undisturbed unless irradiation or chemotherapy is planned.

Hormonal Therapy

The effect of estrogen and the results of antiestrogen treatment in clinical trials are controversial. Jaspers et al. [244] reported that the features and prognosis in gastric cancer associated with pregnancy were the same as in other young patients.

4.2.1.7 Prognosis

Pregnancy-associated gastric cancer is found in the advanced stage in 95.5 % of the patients. In one of the largest studies by Ueo et al., only 44 % of the patients underwent surgical resection and the prognosis was extremely poor, i.e., 1-year survival in 14.5 % and 2-year survival in 10.6 % [240]. In another study patient survival was analyzed based on the data obtained from the 85 patients whose prognostic data were available. The prognosis was very poor: the 1- and 2-year survival rates were 18 and 15 %, respectively, and only five patients survived for more than 3 years with no recurrence [276]. Fazeny and Marosi conducted a 30-year review of the world's medical literature. Among 100 reports of pregnancy-associated gastric cancer, only one survivor was detected. Maternal survival of 9–19 months after diagnosis in pregnancy was observed for all other cases [288]. Even in regard to the 27 patients diagnosed in the most recent 20 years, the 1- and 2-year survival rates were 37 and 32 %, respectively [276]. In conclusion, the prognosis of patients with pregnancy-associated gastric cancer remains poor, although it seems to be somewhat improved compared with that in the report of Ueo et al. [240].

4.2.2 Perforated Gastric Cancer in Pregnancy

4.2.2.1 Incidence

There are four cases of perforated gastric cancer during pregnancy published with extremely poor prognosis. First is a 29-year-old woman from Turkey [289] and three others from Japan, one during Cesarean section [261], another during pregnancy during observation of ovarian tumor [254], and the third during delivery with misdiagnosed abruption of placenta [271]. There is only one case of perforated malignant ulcer in 43-year-old 17th gravid patient, who developed a perforation of a carcinomatous ulcer of the stomach on the 8th day of puerperium [290]. There are no more details about the case.

4.2.2.2 Treatment

Primary Gastric Tumor

The difference between benign and malignant ulcer or carcinoma is the necessity of oncologic curative or palliative surgery. If perforated carcinoma is found during Cesarean section, definitive oncologic surgery could be made or just suturing as the therapy for the perforation and another exploration is made for definitive surgery. If perforation is found during pregnancy, further therapy depends on the stage of pregnancy as in other malignant tumors during pregnancy. In early pregnancy termination of pregnancy with oncologic surgery is made. In advanced pregnancy oncologic surgery can be postponed after delivery, or if pregnancy is around 27th week, then corticosteroids are used for fetal lung maturation and Cesarean section with definitive surgery is made.

Because of this as well as the fact that the peritoneal cavity will already be contaminated by cancer cells, surgery should be as palliative as possible. In view of the poor outcome, a simple closure of the perforation or omentopexy is the usual procedure.

4.2.2.3 Prognosis

One patient died 6 months after initial diagnosis of gastric cancer despite surgical therapy and adjuvant chemotherapy [289]. Unfortunately, the data for three Japanese cases [254, 261, 271], as well as for perforated malignant ulcer [290], were not available.

4.3 Non-peptic Ulcer Nontraumatic Gastric Perforations/Ruptures

4.3.1 Spontaneous Gastric Rupture

4.3.1.1 History and Incidence

Spontaneous rupture of the stomach in general population was the subject of medical speculation as long ago as 1819, but Carson's report in 1845 offered the first proof of its occurrence in human [291]. Glassman in 1929 collected 14 cases of nontraumatic rupture of the stomach from the literature and noted that there was but one survival [292]. Miller has made the first report of *spontaneous rupture* of the stomach during labor or the postpartum period [293]. It is an extremely rare condition with less than ten cases published [44, 199, 293–296].

4.3.1.2 Etiopathogenesis

Spontaneous gastric rupture is rare because the stomach is anatomically protected in the upper abdomen by the liver and ribs and because the stomach has mobile distensible walls and two valves, gastroesophageal and pyloric, to decrease intragastric pressure [297].

It is apparent from the reports of *spontaneous rupture* of the stomach or intestine that distention of the viscera invariably precedes rupture. Acute gastric dilatation is a recognized complication of the postpartum period which is most frequently of functional origin. Pylorospasm, "dropping" of the stomach and intestines to their antepartum position, hypotonicity of the bowel, and "nutritional edema" of the pylorus have also been suggested as etiological factors in acute postpartum gastric dilatation [298]. Harkins has noted that gastric dilatation and intestinal ileus are prone to occur after abdominal operations and especially when peritonitis is present [299]. Carlson and Ortiz in 1960 attributed ileus and gastric dilatation to the exhaustion phase of the stress reaction and have treated their patients with ACTH [300]. Whatever the cause of the dilatation, sustained distention of the stomach may lead to an ischemic necrosis of the mucosa with disruption of this layer and subsequent extension through the remainder of the stomach wall [293, 301]. Nontraumatic rupture of the dilated stomach occurs most frequently near the lesser curvature and explains this predilection by the external fixation of the lesser curvature and the reduced "elastic coefficient" of the "magenstrasse" [301, 302]. These authors describe a symptomatic triad of:

- Tympanitic distention of the abdomen
- Subcutaneous emphysema
- Shock as distinguishing features of *spontaneous rupture* of the stomach

The first factor leading to increased intragastric pressure is dilatation of its walls following sudden consumption of large quantities of food. Historical studies on cadavers by Revilliod in 1885 indicate that the stomach has enormous capacity. Gastric rupture due to overfilling could occur only after a rapid filling of a stomach with 4 l of fluid and that the rents occurred in mid-stomach, both anterior and posterior walls [303]. Key Aberg in 1897 made the experiment in sitting position and found that filling with 4 l made ruptures on the lesser curvature.

Vomiting is a significant contributing factor in Mallory-Weiss syndrome, causing longitudinal cracks in the gastric mucosa near the cardia. The above-mentioned cracks may penetrate into the muscular layer. Sometimes vomiting may lead to the rupture of the distal esophagus (Boerhaave syndrome). The difference is that the esophageal rupture occurs during vomiting with gastric contents, while gastric rupture occurs during nausea and vomiting reflexes. Pathogenesis of gastric

rupture is believed to involve arterial ischemia of the gastric wall despite its excellent blood supply. Inflammation of the gastric mucosa which often is not noticed by the patients is also a significant factor here. Trauma, e.g., indirect cardiac massage or chest thump, is the last of the factors leading to gastric rupture [304].

High position of the diaphragm intensified activity of the valve closing the gastric cardia. Compression of the stomach by the uterine fundus increased intragastric pressure and impaired gastric emptying. The probable inflammation of the gastric mucosa decreased the resistance of its walls.

Spontaneous gastric rupture can be caused by increased intra-abdominal pressure [305]. The pathologically dilated stomach becomes susceptible to rupture during forceful emesis when an abrupt increase in intra-abdominal pressure occurs [306]. Once the stomach becomes critically dilated, the lower esophageal sphincter functionally becomes a one-way valve, allowing contents to only enter into the stomach. Such gastric ruptures typically occur on the lesser curvature where the stomach is less elastic.

All authors have been impressed by the rapidity of onset and depth of the shock and note that these patients die in the first 9–10 h without alleviation of the state of shock by vigorous, supportive treatment. Numerous explanations of the mechanism of this type of shock have been advanced, all pertinent, but none of which are conclusive. Christoph and Pinkhamew in 1961 believed that the pathogenesis of the gastric rupture in the presented case followed a definite sequence [294]. Because of the stress from perforation of the appendix and peritonitis, which may have spread following involution of the uterus, and spontaneous delivery, the basis for acute gastric dilatation was present [299, 300]. The distention was sufficient to cause ischemic necrosis of the gastric mucosa [293, 301] with a subsequent tearing of the outer layers of the stomach wall by the trauma of persistent emesis. Because of the surgical vent in the right lower quadrant, this case did not demonstrate the tympany and subcutaneous emphysema described by others [301]. The depth of shock, however, was disheartening to physician and surgeon alike. In view of the facts that postpartum gastric dilatation and postoperative abdominal distention are frequent complications without causing "unexpected rupture" of a viscus, an additional factor must have had a vital role in the present case. Christoph and Pinkhamew in 1961 believed that stress and chemical imbalance from her several difficulties may have produced changes in the gastric mucosa similar to those produced in major burns [294]. It seems probable that the subtly damaged gastric wall was thus more susceptible to ischemic necrosis and subsequent rupture than the normal stomach.

Some authors believe that the term "spontaneous rupture" of the stomach is a misnomer and that "unexpected rupture" is a more descriptive phrase [294, 307]. In reviewing the available reports of so-called spontaneous rupture of the stomach, a pathologic basis, whether it was ulcer, carcinoma, or gastric dilatation of undetermined cause, was demonstrated at operation or at postmortem examination in all cases.

It should be noted that both cases of gastric rupture in pregnancy were located on the greater curvature [293, 295].

4.3.1.3 Prognosis

In general population during 1930s, in a small number of patients with nontraumatic gastric rupture the survival was almost impossible (1 of 14 patients) [292]. Previous literature indicates high maternal and newborn mortality [44, 199, 304]. There is one case with maternal survival but fetal death in 2002 [296]. The key for maternal survival was early suspicion and diagnosis, early aggressive resuscitation, and emergency laparotomy.

4.3.2 Postoperative Gastric Perforation/Rupture

4.3.2.1 Gastric Ulcer Perforation After Gastric Banding

Laparoscopic placing of an inflating silicon band around the stomach and reducing its orifice, also known as gastric banding, is a surgical procedure that reduces maternal obesity. This procedure is associated with increased unplanned pregnancies. The most common effect reported during pregnancy is repeated/intractable nausea

and vomiting, resolving with deflating of the silicon band. This complication imposes a diagnostic dilemma as to whether bowel obstruction or other intra-abdominal pathologies are involved.

Marginal ulcer is a known complication of bariatric surgery and is a result of tissue ischemia caused by reduced blood supply to the stomach because of the inflated ring [308]. Therefore, when the patient deteriorates under conservative management and a laparotomy is performed, removal of the ring is necessary to resume appropriate gastric blood supply, which is important for a proper gastric healing. Weiss et al. reviewed the results of seven pregnancies, five of which had progressed to delivery [309]. All bands were decompressed because of nausea and vomiting, and two patients had serious complications: one had intragastric migration of the band and the other a balloon defect. Both had to be operated on to remove the band. Laparoscopic gastric banding is considered an efficient and relatively safe procedure for the treatment of maternal obesity. The severely obese pregnant patients with previous gastrointestinal surgery demonstrate one of the unique management dilemmas when presenting with intractable vomiting. This case is even more complicated because a combination of other clinical symptoms suggesting preeclampsia and fetal distress, on top of obesity and vomiting, made the diagnosis even more difficult [198].

4.3.2.2 Gastric Rupture Caused by Diaphragmatic Hernia

This entity is described in Chap. 6.

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Symptomatic Abdominal Wall Hernias

5

5.1 Introduction

Surgical repair of different types of hernia is the most common general surgical procedure. More than 20 million patients worldwide undergo hernia repair each year [1]. As the world population grows, there is continuous increase in absolute number of hernias which should be repaired. Also as the world population grows, it is obvious that there are more and more pregnant women throughout the world. Therefore, there will be more pregnant women with hernias presenting in elective or emergent settings. Minimization of this increase would probably be due to more widespread use of laparoscopy which in turn lowers the incidence of postoperative hernias. During pregnancy, uterine distension raises intra-abdominal pressure making some abdominal wall hernias visible. These hernias are rare and are mostly reported as case reports. This chapter describes the most common abdominal wall hernias during pregnancy with indications for elective and emergency operations. Abdominal wall hernias in pregnancy include surgical and gynecologic aspects of the disease and should be evaluated and treated by an abdominal surgeon and gynecologist in collaboration.

5.2 Groin Hernia

Varices of the round ligament are often mistaken for an inguinal hernia

Verovitz, 1941

5.2.1 Incidence

Estimated rates of the lifetime risk of inguinal hernia repair are 27 % for men and 3 % for women in general population [2]. Operations performed for both elective and emergent inguinal hernias in women have a bimodal age distribution: during the first 9 years of life; thereafter, incidence rises after 30 years of age. The incidence in women is 9–10 times less frequent than in men, and only 9 % of inguinal hernioplasties are performed on women; of these, 17 % are performed on an emergent basis [2]. In nonpregnant women indirect inguinal hernia is 2.5 times more frequent than direct hernia during elective operations (54.3 % vs. 23.1 %), while the difference during emergent operations is significantly smaller (23.5 % vs. 17.2 %). Femoral hernias in an elective setting comprise 15.9 %, while as an emergency these comprise 53.6 % [3]. Inguinal hernia in pregnancy has a reported incidence of 1/1,000–1/3,000 with 75 % occurring in multiparas [4–7].

5.2.2 Etiopathogenesis and Risk Factors

Some authorities from the previous century [8, 9] stated that preexisting hernia frequently disappears during the later months of pregnancy: “the reason being that the enlarging uterus pushes the intestines away from the inguinal ring and presently blocks access to them” [9]. Strangulated inguinal hernias are extremely rare in the later

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months, and, in fact, Gaudier in 1894 stated that a strangulated inguinal hernia and pregnancy are incompatible [10]. Praxagoras of the third to fourth century BC was credited with the first reported operation for obstruction in general population, by relieving strangulated inguinal hernia [11].

The risk factors are the same as for the general population plus the additional increase of intra-abdominal pressure due to an enlarging uterus

- Family history
- Collagen diseases
- Smoking
- Renal failure
- Chronic lung disease
- Diabetes mellitus
- Steroid use
- Malignancy
- Malnutrition
- Cirrhosis
- Ascites
- Obesity

5.2.3 Clinical Presentation

Diagnosis is made by the presence of a reducible or nonreducible groin lump, which demonstrates an expansile cough impulse and the exclusion of other causes of a lump. Palpation of hernia content can differentiate a solid structure (greater omentum or uterine fibroid) from the intestine (gas sounds on pressure). Assessment of the inguinal region is made by applying Valsalva maneuver which increases intra-abdominal pressure. The maneuver is performed when a person tries to exhale forcibly with a closed glottis so that no air exits through the mouth or nose as, for example, strenuous coughing, straining during a bowel movement, or lifting a heavy weight. If incarceration occurs, there is severe abdominal pain with nausea and sometimes vomiting. If bowel is incarcerated, then severe vomiting with absence of stool and flatus is present. Fever develops if perforation due to distension or strangulation occurs. In such cases redness of the overlying skin is commonly present due to the spread of infection through abdominal wall.

5.2.4 Diagnosis

5.2.4.1 Plain Abdominal X-Ray

It is used for the confirmation of bowel obstruction due to incarcerated inguinal hernia in general population. If bowel obstruction is not present, probably the part of the greater omentum is incarcerated. This imaging method is not mandatory because clinical suspicion of incarcerated inguinal hernia is an indication for the emergency operation during pregnancy.

5.2.4.2 Transabdominal Ultrasound

Ultrasound is noninvasive and performed in real time but is operator dependent and has limitations in obese patients. Sensitivity in detecting clinically occult hernias in a non-acute presentation is 33 %, with a specificity of 100 %, and patients with normal ultrasound findings should be considered for further investigation, but hernias with characteristic clinical features need no additional investigation [12].

5.2.5 Differential Diagnosis

There are many causes of a groin swelling/mass and some are listed in the Table 5.1. Some of them, specific to pregnancy, are discussed in detail.

Table 5.1 Possible causes of groin swelling/mass [5, 6, 13–15]

Enlarged lymph node(s)
Subcutaneous lipoma
Cyst in persistent process vaginalis
Round ligament varicosities
Round ligament stretch
Inguinal endometriosis
Inguinal metastases
Lymphoma
Hematoma
Abscess
Mesothelial cysts
Lymphadenopathy
Cyst of the canal of Nuck
Vascular aneurysms/pseudoaneurysms
Soft tissue malignancies
Cystic lymphangiomas

5.2.5.1 Round Ligament Varicosities

Pathophysiology

Anatomically, the round ligament extends from the lateral uterus to the major labia containing veins, arteries, lymphatics, and nerves. Round ligament varicosities (RLVs) are prominent veins within the round ligament and are more common in pregnancy especially in the second or early third trimester because pregnancy promotes increased venous flow and reduced venous tone [13]. There are several mechanisms that cause RLV development. Physiologically, there are progesterone receptors naturally occurring within the round ligament veins [16] and, as progesterone levels increase during pregnancy, they cause dilatation of these veins. Furthermore, with advancing pregnancy, blood volume and cardiac output increase resulting in increase of venous return [17]. This, as well as a gravid uterus causing relative impingement of pelvic veins, results in venous engorgement. RLVs have been rarely described and their true incidence is unknown [5, 16, 18], one study claiming 0.001 % [15]. The RLV was first reported in 1941 by Verovitz who stated that "varices of the round ligament are often mistaken for an inguinal hernia" [19]. The first report of RLV in Korea was in 2010 by Jung et al. [20].

Clinical Presentation

The distinction between groin hernia and RLV is difficult clinically because the symptoms and signs are similar. Both swellings disappear on lying down and reappear on standing, provoked by increased intra-abdominal pressure in cases of coughing or Valsalva maneuver, though a varicocele may return more gradually than a hernia and is a little less circumscribed. A varicocele is of course dull on percussion and more closely resembles a hernia containing omentum than one containing bowel. The absence of varicose veins elsewhere does not exclude the diagnosis of a varicocele of the round ligament. Both traverse the inguinal canal and can be reducible or irreducible. Reducibility of RLV is due to the fact that these veins do not contain valves and therefore can partially empty. RLVs also transmit cough impulses because transmitted abdominal pressure leads to vein distension [6, 13]; a clue that may suggest RLV is in coexistence of lower limb or labial varicosities. RLV most commonly presents with a groin bulge and mild discomfort (Fig. 5.1).

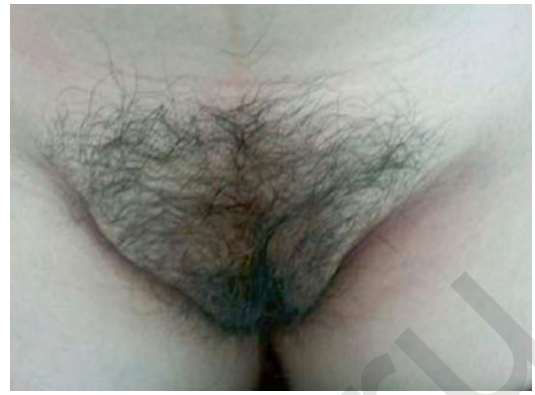

Fig. 5.1 Right inguinal swelling caused by round ligament varicosities [21]

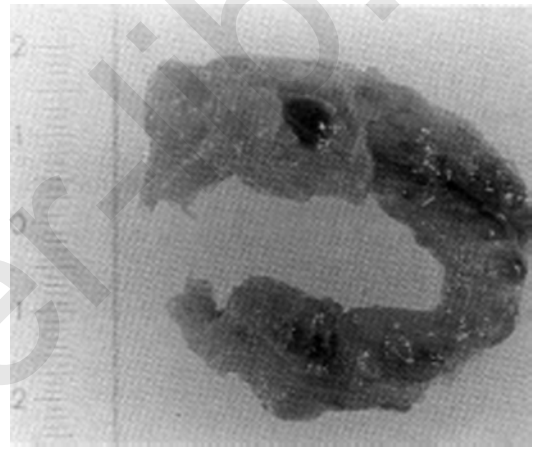

Fig. 5.2 The excised part of the round ligament which is thickened with evident thrombosed varicose veins [22]

5.2.5.2 Round Ligament Varicose Vein Thrombosis

If pain is the predominant symptom, thrombosis of RLV or variceal rupture should be excluded [22]. Thrombosis of the RLV is a complication which still further increases the resemblance between an inguinal hernia and RLV. This complication produces a firm, tender, irreducible swelling simulating a strangulated inguinal hernia. It is more common during postpartum period (Fig. 5.2).

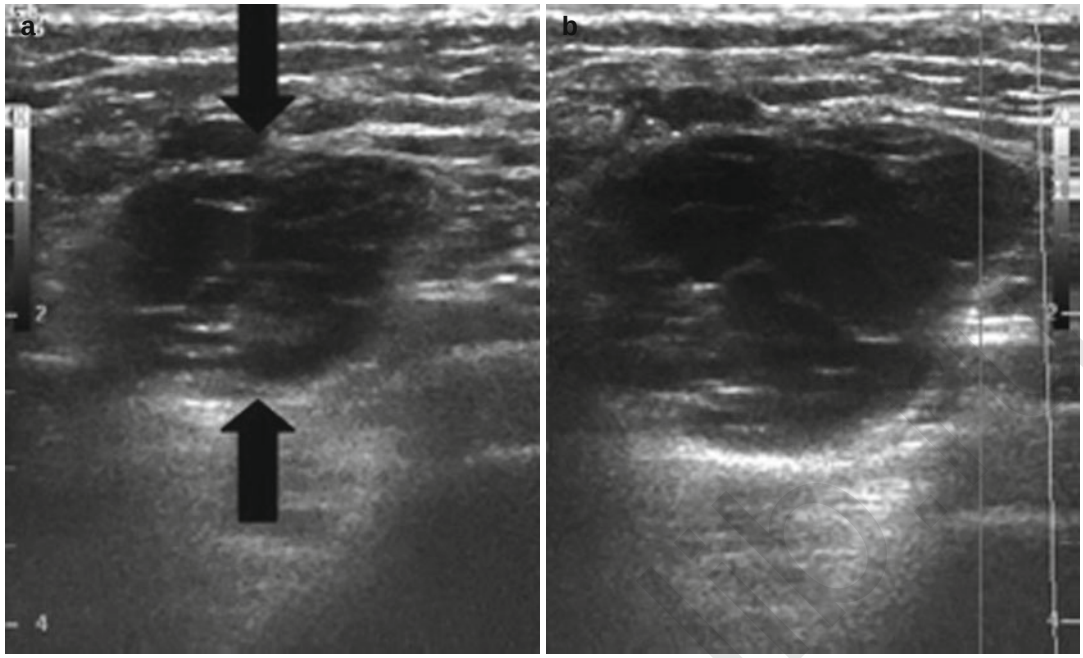

Fig. 5.3 (**a**) Transverse gray-scale sonogram of painful right reducible inguinal mass at rest shows cystic mass (*arrows*). (**b**) Mass enlarged during Valsalva maneuver [11]

Diagnosis

Ultrasonography of the inguinal region can differentiate between multilocular mass which enlarges during Valsalva maneuver (Fig. 5.3) and single mass found in hernia. If the bowel is present in the sac, then peristalsis can be visualized and helps to differentiate it from RLV. It should be noted that hernia sac also enlarges during Valsalva maneuver and is not pathognomonic for either of these diseases. Color Doppler US examination can differentiate RLV from other causes of groin swelling in pregnancy. The characteristic ultrasound appearances of varicosities simulating pelvic masses in pregnant and nonpregnant women include a prominent venous plexus with accompanying dilated draining veins passing through the inguinal canal, veins draining into the inferior epigastric vein, and the typical "bag of worms" appearances of smaller varices [23] with absence of bowel or lymph nodes in the inguinal mass [15]. Duplex imaging can confirm venous flow and augmentation of this flow with Valsalva maneuver (Figs. 5.4 and 5.5). In inguinal hernias, herniated bowel may be recognized by its peristalsis, mucosal blood flow, or mesenteric fat by US and Doppler US examination [18].

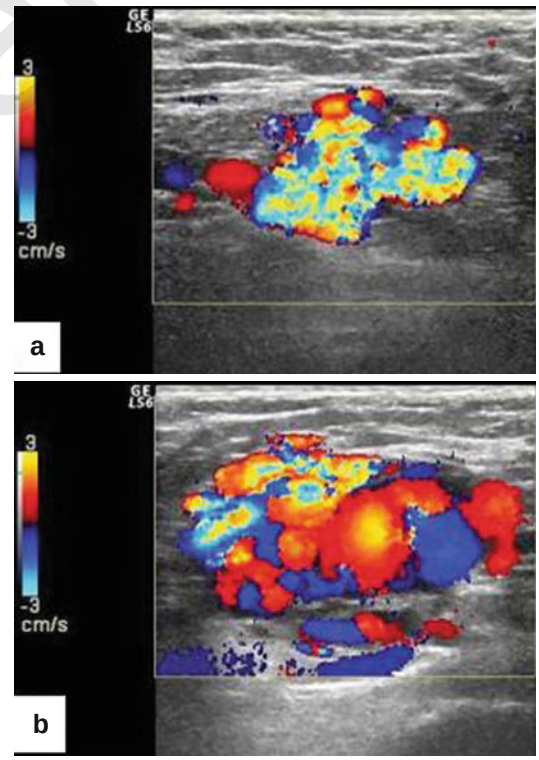

Fig. 5.4 (**a**) Color Doppler US examination confirmed venous flow in the mass. (**b**) Valsalva maneuver caused marked enlargement and flow augmentation in the veins, consistent with round ligament varices [11]

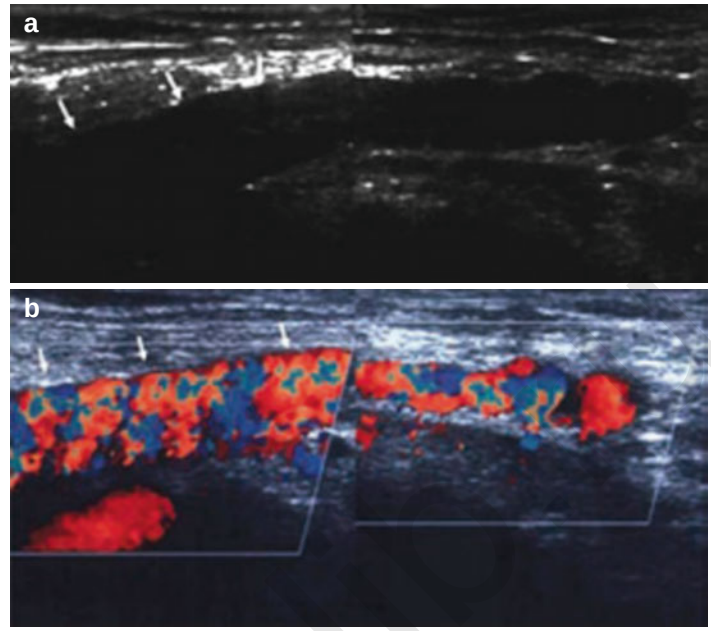

Fig. 5.5 Sagittal gray-scale (**a**) and color Doppler imaging (**b**) reveal the lesion extending from the right inguinal canal to the abdominal cavity (*arrows*) [15]

Lymph nodes have a characteristic appearance, usually hypoechoic with an echogenic central hilum that demonstrates flow on Doppler imaging. The sonographic appearance of endometriosis, hematoma, lipoma, or lymphadenopathy is not easily confused with that of RLV [18]. In doubtful cases CT or MRI can be used. There is no specific treatment and mostly symptoms resolve completely from 2 weeks [21] to 2 months postpartum [15]. A truss may, by giving support, add to the comfort of the patient. Reassurance, with a simple explanation of the temporary nature of the lump during pregnancy and the recommendation of the usual supportive measures for the relief of vulvar and leg varicose veins, is all that has been found necessary.

Thrombosis of Round Ligament Varicosities

The diagnosis of *thrombosis of RLV* has relied historically on surgical evaluation [24], but at imaging they should be suspected if veins are noncompressible, no flow signal can be obtained, and/or there is a visible clot within the lumen. There is no consensus on the management of thrombosed RLV, with patients being treated successfully both with conservative and with surgical management [22]. Surgical exploration is recommended first to rule out a strangulated hernia and secondly to reduce pain or discomfort caused by the inguinal mass.

5.2.5.3 Round Ligament Stretch (Pain)

As the uterus rises in the abdomen, it pulls on the round ligaments like an inflating balloon tugging at its guy ropes (Fig. 5.6). The ligaments usually stretch easily, but occasionally growth rate is too much for them and small hematomas occur. The patient will have sudden localized abdominal pain or hip area that is either on one side or both with little constitutional upset. Some women even report pain that extends into the groin area. Examination shows tenderness well localized over the round ligaments and sometimes radiating to their insertion along the inguinal canal and to the pubic tubercle. Treatment with analgesia, bed rest, and local warmth resolves the situation in a few days.

5.2.5.4 Inguinal Endometriosis

Inguinal endometriosis is rare with the incidence of 0.3 % of endometriosis treated. The incidence of endometriosis in the extraperitoneal part of the round ligament is 0.3–0.6 % among women

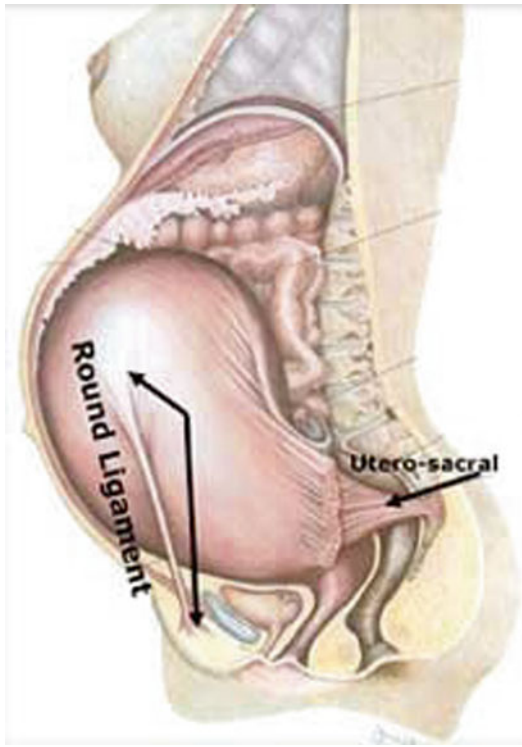

Fig. 5.6 Enlargement of the pregnant uterus causes distension of the round ligament producing abdominal pain [25]

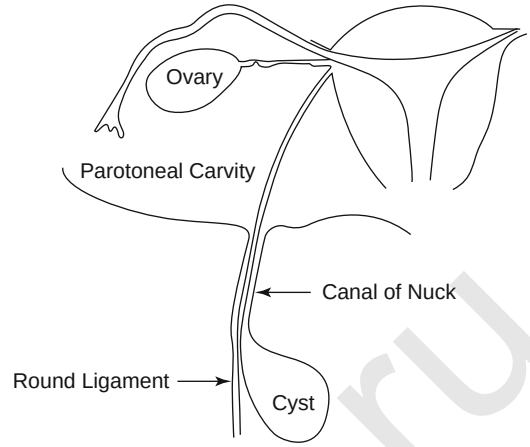

Fig. 5.7 Anatomic diagram of the canal of Nuck. The canal is a small evagination of the parietal peritoneum that accompanies the round ligament through the inguinal ring into the inguinal canal, providing the most likely pathway for endometrial tissue to implant in the superficial inguinal soft tissue [43]

suffering from endometriosis in general [26–32]. Almost all lesions are on the right side and only three patients had left-sided disease and one patient had bilateral inguinal endometriosis [26, 28, 33–35]. Although predominance for the right side is unclear, one possibility for the right-sided predominance is that the sigmoid colon relatively protects the left groin [36]. Also, right inguinal area seems more often affected than the left one because of the clockwise movement of the peritoneal fluid because of the peristaltic movement of the intestinal wall [37, 38].

The size of the mass reported ranges 1–6 cm in diameter [27, 28, 39, 40]. Analysis of published cases showed that 25 % are associated with an inguinal hernia. Endometriosis in the inguinal region was first reported by Cullen in 1896 which he referred to as an adenomyoma of the round ligament [41], and since then less than 100 cases have been published.

Direct extension of endometrial tissue along the round ligament is a possible pathogenesis of inguinal endometriosis [42]. The prevalence of the round ligament of uterus endometriosis in females with deep infiltrating endometriosis is 13.8 % [44]. The canal of Nuck, which is a small evagination of the parietal peritoneum that accompanies the round ligament through the inguinal ring into the inguinal canal, provides the most likely pathway for endometrial tissue to implant in the superficial inguinal soft tissue (Fig. 5.7) [45, 46].

The symptoms commonly fluctuate with menses. Catamenial pain was the pathognomonic symptom in the differential diagnosis of the inguinal mass. Symptomatic complaints ranged from 3 months to 10 years, with an average interval of 3 years [26, 28]. It is essential to point out that cyclicity is not always demonstrable and is not essential for diagnosis. Despite fluctuating symptomatology inguinal endometriosis should be included in a differential diagnosis because it is often diagnosed as inguinal hernia preoperatively. Until the 1960s correct preoperative diagnosis was made in 25–35 % [31]. Ultrasound of inguinal region was not described in this paper.

The sonographic findings of inguinal endometriosis have been presented for fewer than 15 cases [36, 43, 47–51]. The sonographic features of inguinal endometriosis are variable. The presence of solid masses [47–49], cystic masses [36, 51], and combined cystic and solid masses [50] has been described. Most of the cystic masses

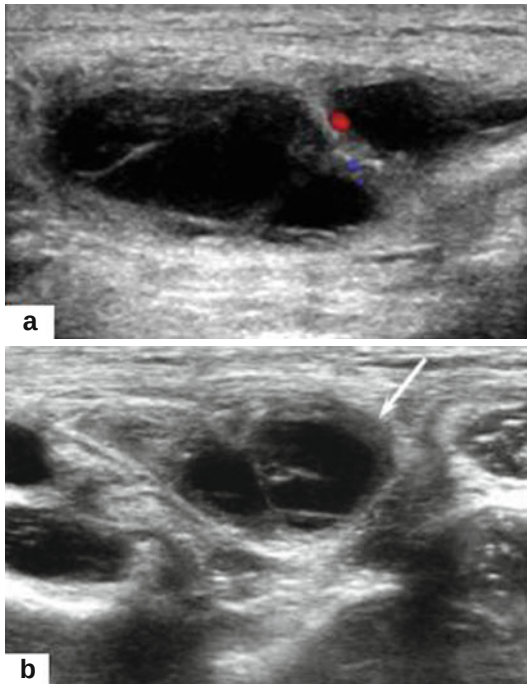

Fig. 5.8 Imaging findings for inguinal endometriosis in a 29-year-old woman. Longitudinal color Doppler (**a**) and transverse gray-scale (**b**) sonograms showing a cystic mass with an internal septum in the right inguinal area (*arrow*). There are flow signals within the septum [43]

have internal septa (Fig. 5.8) [36, 44, 51]. These sonographic findings are different from findings for abdominal wall endometriosis that arises near Cesarean delivery scars. Most abdominal wall endometriosis shows a solid appearance with an irregular margin on sonography, and internal vascularity has been seen within these masses on color Doppler sonography [52, 53].

Young et al. believe that this difference is due to the different environmental situation between the two types of lesions. Inguinal endometriosis usually develops in the canal of Nuck, which is a cavity filled with fluid. If bleeding occurs within the implanted endometrial tissues, the canal of Nuck may be obliterated, and the structure may be vulnerable to formation of a cystic mass. In contrast, cyst formation is difficult for abdominal wall endometriosis because this lesion usually occurs in Cesarean delivery scars, which is a limited space rather than the canal of Nuck [44].

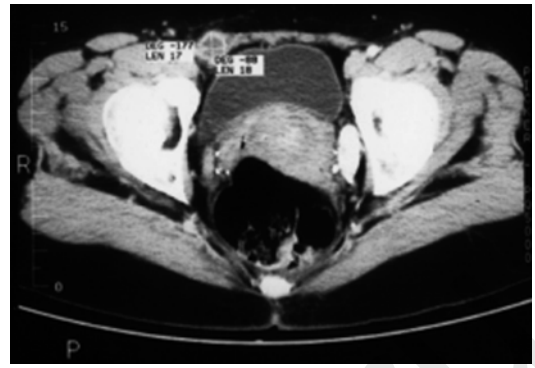

Fig. 5.9 CT scan of the right inguinal extraperitoneal endometriosis. Low-density area with an enhancing rim in the right inguinal region medial to the inferior epigastric vessel lying lateral to the inferior insertion of the rectus abdominis muscle. There was no evidence of bowel obstruction but there were inflammatory changes around the area suggestive of a strangulated direct inguinal area [54]

Sonographically guided fine-needle aspiration is helpful for rapid and accurate diagnosis of inguinal endometriosis and enables a malignancy to be excluded [52]. On CT, inguinal endometriosis shows the presence of a soft tissue mass which is mainly solid in nature with the same density as muscle and follows the course of the round ligament (Fig. 5.9) [43, 55].

An additional diagnostic modality in unequivocal cases is MRI with a characteristic “shading sign” representing an endometriotic nodule [56]. MRI clearly showed the change of tumor size depending on the menstrual cycle, which aided in arriving at the correct diagnosis of endometriosis in this unusual location [55]. However, in half of the reported cases of inguinal endometriosis, MRI features were not specific and included intermediate or high signal intensity on T2-weighted images [47, 55].

When inguinal endometriosis presents as a solid mass on sonography, the differential diagnosis includes neoplasms such as sarcoma, lymphoma, metastasis, an abscess, and hematoma. When inguinal endometriosis presents as a cystic mass on sonography, it should be differentiated from a hydrocele of the canal of Nuck (usually presents as a unilocular cyst [45, 46] and an inguinal hernia). A definitive diagnosis is made during operation for inguinal hernia repair and the condition is treated by complete excision of

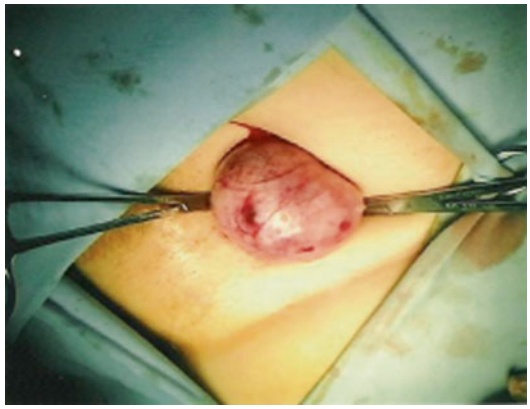

Fig. 5.10 Right inguinal mass (endometriosis) during exploration [37]

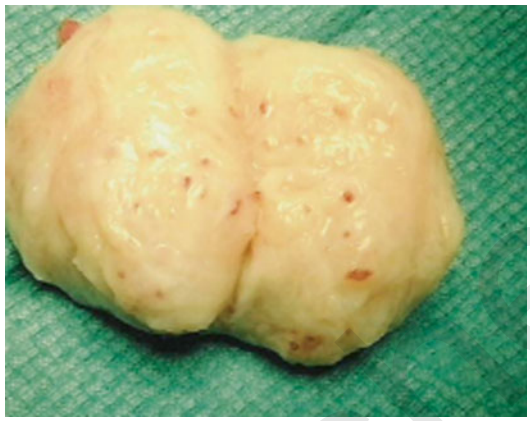

Fig. 5.11 Gross specimen of right inguinal endometriosis [37]

the inguinal endometriosis, including the extraperitoneal portion of the round ligament (Figs. 5.10 and 5.11), otherwise recurrences are frequent [57].

Intraperitoneal endometriosis is demonstrated in most patients. Majeski recommends performing pelvic laparoscopy for all patients who have endometriosis in the extraperitoneal part of the round ligament or in a scar [58]. This view is shared by other authors because of the association with pelvic endometriosis and subfertility (Fig. 5.12) [27, 28].

On the other hand, Seydel et al. did not see the need to perform laparoscopy in patients who do not present with signs of pelvic endometriosis [59].

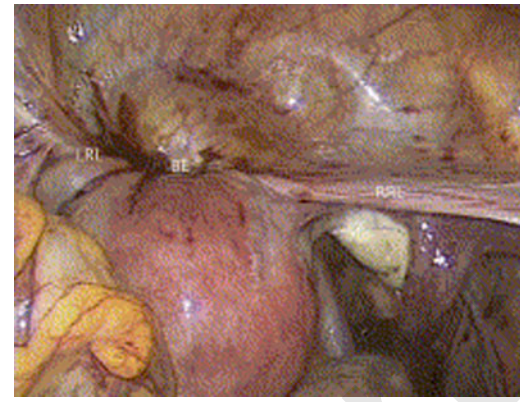

Fig. 5.12 Macroscopic aspects of the round ligament of the uterus. LRL = a left round ligament that is shortened, widened, and deviated in the direction of the bladder due to endometriosis. RRL = a right round ligament that is thickened and pressured by uterine deviation to the left. BE = bladder endometriosis [59]

5.2.5.5 Hydrocele of the Canal of Nuck

In the female, the round ligament is attached to the uterus near the origin of the Fallopian tube and a small evagination of parietal peritoneum accompanies the round ligament through the inguinal ring into the inguinal canal [60]. This small evagination of parietal peritoneum is the canal of Nuck in the female, homologous to the processus vaginalis in the male. The canal of Nuck normally undergoes complete obliteration during the first year of life. Failure of complete obliteration results in either an indirect inguinal hernia or a hydrocele of the canal of Nuck [60, 61]. If obliteration fails in the distal portion of the canal, a sac containing serous fluid remains, the so-called hydrocele of canal of Nuck [60, 61]. Hydrocele of the canal of Nuck is rare condition.

Clinically, the hydrocele of the canal of Nuck manifests as a painless swelling in the inguinal area and major labia. The cysts are usually small averaging about 3 cm in length and about 0.3–0.5 cm in diameter [62].

Ultrasound finding of a hydrocele of the canal of Nuck is typically sausage shaped, extending along the route of the round ligament [61], or comma shaped with a surface beak representing a continuation of the peritoneal cavity through the inguinal canal on ultrasound [46]. MRI shows a hydrocele of the canal of Nuck as a thin-walled tense cystic mass in inguinal area (Fig. 5.13).

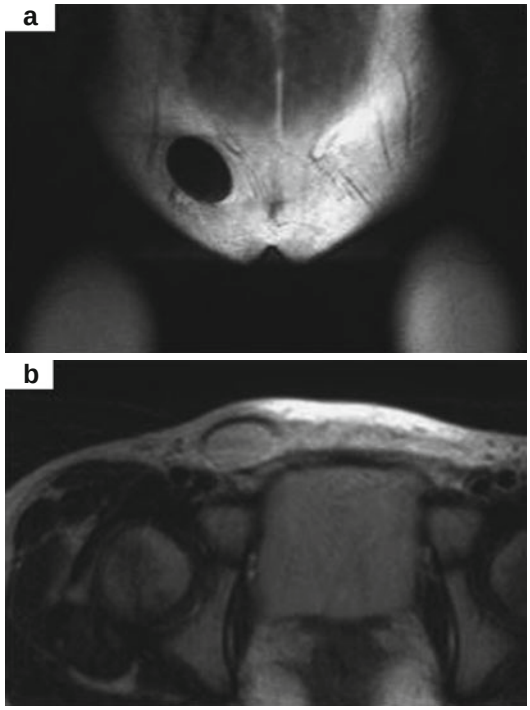

Fig. 5.13 MRI findings of a hydrocele of the canal of Nuck. (**a**) Coronal T1-weighted and (**b**) axial T2-weighted images show the mass is true cystic and thin walled in the right inguinal area [46]

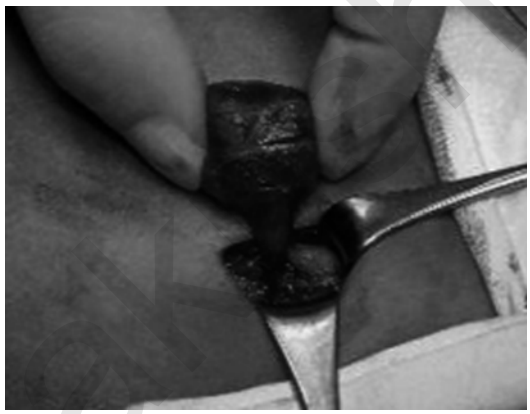

Fig. 5.14 Photograph at surgery shows a comma-shaped cyst with surface beak continuing the round ligament that extends peritoneal cavity through the inguinal canal. The round ligament with cystic tense mass was excised [46]

During operation cystic mass adjacent to round ligament is found (Fig. 5.14). It should be excised completely with excision of the adjacent round ligament because definitive diagnosis is sometimes established only during pathohistological analysis.

5.2.6 Therapy

In general population a higher proportion of emergency operations is carried out in women (16.9 %) than men (5.0 %), leading to bowel resection in 16.6 and 5.6 %, respectively. During reoperation femoral hernias were found in 41.6 % of the women who were diagnosed with a direct or indirect inguinal hernia at the primary operation. The corresponding proportion for men was 4.6 % [63]. These data should be kept in mind when operating on a pregnant patient. Sciannameo et al. reported a case of incarcerated inguinal hernia during pregnancy in which the content of the hernia sac was a distorted uterine fibroid [57]. The role of abdominal binder during the postoperative period is not known.

5.2.6.1 Perioperative Considerations

It has been documented that the rate of serious postoperative complications is lower under local anesthesia, including fewer postoperative analgesic requirements and fewer micturition problems [64].

5.2.6.2 Combined Surgical Procedures and Cesarean Section

The dilemma is whether to perform herniorrhaphy in a pregnant patient with an abdominal wall hernia and indication for Cesarean section. The combination of inguinal hernia repair with Cesarean section was first reported in 1987 by Altchek and Rudick [65]. Cesarean section in a woman with umbilical hernia, inguinal hernia, and incisional hernia after midline, lower midline, or paramedian incision can be made with a single incision and operation time less than 120 min [66]. In patients with bilateral inguinal hernia, the procedure is significantly prolonged [67]. This corresponds to wound infection rate in general population: in operations lasting 61–90 min (4.0 % infection rate), as opposed to 91–120 min (6.2 %) or greater in operations longer than 120 min (8.0 %) [4]. Cesarean section with repair of more distant

hernias requires combined procedures with separate incisions and significant prolongation of operation. Longer duration of operation is associated with an increase in wound infection rates [4]. Prolonged hospitalization and increase in complication rate were not observed in the combined procedures with single incision. In one study no complications were recorded during the perinatal and follow-up periods, and no recurrences observed [67]. The practical benefits are obvious: a 2-in-1 operation, with a single incision, single anesthesia, and single hospital stay, confers valuable advantages for both the patient and hospital in terms of time, cost, convenience, and avoidance of the separation of mother from her newborn baby entailed by reoperation. The operation could be done in general or spinal/epidural anesthesia.

5.2.7 Prognosis

Postoperative course of incarcerated inguinal hernia depends on the content of the hernia sac and duration of the incarceration. There are several important postoperative complications that can occur after inguinal hernioplasty.

5.2.7.1 Recurrence

Recurrence in the general population is 1–20 % [68]. Recurrence rates are not known for inguinal hernioplasty during pregnancy. It is often secondary to deep infection, undue tension on the repair site, or tissue ischemia as in nonpregnant patients. The high postoperative morbidity rate in nonpregnant women compared with men is due both to their high proportion of femoral hernia and to an increased risk for emergency procedure in all types of groin hernias [3]. Because femoral hernias are more frequent in recurrent hernias than in primary hernias, it has been suggested that femoral hernias may be overlooked during repair of inguinal hernias. Possible reasons for the high rate of emergency operation in femoral hernias are no or vague symptoms prior to incarceration, and diagnostic difficulties, even at incarceration [3]. McEntee et al. concluded that strangulated hernias were misdiagnosed by the general practitioner in 33 % of patients and by the hospital registrar in 15 % [69].

5.2.7.2 Postherniorrhaphy Pain

Postoperative groin pain (inguinal neuralgia and inguinodynia) is common. It follows the distribution of the regional nerves, including the ilioinguinal, iliohypogastric, lateral femorocutaneous, and genital branch of the genitofemoral nerve. Nerve injury is usually due to the entrapment of a portion of the nerve in the mesh or suture line.

5.2.7.3 Infection

Infection of the hernia wound or mesh is an uncommon postoperative complication but represents another etiology of recurrence. In specialized hernia centers, the incidence of wound infection is <1 %. When an infection does occur, skin flora is the most likely etiology, and appropriate gram-positive antibiotics should be initiated. If mesh (nonabsorbable) is present, most postoperative groin hernia infections could be treated with aggressive use of antibiotics after the incision is opened and drained expeditiously [70]. Mesh removal is rarely indicated.

5.3 Umbilical Hernia

5.3.1 Incidence

Approximately 5–7 % of all primary hernias in the adolescent/adult general population are umbilical [71]. Infantile umbilical hernia is the result of an abnormally large or weak umbilical ring that fails to close in an otherwise normal abdominal wall. The herniation is typically at the umbilicus, but it may be above (supraumbilical) or below that level (infraumbilical). The defect is covered by skin. The umbilical ring is not covered by fat. Adult umbilical hernia may be the result of untreated infantile hernias that fail to close spontaneously. Only 10.9 % of adults with umbilical hernias recalled having hernias from childhood with a male to female ratio 1:1 [72]. Umbilical hernias (protrusions of >5 mm and diameters of >10 mm from the abdominal skin surface) are present in about 15 % of pregnant West African women [73].

First description found of umbilical hernia in pregnancy was in 1907 by Ernest F. Robinson

Fig. 5.15 Ernest F. Robinson (1872–1945) upon settling in Kansas City became chief surgeon for two railroad companies and, in 1905, joined the University of Kansas School of Medical as a Professor of Surgery – an association that lasted until 1909 [74]

(Fig. 5.15) [75] and the first incarcerated umbilical hernia in 7th month of pregnancy that was complicated with wound infection after hernioplasty and subsequent recurrence was found in the study by Coley and Hoguet published in 1918 [76].

5.3.2 Etiopathogenesis

Mostly, adult hernias present de novo pathology because of either a weakness of the abdominal wall or an increase in abdominal pressure (as in pregnancy), cirrhosis, ascites, or obesity [71]. The neck of the umbilical hernia is usually narrow (1–2 cm) compared with the size of the hernia mass, and strangulation is common [71].

Hypothesis on the mechanism of the incarceration of fibroids without pedicle is as follows. Since the free movement of such fibroids is very limited, their risk of incarceration is much lower than those of their pedicled counterparts. The

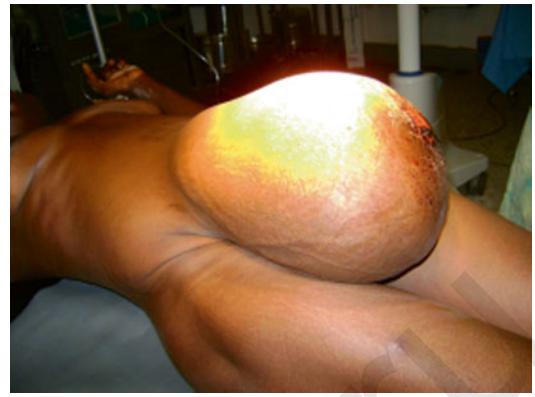

Fig. 5.16 A 42-year-old multiparous woman with a huge umbilical hernia with skin necrosis over the umbilicus in 38-week pregnancy presented to the outpatient clinic stating that she was in labor. She had vaginally delivered her previous children at home with the assistance of a traditional birth attendant. She had never had abdominal operation [79]

progression of pregnancy makes the fibroid displace cranially onto the anterior wall of the uterus. During this process, compression of uterus in the posterior to anterior direction in the abdominal cavity may cause the fibroid to be easily entrapped in the umbilical opening of the hernia sac. The increase in the intra-abdominal pressure due to pregnancy may be a contributing factor to the hernia formation or enlargement of underlying umbilical hernia. The neck of the umbilical hernia is usually quite narrow compared with the size of the hernia mass, and strangulation is therefore common [77].

Finding a gravid uterus in an anterior abdominal wall hernia is rare, and is usually found, in multiparous patients [67, 78, 79].

5.3.3 Clinical Presentation

There are two parts of the diagnostic process. First is the definition of umbilical hernia and second is the definition of the contents of the hernia sac, both important for the type of treatment. Diagnosis is definitive if there is a dilated umbilical ring with or without contents in a hernia sac (Fig. 5.16). If incarceration is present, symptoms depend on the incarcerated organ and duration of incarceration: incarcerated bowel causes vomiting, distension, and absence of stool passage;

uterine fibroid or greater omentum causes only pain and local tenderness. If the bowel becomes necrotic, perforation ensues into the surrounding tissue of the abdominal wall with erythema and edema overlying the hernia.

Postoperative hernia after laparoscopic surgery with supra- or infraumbilical incisions can be differentiated with history taking and evidence of surgical scars.

5.3.4 Diagnosis

5.3.4.1 Plain Abdominal X-Ray

Plain abdominal X-ray can confirm or exclude bowel obstruction but if the diagnosis is clinically evident, it is not necessary, avoiding the risk of fetal exposure.

5.3.4.2 Transabdominal Ultrasound

Abdominal ultrasound is diagnostic in doubtful cases to exclude other possible etiologies of painful periumbilical lumps (see next section "Differential diagnosis") or to confirm or exclude the presence of the bowel in hernia sac.

5.3.5 Differential Diagnosis

5.3.5.1 Omphalitis/Periumbilical Abscess

History taking is important because in omphalitis there is no previous hernia and in periumbilical abscess there is often the history of cleansing of umbilicus with small sticks which cause skin abrasions with inoculation of bacteria. Furthermore, systemic symptoms are rarely present in omphalitis and periumbilical abscess.

5.3.5.2 Umbilical Endometriosis

Incidence

Cutaneous EM (CEM) accounts for less than 5.5 % of all EM cases [80–82]. Less than 30 % of CEM cases appear in the absence of prior surgery and are then referred to as primary or spontaneous CEM [80–82]. Cutaneous EM of the umbilicus is also known as *Villar nodule*, with reference to the physician who first described it in 1886.

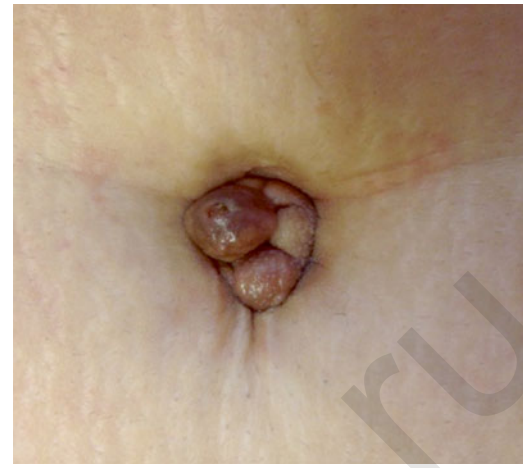

Fig. 5.17 A 37-year-old woman presented with a multilobulated, *red-brownish* nodule that had developed 10 years earlier over her umbilicus, 2 years after the delivery of a single healthy baby. This lesion had slowly grown in size and was reportedly tender and exhibited occasional bleeding during the menses [88]

Cutaneous endometriosis can develop spontaneously during pregnancy and is then most often located on the umbilicus [83, 84]; it may regress spontaneously after delivery [83]. Umbilical EM (UEM) accounts for up to 30–40 % of all CEM cases [80, 81, 85]. Up to 2008, 234 cases of umbilical endometrioses have been described in the literature and only two of umbilical endometriosis in pregnancy [83, 84].

Clinical Presentation

It manifests as a rubbery or firm nodule ranging in size from some mm to 6–9 cm (mean 2–2.5 cm). Its color varies from red and blue to brown-black, depending on the amount of hemorrhage and the penetration depth of ectopic endometrial tissue. Occasionally, the nodule is flesh colored [86, 87]. It is usually single and often multilobulated, although multiple discrete nodules may be present (Fig. 5.17) [89].

Clinical symptoms include tenderness, pain, bleeding, swelling, and growth correlated with the menstrual cycle. However, not all symptoms are present in a given patient and some patients are totally asymptomatic [90]. It is essential to point out that cyclicity is not always demonstrable and is not essential for diagnosis. Other

authors have described noncyclical pain as being more common, and hence the diagnosis of endometriosis must not be disregarded if the pain is not cyclical [91, 92]. Umbilical EM may be associated with umbilical hernia [93]. When UEM is associated with pelvic EM, general symptoms such as dysmenorrhea and dyspareunia may be present. EM has been described in connection with umbilical hernia [94].

Diagnosis

The diagnosis of CEM can be suspected clinically on the basis of the clinical appearance and a good history but relies mainly on histopathological examination. Other diagnostically helpful imaging methods include dermatoscopy, MRI, and ultrasonography. Dermatoscopical findings of EM include a homogenous reddish pigmentation with small, well-defined, globular structures of a deeper hue, termed "red atolls" [95]. The findings in MRI include a low signal on T1 weighting and a low or high signal on T2 weighting, depending on the presence or lack thereof, respectively, of hemosiderin [90, 96]. Ultrasonography and computed tomography are more accessible than, but not as sensitive as, MRI. Fine-needle aspiration cytology has been used, but its results may be inconclusive [37, 82, 97]. Serum CA-125 levels may be increased (up to 260 U/ml) [83, 97, 98], but this finding is not specific for EM.

Therapy

The treatment of CEM is mainly surgical, preferably performed at the end of the menstrual cycle when the lesion is small in order to achieve a minimal excision [99]. The technique of removal varies depending on the size and extent of the lesion, from simple excision with wide margins under local anesthesia to laparoscopic excision en bloc of the umbilicus [87]. A polypropylene mesh may be necessary to prevent the development of hernia, if the defect in the rectus sheath is large [82, 100]. Treatment with gonadotropin-releasing hormone agonists, danazol, and contraceptive pills can be given in order to reduce tumor size before excision or provide relief from the symptoms [81, 101]; these are insufficient as sole treatments [101] and may lead to incomplete excision [82]. Gynecologic examination and hormonal evaluation are recommended after excision of CEM in order to detect an associated pelvic EM. Abdominal and transvaginal ultrasonography or MRI scan should be performed in all asymptomatic patients, but whether laparoscopic examination should be systematically performed is still debated [37, 82, 87, 98, 101].

Prognosis

The prognosis of CEM is good. Recurrences are uncommon if excision is performed with clean and wide margins. However, malignant transformation has been reported in 0.3–1 % of scar EM and should be suspected in the case of rapidly growing or recurrent lesions [102, 103]. The most common histological subtype is endometrioid carcinoma (69 %) followed by clear-cell carcinoma (13.5 %), (adeno)sarcomas (11.6 %), and serous carcinoma [102, 103].

5.3.5.3 Umbilical Endosalpingiosis

Endosalpingiosis is a rare clinical entity that describes the ectopic growth of Fallopian tube epithelium [104]. Endosalpingiosis, endometriosis, and endocervicosis constitute the triad of nonneoplastic disorders of the Müllerian system. These pathologies are found in isolation but are more commonly found in association with one another [38, 105]. The term endosalpingiosis was employed for the first time by Sampson et al. in 1930. Under that term, the author designated any unusual growth and invasion of tubal epithelium in tubal stumps, in subjects who had undergone previous salpingectomy or tubal sterilization [104].

Pathogenesis

The different theories for the pathogenesis of endosalpingiosis are similar to those for endometriosis, since those two entities, together with endocervicosis, constitute the nonneoplastic disorders of the Müllerian system. The different models can be traced back to two basic ideas. One group of theories is based on the fact that endometrial cells (or their precursors) are transported by various routes (transtubal, hematogenous, lymphogenous, or direct apposition) and implanted in the affected organ. The other group of theories

suggests that Müllerian ectopias are the result of metaplastic processes in the target organ (coelomic metaplasia theory, secondary Müllerian system) or from scattered embryonic rest [106–108].

Clinical Presentation

These lesions appear as nodules of the umbilicus and are usually brownish in color. The main symptoms (besides the esthetic) are pain and size fluctuation with menstruation. In the international literature, there are five cases of umbilical endosalpingiosis. The first four cases refer to patients with previous medical history of gynecologic procedures [109–111], while the last case is the first case of spontaneous appearance [112].

Diagnosis

The diagnosis of these pathologies is made histologically. In the case of endosalpingiosis, pathology confirms the presence of a tube-like epithelium containing three types of cells: ciliated, columnar cells; non-ciliated, columnar mucous secretor cells; and the so-called intercalary or peg cells [109, 113].

Therapy

The treatment of choice is surgical excision. Excision should be done under local anesthesia, in order to minimize morbidity and hospitalization if small. However, the patient has to be notified that in the case of a reappearance of abdominal pain (especially in the lower quadrant), a laparoscopy should be performed in order to exclude abdominal endometriosis.

5.3.6 Complications

Multiple complications have been reported in association with pregnancies in anterior abdominal wall defects. These include excessive stretching of the skin, causing ulceration due to friction between the hernia sac and other parts of the patient's body and clothing with possible pressure skin necrosis and rupture. Other reported complications, many of which can threaten the mother or fetus, include incarceration, miscarriage, premature labor, intrauterine hemorrhage, intrauterine growth retardation, intrauterine death, rupture of the lower uterine segment, ruptured abdominal wall, and death [78].

Fig. 5.18 Bruce Kenneth Young from NYU Langone Medical Center published one of the first cases of ruptured umbilical hernia in pregnancy

5.3.7 Therapy

Therapeutic goals consist of two parts. First is the treatment of hernia itself and second the treatment of concomitant complications and the cause of the herniation. Incarceration and strangulation are considered relatively uncommon, but when they do occur, these complications are responsible for 10–20 % of the indications for umbilical hernia repair [114]. One of the first published cases of ruptured umbilical hernia during pregnancy by Bruce Kenneth Young (Fig. 5.18) was in 1965 [115].

Umbilical hernias in adults do not close spontaneously; slow enlargement over a period of years is common and strangulation is much more frequent than in pediatric umbilical hernias therefore elective operation is mandatory at presentation in general population.

In elective and emergent settings, as in the general population, the recurrence rate correlates with the body weight and width of the hernia orifice. The recommendation is that mesh should be used to repair hernia in patients whose BMI is higher than 30 and the hernia orifice is larger than 3 cm because mesh repair has significantly lower recurrence rate in the general population [116]. However, when the orifice is in the range of 2–3 cm, the decision to use mesh should be made on the basis of individual variations [117]. It has been reported recently that the laparoscopic repair is an alternative to the open mesh repair in the umbilical hernia [118]. The role of abdominal binder during the postoperative period in pregnancy and puerperium is not known.

Irreducible umbilical hernias without symptoms should be repaired in a semi-urgent basis before the enlarging uterus causes possible organ (most often small bowel) strangulation. Symptomatic irreducible umbilical hernia is absolute indication for urgent operation. Skin necrosis is the semi-urgent situation when frequent controls are necessary, and if progression of necrosis or rupture develops, then urgent operation is mandatory. The indication is the same if skin necrosis (Fig. 5.16) occurs in a previously repaired umbilical hernia with mesh.

5.3.7.1 Combined Procedures

Combined procedure could be done in elective or emergent settings. The combination of umbilical hernia repair with gynecologic surgery or Cesarean delivery is virtually undocumented except for a case report from 1987 [65]. The practical benefits were obvious: a 2-in-1 operation, with a single incision, single anesthesia, and single hospital stay, conferring valuable advantages for both patient and hospital in time, cost, and convenience, not to mention avoiding the separation of mother from newborn entailed by reoperation. The intraoperative difficulty of mesh fixation and to a lesser extent primary suture repair is the main problem, which always requires assistance to achieve good traction. Proponents of postpartum hernia repair may argue that the combined procedure increases the complication rate, because of blood loss and wound infection resulting from the longer operation time, and prolongs hospitalization. Hernia repair prolonged the average duration of Cesarean delivery, but the time remained within the normal range reported for hernia repair in the literature. In all patients undergoing paraumbilical hernia repair, operation times remained below 120 min with a wound infection rate of 4.2 % [66]. Other study confirmed these results with duration of combined procedure of 50 ± 7 min compared to 37.4 ± 12.6 min for Cesarean sections alone. No complication was recorded during the perinatal and follow-up periods, and no recurrences were observed. In the third study with three patients, there was even no prolongation of operation time. Unfortunately, the diameter of the umbilical hernia and the type of the procedure for umbilical hernia repair were not mentioned [67].

Surgical technique consists of standard Cesarean delivery and standard umbilical hernia repair with the technique depending on the diameter of the umbilical defect. Anesthesia could be general or epidural/spinal. Cesarean delivery was conducted as follows: the skin is disinfected with povidone-iodine, a Pfannenstiel skin incision is made in the lower crease, the fetus is delivered, and the uterine wound is closed, all the while maintaining good hemostasis. Patients receive antibiotic prophylaxis in the form of intravenous cefotaxime 1 g after placental extraction. In 36 patients who had a defect less than 3 cm, umbilical hernia repair was performed by means of a primary suture from the inside. In 12 patients with a defect more than 3 cm, repair was performed by inside mesh hernioplasty fixed to the peritoneum and sheath by nonabsorbable polypropylene suture. Good peritoneal toilette and closure of the Cesarean wound was done as usual [66].

5.3.7.2 Uterine Fibroids

Most of the uterine fibroids are symptom-free [119] and no treatment needed during pregnancy if intramural and subserosal fibroids of 3 cm or smaller are present. Only 10 % of previously diagnosed fibroids are causing complications during pregnancy or delivery. Although some complications are reported as a result of changes in the anatomical localization of the fibroids during

pregnancy, the most common complication is pain due to degeneration [120]. The first report of incarcerated umbilical hernia with a fibroid during pregnancy was published by Ehigiegba and Selo-Ojeme in 1999 [121]. As a general rule if there are no signs of bleeding, hematoma, or necrosis or rupture, the fibroids are not resected and are gently pushed it into the abdominal cavity after which umbilical hernia repair is performed [77]. If aforementioned changes are present, myomectomy is performed [121].

5.3.7.3 Gravid Uterus

> *When the patient stood upright the fundus of the uterus was at a lower level than the symphysis pubis. Per vaginam the cervix could not be reached. The uterus was thus almost completely upside down and it was acting as a lever with the lower edge of the hernial orifice as the fulcrum*
>
> Thomsom SW, 1962

The first descriptions of gravid uterus in umbilical hernia found were by Thomson (Fig. 5.19) [122] and Wydell [123].

Less than ten cases of gravid uterus in umbilical hernia have been published. It has been suggested that the laxity of the abdominal wall and the presence of an enlarged, hypertrophied uterus could weaken a repair. Despite these theoretical concerns, herniorrhaphy has been successfully performed as part of the Cesarean section with no increase in wound infection rates and no recurrences [6]. Therefore, recommendation is to always repair hernia after Cesarean section (Fig. 5.20). If there are indications for mesh placement as in non-pregnant population, it should be used. Another possible indication for Cesarean section is that even Thomson found almost upside-down position of the uterus in giant umbilical hernia preventing normal vaginal delivery: "When the patient stood upright the fundus of the uterus was at a lower level than the symphysis pubis. Per vaginam the cervix could not be reached. The uterus was thus almost completely upside down and it was acting as a lever with the lower edge of the hernial orifice as the fulcrum" [122]. There is a case of ruptured umbilical hernia in 28 weeks gestation with gangrenous ileum. The sac ruptured at the inferior surface which was the most dependant part and the site attached to the overlying inflamed, ulcerated, and damaged skin. The bowel was resected

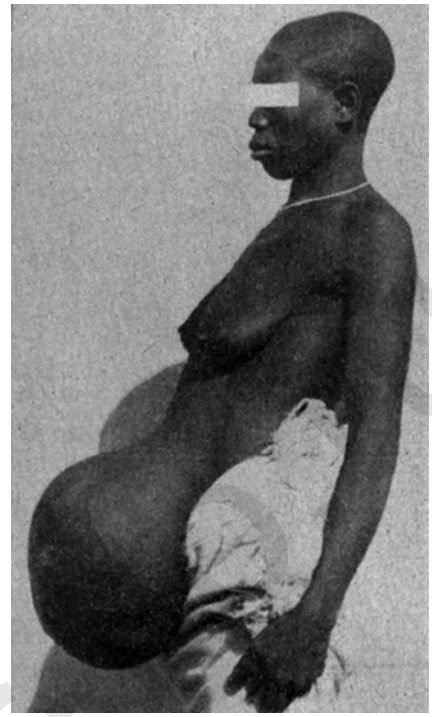

Fig. 5.19 The blanket which passes round the abdomen shows the lower limit of hernia neck. The level of the fundus can be gauged from that of the hand [122]

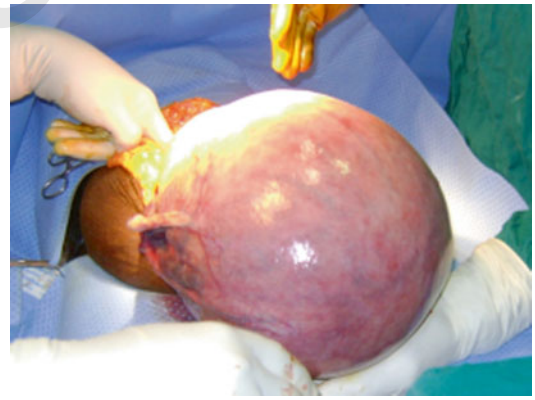

Fig. 5.20 Full-term pregnancy in umbilical hernia. Cesarean section was performed followed by suture repair of giant umbilical hernia (mesh was not available during operation). Patient's repair was intact at follow-up >1 year after surgery; the baby was healthy and developing normally [79]

with terminoterminal anastomosis and there was no fetal distress and the pregnancy was continued. The umbilical hernia defect was 12 cm and Mayo technique was used because there was no mesh available. Six weeks later, she went into spontaneous labor and had assisted vaginal delivery of a live baby. She had remained well at 9 months follow-up [124]. The suture repair of a large defect may result in tissue tension which is associated with high recurrence. In addition, such repair may cause raised intra-abdominal pressure particularly when the abdomen contain a gravid uterus. This can lead to respiratory complications such as atelectasis and pneumonia that could be prevented by chest physiotherapy and early ambulation. General recommendations are that emergent indications are the same as in nonpregnant patient and decision to continue pregnancy depends on the week of presentation and fetal distress.

5.4 Postoperative (Incisional) Hernia

5.4.1 Incidence

The incidence of incisional or postoperative hernia in general population is up to 18.7 % at 10-year follow-up [125]. It must be differentiated from early wound dehiscence with evisceration and has a reported incidence of 1–3 % in laparotomies and always requires immediate reoperation [126]. The incidence of postoperative hernia is 3 % following Cesarean sections [127] and is associated with midline incisions, the need for additional operative procedures, longer than usual administration of antibiotics and more potent antibiotics, presence of postoperative abdominal distension, intra-abdominal sepsis, residual intra-abdominal abscess, wound infection, wound dehiscence, and postoperative fever [127].

The incidence of postoperative hernia in pregnancy is unknown. There are only case reports regarding the condition in the literature. There may be several reasons for the condition's estimated low incidence. First, pregnant patients mostly represent young and healthy adolescents that have either been operated on successfully in the earlier neonatal or childhood period or were never operated on. Second, patients with incisional hernias who plan future pregnancy probably subdue to operation before pregnancy.

Approximately ten cases of gravid uterus in incisional hernia have been reported. The first case has been described in 1977 when a woman presented with pressure necrosis of a Cesarean section scar with protrusion of the gravid uterus through the wound [78]. Herniation of a gravid uterus through an incisional hernia of the anterior abdominal wall is a rare condition because, in most instances, by the time the uterus is large enough to reach the fascial defect on the abdominal wall, it is also too large to protrude through the hernia [128]. Also the patients with such large defects seek help because such large incisional hernias are mostly symptomatic before conception.

5.4.2 Clinical Examination

History (previous operations), symptoms and signs (abdominal pain, vomiting, absence/presence of flatus, and stool passage), and clinical examination (abdominal wall scars with palpable defect in the abdominal wall and distension) are mostly sufficient for the diagnosis.

5.4.3 Diagnosis

If in doubt, abdominal ultrasound examination could define hernia and structures in the hernia sac. A rare but serious obstetric situation can present when a gravid uterus herniates into an anterior abdominal wall through an incisional hernia [129, 130]. Complications include strangulation, abortion, premature labor, accidental hemorrhage, intrauterine death, and rupture of the lower uterine segment [130]. Excessive stretching of the skin could cause skin ulceration.

5.4.3.1 Gravid Uterus

Herniation of a gravid uterus through an incisional hernia of the anterior abdominal wall is a

rare but serious condition due to the potentially severe maternal and fetal risks [131, 132]. Diagnosis of a gravid uterus in an incisional hernia is made by the history of hernia between pregnancies, presence of an unusual bulge of the abdomen with stretched skin [128, 133], and easily palpable uterus and fetal parts [129, 134]. Imaging studies like ultrasound and MRI can also assist in diagnosis [129, 135]. Potential complications include spontaneous abortion, preterm labor, accidental hemorrhage, intrauterine fetal death, and rupture of the lower uterine segment during labor [136]. In one case, complete evisceration of the gravid uterus due to protrusion through an incisional hernia and skin necrosis was reported to occur in a woman at 28 weeks gestation and required emergent Cesarean section and abdominal wall closure but, unfortunately, led to fetal demise [137]. Therefore, pregnant women and fetuses should be monitored closely because the uterus in an abdominal wall hernia could interfere with proper growth and may cause intrauterine growth retardation.

5.4.4 Therapy

Patients can be operated in elective or emergent settings. Emergent operation is indicated when herniation of gravid uterus leads to incarceration, strangulation, or burst abdomen. Cesarean section is recommended in cases with a previous Cesarean section. The management in emergent conditions depends on the gestational age at presentation. If strangulation of the uterus occurs at or near term, emergent laparotomy, Cesarean delivery, followed by immediate repair of the hernia is recommended. If the uterus is strangulated early in pregnancy, immediate repair should be undertaken and pregnancy taken to term. Despite advances in surgical technique and materials, adequate fascial closure is mandatory. The best method is mass closure using wide bites with the sutures sufficiently close together so as to comply with *Jenkin's rule* which declares the need for four times the length of material as the length of the wound [138]. *Smead-Jones mass closure* is the closure of all the layers of the abdominal wall (except the skin) as one structure. Layered closure is described as the separate closure of the individual components of the abdominal wall and is associated with a significantly higher dehiscence rate compared to mass closure (3.81 % vs. 0.76 %) [139]. If a hernia is large, different surgical techniques using mesh should be used. If an incisional hernia is operated before planned pregnancy, mesh closure is strongly recommended. If operating on a pregnant patient with a large abdominal wall hernia, consultation with an abdominal surgeon for proper abdominal wall closure is mandatory because every subsequent postoperative hernia has a higher incidence of recurrence. Prosthetic mesh tends to contract and harden and may seriously interfere with abdominal expansion in pregnancies so these hernias are probably best repaired by the *shoelace technique* [140]. The role of abdominal binder during the postoperative period is not defined.

5.4.4.1 Gravid Uterus

When it is diagnosed early and causes no symptoms, it can usually be managed conservatively until Cesarean section is performed at term. Because of the rarity of the condition, no consensus exists regarding the timing of the surgical repair or the ideal technique to be used. Among the published cases, the authors have reported immediate and delayed repairs, with some favoring mesh repair and others opting for direct fascial closure [130, 134, 136, 137]. Some authors have reported on the antenatal repair of incisional hernia containing a strangulated uterus early in the pregnancy, followed by normal completion of gestation at term [132]. As this is obviously necessary in instances where strangulation occurs early during gestation, an antenatal approach cannot be used in all patients because of the obvious operative and anesthetic risks associated with the surgery, as well as the potential detrimental effect that progression of pregnancy may have on the hernia repair [136].

Since its initial description by Ramirez [141], the "component separation technique" has proven to be effective for the treatment of those giant abdominal hernias in which prosthetic material utilization is not indicated (Figs. 5.21, 5.22, 5.23 and 5.24) [143].

It can be used in emergency and elective settings. First step in standard component separation

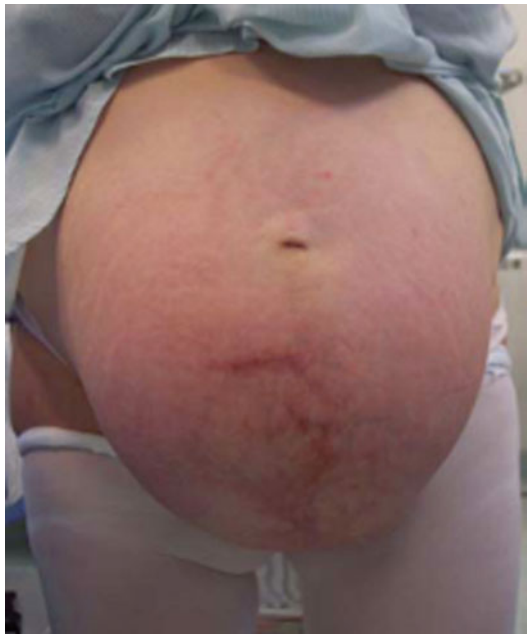

Fig. 5.21 Preoperative frontal view of a 35-year-old woman after four vaginal deliveries. The incisional hernia was secondary to a laparotomy via an infraumbilical incision and right oophorectomy performed for ovarian cystadenoma [142]

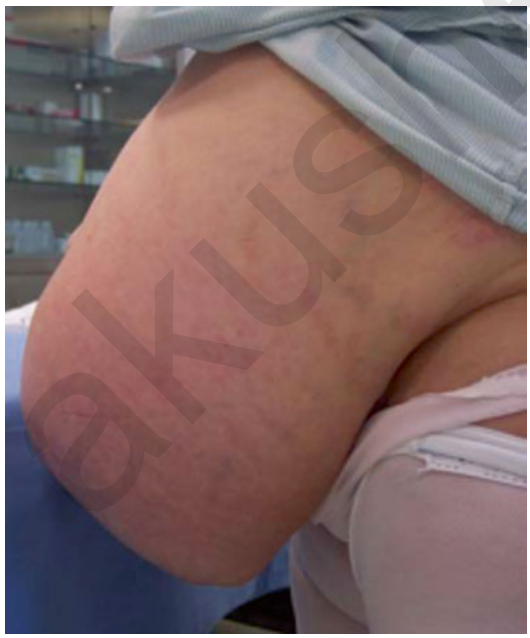

Fig. 5.22 Preoperative lateral view of the same patient [142]

technique is separation of the skin and subcutaneous tissue from the anterior rectus sheath and external oblique aponeurosis. The latter is incised

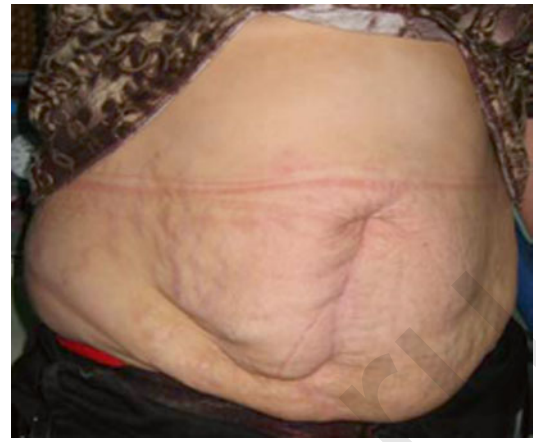

Fig. 5.23 Postoperative (after component separation technique) frontal view (see text for details) [142]

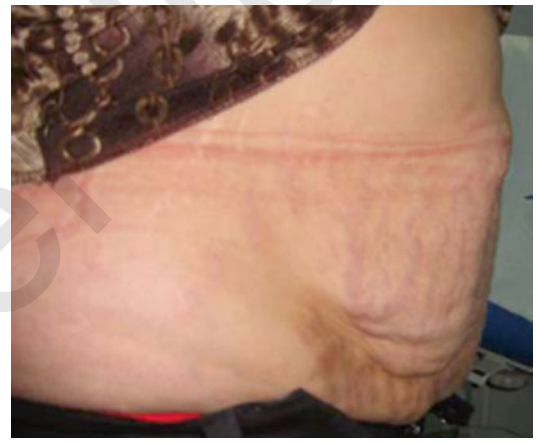

Fig. 5.24 Postoperative (after component separation technique) lateral view (see text for details) [142]

2 cm lateral to the linea semilunaris to allow for separation of the external oblique from the internal oblique in their avascular plane, thus, allowing the rectus abdominis complex to be brought medially and approximated with interrupted nonabsorbable suture. Redundant skin is excised and the incision approximated over two closed suction drains. The postoperative course in the only published case was unremarkable and the patient was discharged on postoperative day 5 with an abdominal binder recommended for the first 4 weeks postoperatively [142]. Drains were removed on postoperative day 7. Follow-up at 1, 6, and 12 months has confirmed the absence of recurrence (Figs. 5.23 and 5.24).

5.5 Parastomal Hernia

5.5.1 Definition, Classification, and Types (General Population)

5.5.1.1 Definition

A parastomal hernia is an incisional hernia related to an abdominal wall stoma [144].

5.5.1.2 Classification

Devlin classified parastomal hernias into four subtypes [145]:

- *Interstitial*, where the hernia sac lies within the layers of the abdominal wall
- *Subcutaneous*, where the sac of the hernia lies in the subcutaneous plane
- *Intrastomal*, where the sac penetrates into a spout ileostomy
- *Peristomal* (*prolapse*), where the sac is within a prolapsing stoma

No data are available to show differing complication rates, or increased incidence of symptoms, attributable to each of these different subtypes of hernia. The classification system is, however, useful in enabling a specific comparison between different types of repair based on the subtype of hernia. It also allows a specific description of any hernia detected by CT.

5.5.1.3 Ostomy Types

Three types of ostomies commonly seen in pregnant women include ileostomy, urostomy, and colostomy. The *ileostomy* (Fig. 5.25) is the most frequent. An ileostomy is the surgical creation of an opening into the ileum on the abdominal wall for fecal diversion. The principal indication for ileostomy in younger population which includes pregnant patients is alimentary diversion due to ulcerative colitis and Crohn's disease. The *colostomy* is the least frequently performed for fecal diversion in young adults. A *urostomy* (ureterostomy), or urinary diversion, is an opening created in the abdominal wall that allows urine to pass directly out of the body. It is made in cases where long-term drainage of urine through the bladder and urethra is not possible (e.g., after extensive surgery or in the case of obstruction). In women

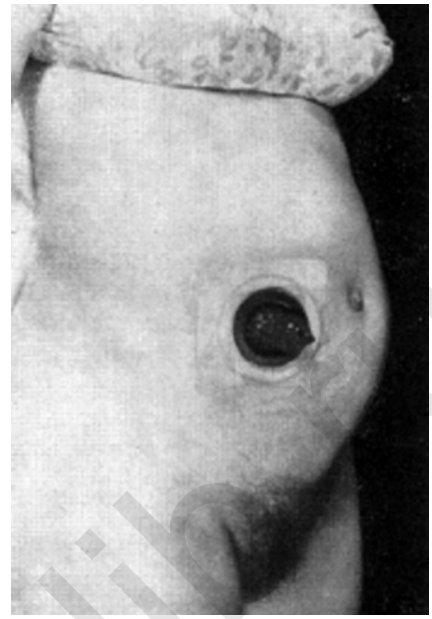

Fig. 5.25 Normally functioning ileostomy in late pregnancy [146]

of childbearing age, fecal or urinary diversion is related to inflammatory bowel disease, neoplasm, congenital anomalies, trauma, malignancy, and polyposis syndromes [147]. The stoma may be located on the abdomen over the right, transverse, or left side. Some degree of paracolostomy herniation is considered to be an almost inevitable complication of colostomy formation [148], but complications are few and normal pregnancy, birth, and postpartum period are expected [149].

5.5.2 Incidence

A parastomal hernia is an incisional hernia related to an abdominal wall stoma. Parastomal hernia affects 1.8–28.3 % of end ileostomies and up to 6.2 % of loop ileostomies in general population. Following colostomy formation, the rates are 4.0–48.1 % and 0.3–31 %, respectively [150]. Direct tissue repair or stoma relocation has recurrence rates of up to 50 % although the use of mesh lowers this considerably to 0–25 % [151]. However, mesh placed in this onlay position around the stoma as a circumferential onlay can cause

problems of erosion into the stoma or fistula formation in up to 5 % of patients [152]. Jones et al. in 2004 have reported the use of prophylactic mesh in the prevention of parastomal hernia by the placement of a lightweight sublay mesh at the time of stoma formation [153]. Possible explanation for extremely rare incidence of incarcerated parastomal hernias in pregnancy is due to:

- Elective closure before planned conception
- Pregnancy as relatively short period for the development of clinical parastomal hernia
- Extremely rare possibility of incarceration due to protective effect of enlarging uterus

Incidence in pregnancy is not known, but due to increasing incidence of inflammatory bowel disease, it could be stated that more and more pregnant patients with stomas would be present. Therefore, increased incidence of (incarcerated) parastomal hernia could be expected.

5.5.3 Clinical Presentation

Literature search did not find any case reports dealing with incarcerated parastomal hernias. Fortunately, principles of diagnosing and treating such conditions are the same as in nonpregnant patients. The diagnosis of parastomal hernia of the small or large bowel, especially incarcerated, is more difficult to make in the pregnant population because nausea and vomiting affects up to 80 % of pregnant women in developed countries [149]. Constipation is common in the third trimester and may also indicate a bowel obstruction of the pregnant ostomy patient. Self-care measures to prevent and treat constipation include increasing fluid intake and exercise, regular bowel habits, and use of stool softeners. Intestinal obstruction is more likely to occur in mid to late pregnancy when the fetal head descends and immediately postpartum when there is an acute change in the uterus size [149].

5.5.3.1 Physical Examination

Examination involves removal of the appliance and inspection of the surrounding skin. Examination should be performed with the patient in standing and supine position performing a Valsalva maneuver [154]. The hernia appears as a bulge around the stoma. Digital examination of the stoma enables fascial aperture and parastomal tissue assessment.

5.5.4 Diagnosis

If the history is suggestive of a hernia that cannot be demonstrated clinically or by plain abdominal X-ray or ultrasound, consideration should be given to abdominal CT scan which may detect subclinical hernias [155].

The diagnostic approach is the same as for other causes of obstruction. Prevention and management of fluid and electrolyte imbalances are a challenge for a pregnant woman with an obstructed ileostomy who has lost the absorptive functions of the colon. Fluid and electrolyte substitution is necessary even if the patient is not vomiting due to intraluminal fluid accumulation.

5.5.5 Therapy

5.5.5.1 Conservative Management and Elective Repair

The traditional approach is proposed for hernia repair during pregnancy only in cases of incarceration, strangulation, and/or perforation [156]. In the absence of emergency indications, conservative management is preferred in the form of rest, weight control, abdominal binders, and stool softeners [129]. Repair should be deferred until uterine involution postpartum to avoid the induction of collagen remodeling by relaxin during pregnancy [157], with the softened tissue predisposing to hernia recurrence. The need for anesthesia and surgery during pregnancy is 1.5–2.0 % [158]. According to a study of a large number of operated patients, the safety of non-obstetric surgery and anesthesia in pregnancy for the mother or fetus has been well established [159].

5.5.5.2 Emergent Operation

Recognition and treatment of the obstruction requires immediate relief of the obstruction, generally by nasogastric suction or surgical intervention. In cases of peristomal erythema and tenderness,

emergent operation is also indicated. If an obstruction is present, then a perforation of a bowel in hernia should be suspected. Without obstruction other diagnoses should be presumed as an abscess or necrosis from different primary diseases. Emergent operation is also indicated, but different surgical procedures are performed depending on the underlying cause. Cephalosporins (FDA Class B) are introduced 30 min before incision and continued if indicated by intraoperative findings. In cases of incarcerated organ perforation (especially if contents are spilled into the free abdominal cavity) or obstruction of large bowel, metronidazole (FDA Class B) should be administered. There are several techniques for the elective repair of different types of hernia in both men and women: open suture, open mesh, or laparoscopic mesh. In nonpregnant women, higher reoperation rate after inguinal hernia repair is not related to a particular technique. Consequently, routine use of open mesh methods in females is not recommended [159]. The situation is similar in an emergent situation. If the incarcerated content is the bowel, vitality is most important. If gangrene is present, the bowel should be resected, and if Fallopian tubes and/or ovaries are necrotic, then resection (adnexectomy) should be performed. In these situations hernioplasty with mesh is absolutely contraindicated because of a significant increase in incidence of wound infections. Suture techniques are still widely used for the repair of umbilical hernias and have a recurrence rate of 20 % [71]. Thus, mesh repairs are performed more frequently with lower recurrence rates [118]. There are no final conclusions in terms of technique, material, or mesh position.

Surgical options for repair include peristomal hernia repair with or without mesh or stomal transposition with or without mesh repair. These operations could be done in open or laparoscopic fashion.

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Symptomatic Diaphragmatic Hernia

6

6.1 Etiology

6.1.1 Acute Diaphragmatic Fatigue

Acute diaphragmatic fatigue has been experimentally shown to occur in normal healthy subjects and in patients with chronic obstructive pulmonary disease by asking them to modify their pattern of breathing or to breathe against high inspiratory resistances. During the expulsive period of labor, women are asked periodically to make strong expulsive efforts and to sustain them isometrically for many seconds; this is likely to produce "natural" diaphragmatic fatigue. To investigate whether this was the case, six women were studied in the delivery room from the moment of the rupture of the amnion until delivery of the infant occurred. The development of diaphragmatic fatigue was assessed both by measuring the static maximal inspiratory pressure and by analyzing the electromyographic power spectrum of the diaphragm. This study demonstrates that (1) the diaphragm is active in the expulsive efforts during labor and (2) the tension developed and the time each contraction is maintained may lead to the development of diaphragmatic fatigue. Therefore, this study provides evidence of acute diaphragmatic fatigue in a natural condition [1].

6.1.2 Diaphragmatic Hernia

A diaphragmatic hernia (DH) is a defect in the diaphragm (the muscle that separates the chest cavity from the abdominal cavity). DH have been classified by Astley Cooper into three categories: (1) *congenital*, due to defects in the diaphragm arising from faulty embryologic development; (2) *acquired*, which develop at points of anatomic weakness, e.g. at the esophageal hiatus, aortic, or caval openings; and (3) *traumatic*, caused by rents in the diaphragm arising from direct or indirect trauma [2]. DH was described for the first time by Sennertus in 1541, while the first two deaths were described by Ambrose Paré in 1575, one deriving from a strangulated bowel [3, 4]. Only 30 reports of DH in pregnancy have been published on this subject in English between 1959 and 2009 [5] and less than 40 cases reported since 1928 [6–8].

6.1.2.1 Congenital

Congenital DH (CDH) occurs when the diaphragm does not form completely, leaving a hole. If the defect is in the posterolateral aspect, it is called hernia of Bochdalek, and if it is in the presternal region, it is called hernia of Morgagni [9]. The prevalence is 1/2,000–1/5,000 live births [10]. The incidence of asymptomatic Bochdalek's hernia in the adult population was reported to be at least 0.17 %, with a female-to-male ratio of 17:5 [11]. Despite such a high incidence, the number of pregnancies complicated by unrecognized CDH is extremely small – less than 40 cases have been reported since 1928 [6–8]. The pathogenesis of CDH is not well understood. The latest data suggest that many cases of CDH are caused by gene mutations (many CDHs occur in association

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with another major anomaly or syndrome) and indicate that CDH is etiologically heterogeneous [10]. Other causes are toxic (pesticides, nitrofen) [12] which cause increased expression of vascular cell adhesion molecule [13], decreased expression of vascular endothelial growth factor [14], and downregulation of fibroblast growth factors 7 and 10 [15]. Hernia of Bochdalek is the most common CDH. Posterolateral defect occurs in the left hemidiaphragm in 80 % of cases because the right diaphragmatic space is stronger and further protected from a sudden increase in abdominal pressure by the liver [16]. Small hernias are usually asymptomatic and have an estimated incidence of 0.17 %, with a female-to-male ratio of 3:1 [17]. Women may be asymptomatic until pregnancy, when further herniation is caused by increased stress on the diaphragm by repeated vomiting in the first half of the pregnancy, a rapidly enlarging uterus in the second trimester, and Valsalva maneuvers during labor. The symptomatic phase includes flatulent dyspepsia, postprandial substernal discomfort relieved with vomiting, reflex cardiac irregularities (tachycardia and arrhythmia), and dysphagia. Recurrent vomiting in the second or third trimester associated with epigastric pain, hematemesis, or respiratory symptoms should raise the suspicion of complicated DH. With progression, potentially fatal complications could occur, such as obstruction, torsion, strangulation, or infarction of the herniated viscera [18]. Kurzel et al. reported that 65 % (11/17) of strangulated hernias during labor resulted in five maternal and three fetal deaths [9]. Other life-threatening complications include acute dyspnea with hypoxia caused by compression atelectasis and mediastinal shift [6, 19]. Compression on the vena cava may impair venous return producing hypotension [20]. Pleural effusion or pneumothorax may be mimicked, leading to inappropriate thoracocentesis or tube thoracostomy and inadvertent perforation of the herniated viscera [21] illustrating why chest drains should always be inserted using blunt dissection [22].

6.1.2.2 Traumatic

Penetrating Trauma

Traumatic (acquired) diaphragmatic injuries occur frequently after penetrating thoracoabdominal trauma. Kessler and Stein reported an incidence of 1.3 % in 1,000 consecutive lower chest stab wounds [23]. The interval between injury and the onset of symptoms may range from 2 weeks to 40 years [24].

Blunt Trauma

Diaphragmatic rupture after blunt trauma is less common, with an incidence of 5 % [25, 26]. About 88 % of blunt diaphragmatic injuries reported in the literature were the result of motor vehicle accidents [27]. It increases intra-abdominal pressure and tears diaphragmatic fibers [28]. The compression of the abdominal contents causes a bursting force to act on the under surface of the diaphragm, which results in a linear tear in the line of the fibers from the region of the left central tendon toward the esophageal ring, but rarely into intact abdominal viscera for its transmission. The thoracic cage is rarely extensively damaged and if any ribs are fractured, they are usually below the level of the 8th; this fact is also consistent with the force acting from the abdomen, rather than the chest. Commonly there is no pneumothorax, hemopneumothorax, or surgical emphysema, one of which is usually present in severe injuries of the upper chest. In the nonpregnant patient, 90 % of these hernias occur on the left side, because the liver offers protection to the right side and the left hemidiaphragm is weaker [24, 29]. Because the diaphragm is in constant motion, spontaneous healing after injury is unlikely. The diaphragmatic hernia becomes evident mostly in advanced pregnancy [30].

Strangulation of abdominal viscera in a preexisting congenital or traumatic diaphragmatic defect is more common than in spontaneous rupture of the diaphragm; 21 such cases have been reported during pregnancy (16 congenital, four acquired, one spontaneous) up to 2004 [31–33].

Iatrogenic

The third cause of traumatic DH is iatrogenic and usually develops from thoracoabdominal surgery, such as esophagogastric surgery for esophagus cancer or gastric cancer or extensive oncologic operations in upper abdomen [18]. Presumption is that an unnoticed tear occurred during the

previous splenectomy or that the left leaflet was weakened by the hemorrhagic surgical procedure [31, 34]. Since this patient's surgery, repeated increases in intra-abdominal pressure (caused by coughing, sitting positions, constipation, and straining) likely enlarged the unnoticed tear or contributed to further stretching of the weakened diaphragm fibers, eventually resulting in a rent. Pregnancy provides additive factors of increased intra-abdominal pressure: nausea and vomiting until the 16th week and the enlarged pregnant uterus in the second trimester. With advancing pregnancy, as the uterus enlarges, it forces an increasing amount of abdominal content into the chest. All these factors may convert an occult defect to one that is symptomatic and increase the risk of twisting and torsion of herniated viscera.

Spontaneous Rupture During Labor

Spontaneous rupture of the diaphragm during normal labor is extremely rare. It could result from a sudden sharp rise in the intra-abdominal pressure during the second stage of labor, exacerbated by application of external pressure to the uterine fundus or the upper abdomen. Pathophysiological mechanism is similar to spontaneous rupture during cough and sometimes these two conditions could not be differentiated as a cause of spontaneous rupture of the diaphragm. A cough has three different phases: the inspiratory phase, the compressive phase, and the expulsive phase [35]. A sudden sharp rise in the intra-abdominal pressure during labor is similar to first and second phase of cough process. The inspiratory phase of a cough starts with a deep inspiration resulting in increased lung volumes and increased elastic recoil pressure. During the compressive phase, the glottis is closed and the expiratory muscles start to contract. As a result, the intrathoracic pressure increases to generate high-velocity flows for the expulsive phase of the cough. With the expulsive phase, the glottis opens and the high-pressure gradient generates rapid airflow. Both inspiratory and expiratory muscles are actively involved in coughing, and extreme changes in intrapleural pressure occur due to active contraction of these muscles [36]. The fracture of ribs as a complication of excessive strain during cough can be explained by either of two different theories. The first mechanism of rib fracture in cough is similar to that of stress fractures [37, 38]. When force (muscle contraction) is applied to an object (a rib), the object is subjected to stress. The stress will cause deformation of the object. When the deformation exceeds the elastic limit of the object, it undergoes inelastic deformation. Repeated trauma, as in paroxysms of cough, can produce inelastic deformation in the most vulnerable part of the ribs, the middle third. This will result initially in minor cracks of the ribs and later, as the trauma continues, in fractures. Fractures can occur in any rib, but the ones most commonly involved are the fifth to tenth ribs [38]. The second mechanism of rib fracture may be due to opposing muscle forces acting on the ribs. The diaphragm is mainly an inspiratory muscle. The costal part of the diaphragm is attached to the lower six ribs and their cartilage. The muscles of expiration are the chest wall muscles, which include the internal intercostals, the triangularis sterni, the serratus posterior, the quadratus lumborum, and the abdominal muscles (including the external and internal oblique, the rectus abdominis, and the diaphragm) [39]. The diaphragm also acts as an expiratory muscle during activities requiring high intrathoracic pressure like coughing, vomiting, and sneezing [36]. This expiratory activity of the diaphragm is related directly to the intrapleural pressure and follows the expiratory activity of the transversus abdominis muscle. It is speculated that the diaphragmatic contraction will help to stabilize the thoracic cavity during the expulsive phase of cough. The study by Oechsli describes a fracture line starting from a point 4 cm from the costochondral junction of the fourth rib running obliquely caudal and laterally to the ninth rib in the midaxillary line [39]. This line falls on the muscular attachments of the external oblique and serratus anterior muscles. The opposing actions of these muscles on the same ribs can result in fractures. Simultaneous contraction of the shoulder girdle muscles, especially of the serratus anterior, also contributes to the rib fractures by pulling the ribs upward and laterally while the abdominal muscles pull the ribs medially and downward [39]. The development of a hernia during pregnancy is multifactorial, relating to the

mass effect of the gravid uterus, smooth muscle relaxation, and softening of ligaments.

Obstructive shock during labor could have been offset by the increase in the venous blood return to the heart due to the spontaneous contractions of the uteroplacental circulation, to the catecholamines release in response to labor pain, to the autotransfusion from the contracted uterus, and to the release of the aortocaval compression occurring during labor or immediate postpartum period [20, 40, 41].

It requires emergency surgical correction. There are only several case reports of spontaneous rupture during labor. In one case, 11 h after delivery of a male infant, a 27-year-old woman experienced severe epigastric pain, vomiting, and dyspnea, followed by cardiopulmonary arrest. Although the ruptured diaphragm was diagnosed and repaired, she suffered severe anoxic encephalopathy and died 3 weeks after operation without regaining consciousness [42, 43]. Similar causes of short and excessive increase of intra-abdominal pressure such as coughing in patients at risk especially chronic obstructive pulmonary disease [44, 45] or vomiting [46] could also cause spontaneous rupture that could become evident during pregnancy and/or labor.

Hill et al. reported a patient with history of a repaired congenial diaphragmatic defect who became symptomatic after early postpartum discharge. She had undergone four previous uncomplicated vaginal deliveries [19].

6.1.2.3 Hiatal Hernia

Hiatal hernias (HH) are herniations of parts of the abdominal contents through the esophageal hiatus of the diaphragm. HH are six times more common in pregnant patients than the other two types [9, 18] and occur in up to 18 % of multipara and 5 % of primipara women [17]. There are three types. *Type I* (*sliding*), the most common type, is characterized by widening of the muscular hiatal aperture of the diaphragm, with laxity of the phrenoesophageal membrane, allowing some of the gastric cardia to herniate upward. A sliding HH is probably related to loss of elasticity of these ligaments caused by factors such as excessive contraction of the longitudinal esophageal muscles, increased abdominal pressure, genetic predisposition, and age-related degeneration. Paraesophageal hernia represents 5 % of all HH [17]. This condition is rare before the fourth decade of life; however, the patients involved are generally 20 years older than those with a sliding HH, suggesting that this is an acquired disease, evolving over the years [47]. These are true hernias surrounded by a peritoneal sac and when the defect is large, incarceration with obstruction gastric volvulus and strangulation may occur [6, 9, 48]. *Type II* (*paraesophageal*) results from a localized defect in the phrenoesophageal membrane. The gastroesophageal junction remains fixed to the preaortic fascia and the arcuate ligament, and the gastric fundus forms the leading part of the herniation. *Type III* hernias are a mix of types I and II. There is also a *type IV* that is also called *complex HH*.

In the period 1928–2012, 38 cases of this event have been published in the English literature [49–51]. The mean age of presentation was 28 years and 67 % of the patients were multiparous [49]. In the period 1903–1951, there were 19 cases of HH complicating pregnancy published [52].

6.2 Clinical Presentation

Mild symptoms of maternal diaphragmatic hernia can imitate hyperemesis gravidarum and therefore especially cases without more obvious symptoms are often misdiagnosed as hyperemesis gravidarum. In most of the cases maternal diaphragmatic hernias become clinically obvious in the third trimester, when intra-abdominal pressure is rising because of the enlarging uterus. In contrast to this, some form of nausea and vomiting normally occurs in up to 80 % of pregnant women the first trimester [53]. In elective presentation, the diagnosis of HH should be suspected if:

- Symptoms persist after 12 weeks of pregnancy
- The onset of symptoms after the first trimester

The emergent clinical presentation is made up of a combination of the mechanical effect on the cardiorespiratory function by the displaced

viscera and the pathological changes in the viscera themselves consequent upon their displacement. The clinical entity is readily divided into three phases:

1. Immediately following the trauma
2. Quiescent period
3. Associated with strangulation, if it occurs

1. The early symptoms and signs become confused owing to the multiplicity of injuries likely to be associated with this condition. The symptoms of pain in the left chest, pain in the left upper quadrant of the abdomen, left shoulder tip pain, vomiting, and shortness of breath associated with shock [54, 55]. An expanding mass in the chest may displace mediastinal structures with compression of the vena cava and this may impair venous return producing hypotension [20]. Compression and displacement of the lung causes striking collapse of the lungs (atelectasis) which leads to hypoxia and dyspnea [19]. There is usually diminished air entry to a varying degree at the affected base and the percussion note may be impaired or unduly tympanitic. Tenderness and rigidity are common in the left upper quadrant of the abdomen. In none of the cases in this series was there good enough evidence to suggest peritoneal soiling. The salient feature of this phase is the plain X-ray of the chest, which gives an unmistakable picture, whether in the supine or erect position. The consistency of this picture has been demonstrated by all left-sided lesions in this series. It is considered, therefore, that if the X-ray shows an appearance, suggesting elevation of the left leaf of the diaphragm above its normal position, particularly if there is a large gas bubble and fluid level in the erect position, in a patient involved in the type of accident mentioned, the findings are pathognomonic of ruptured diaphragm. The sequence of events from this point varies considerably. The lesion may continue directly to strangulation with a false "quiescent" period of only a few hours or may pass into a true quiescent phase, which may last up to several years. If strangulation follows immediately on the trauma, this is characterized by intractable vomiting. The vomitus may be of non-bile-stained material or in the form of repeated hematemesis or merely dry retching. Severe pain develops in the left chest, left upper quadrant of the abdomen, and left shoulder tip. The patient becomes profoundly shocked and rapidly moribund. The elevation of the diaphragm and the size of the gas bubble are likely to be greater with strangulation than in nonobstructed cases. Carter has reported that the aspiration of serosanguinous fluid from the chest, when none was present before, is strongly suggestive of strangulation. It is of vital importance to recognize the onset of strangulation because if gangrene occurs, the mortality, even with operation, approaches 100 %, instead of being negligible, as it is in the absence of obstruction [56].
2. It is more common for the lesion to pass into a "quiescent" phase with the response to treatment of shock. The improvement may be so rapid, that the medical attendant is completely hoodwinked only to be rudely awakened by the sudden onset of strangulation after hours, days, months, or years. This rapid "recovery" in spite of the constant danger of delayed strangulation strengthens the case for performing a routine chest X-ray before discharge, on all persons suffering this type of trauma. If there is any doubt after plain X-ray examination and screening, barium studies will usually establish the diagnosis. If the quiescent phase is prolonged, there may be no symptoms or only vague symptoms, such as shortness of breath on exercise, substernal discomfort after meals, vague upper abdominal discomfort, sometimes relieved by vomiting or attacks, or subacute intestinal obstruction. These symptoms may be insufficient to make the patient seek medical attention.
3. Strangulation has been recognized to be one of the most serious complications of the diaphragmatic hernia. The onset of strangulation is said to occur most commonly within 3 years of the injury and its onset is usually sudden. It may follow raised intra-abdominal pressure due to unwonted straining and cases have been reported as coming on in the later months of pregnancy. In many cases the existence of

the traumatic hernia is unsuspected and the history of a previous accident may not be volunteered. The presence of intestinal obstruction is probably recognized, but in the absence of abdominal distension and with the bizarre pattern of upper abdominal, chest and shoulder tip pain, conservative management may be continued too long. A "wait-and-see" policy may be encouraged by improvement after the passage of nasogastric tube or the obtaining of encouraging returns from enemata. If gangrene occurs, the outlook is almost hopeless. There are cases where the compression of the left gastric vessels by the intact esophageal ring appeared to play a major part in the causation of gangrene or more commonly gangrene is associated with "direct" diaphragmatic hernia when the opening is smaller. Rare cases have been reported with a normal X-ray immediately after admission, but in whom herniation and even strangulation occurred later. It is presumed in these circumstances that omentum or the spleen temporarily covered the opening, but raised intra-abdominal pressure later caused the herniation.

The presentation on the right side may be quite different from that on the left, in that bowel is rarely herniated into the chest unless the tear is large and consequently the risk of strangulation is minimal. The symptoms of cardiorespiratory dysfunction are more in evidence because of the gross displacement of the lung, the paradoxical movement of the viscera through the large opening, and the gross loss of function of the right half of the diaphragm.

The main complications described in these diaphragmatic hernias include visceral obstruction [9, 31], spontaneous [19, 32] or thoracocentesis-induced [21, 33] visceral perforation, visceral strangulation with or without subsequent gangrene and perforation [57], maternal respiratory distress [19, 58, 59], tension pneumothorax [21], and maternal death [60]. They are more frequent during the third trimester delivery and in the early postpartum period.

If intrathoracic perforation is present, it includes nonsolid organ such as stomach and small or large intestine. Clinical presentation depends on the underlying pathophysiology. If strangulation precedes perforation, acute and significant abdominal and thoracic pain is present with development of fever and shock. If strangulation with ischemia is not the cause of perforation as in patient with perforated intrathoracic peptic gastric ulcer due to excessive use of pain killers due to the persistence of a pelvic pain after the delivery, symptomatology could be less pronounced in the early stages [50]. This patient presented as subacute onset (3–5 days) of a clinical syndrome characterized by severe epigastric pain, moderate but worsening dyspnea, and fever.

Gibson in 1929 reported three cases of strangulated diaphragmatic hernia which he diagnosed clinically without aid of roentgenology. He stressed the following diagnostic symptoms in general population [61] which should be searched for also in pregnant population:

- Diminished expansion of the chest
- Impairment of resonance
- Adventitious sounds
- Cardiac displacement
- Circulatory collapse
- Cyanosis and dyspnea
- Asymmetry of hypochondria

Diminished breath sounds on the ipsilateral side are the most common physical finding. The absence of abdominal distension is present if stomach alone, unaccompanied by intestine, is being herniated through the rent in the diaphragm with the presence of bloody fluid in the left chest.

6.3 Diagnosis

6.3.1 Chest Radiography

The key to diagnosis in an elective or emergent setting is a chest radiograph which may show elevated diaphragm, retrocardiac air in bowel lumen, air-liquid levels if obstruction is present, nasogastric tube in the herniated stomach above the diaphragm, or only mediastinal shift to the contralateral side due to compression (Figs. 6.1 and 6.2) [62, 63].

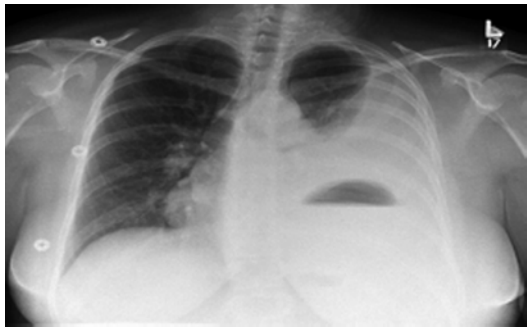

Fig. 6.1 Posteroanterior and lateral chest roentgenogram on the second admission, demonstrating a large left pleural effusion and gastric air-fluid level in the left hemithorax [57]

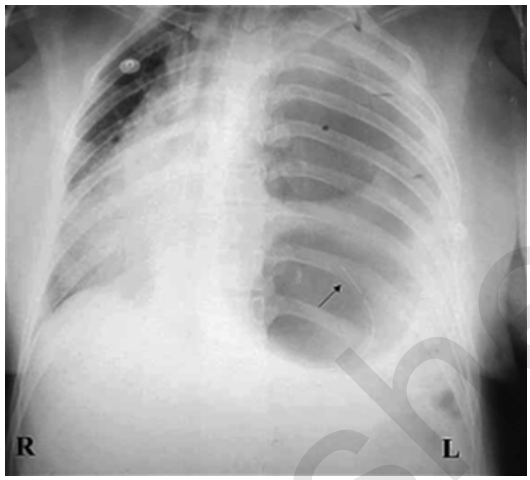

Fig. 6.2 Chest radiograph showing marked mediastinal shift to the right. In the left hemithorax are two large bullae. The *arrow* indicates the nasogastric tube in the herniated stomach above the diaphragm [62]

There is a general reluctance to use X-rays in the pregnant population, but the dose is small, and in a selected population with a clear indication, the consequences of not performing the X-ray may far outweigh this small risk. The results are either diagnostic or abnormal and suggestive of diaphragmatic rupture in 75–97 % of cases [63–65]. In the postpartum period X-rays with contrast media can be used for the definition of suspected diaphragmatic hernia (Fig. 6.3) [62].

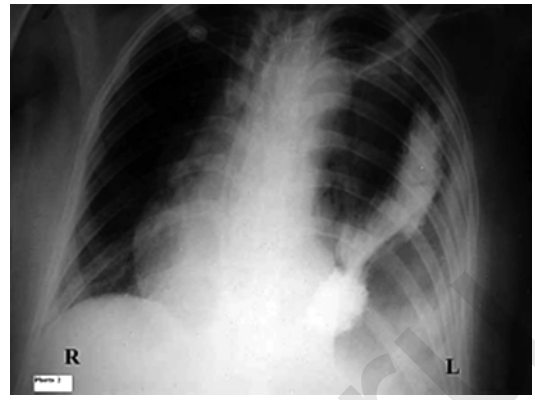

Fig. 6.3 Herniation of the stomach in the left hemithorax seen after Gastrografin ingestion [62]

6.3.2 Thoracic CT

Thoracic ultrasonography and CT scans are possible auxiliary diagnostic methods. If diaphragmatic hernia is suspected or proved, CT of the thorax and abdomen should be made. If perforation is suspected, water-soluble peroral contrast should be used to detect the perforation and its localization. If perforation is present, pleural effusion will be evident (Fig. 6.4). Also if partial obstruction/strangulation of the stomach is present, then typical form of hourglass (*the Collar sign*) is visible (Fig. 6.5).

6.3.3 Thoracic MRI

Recently, to eliminate the radiation exposure to both mother and fetus, MRI has been used for the diagnosis (Fig. 6.6) [6].

6.4 Therapy

6.4.1 Conservative Treatment

Treatment of nausea and vomiting with drugs or by nasogastric suction in form of preparation for the emergent operation is therapeutic because it allows decreased intra-abdominal and intragastric

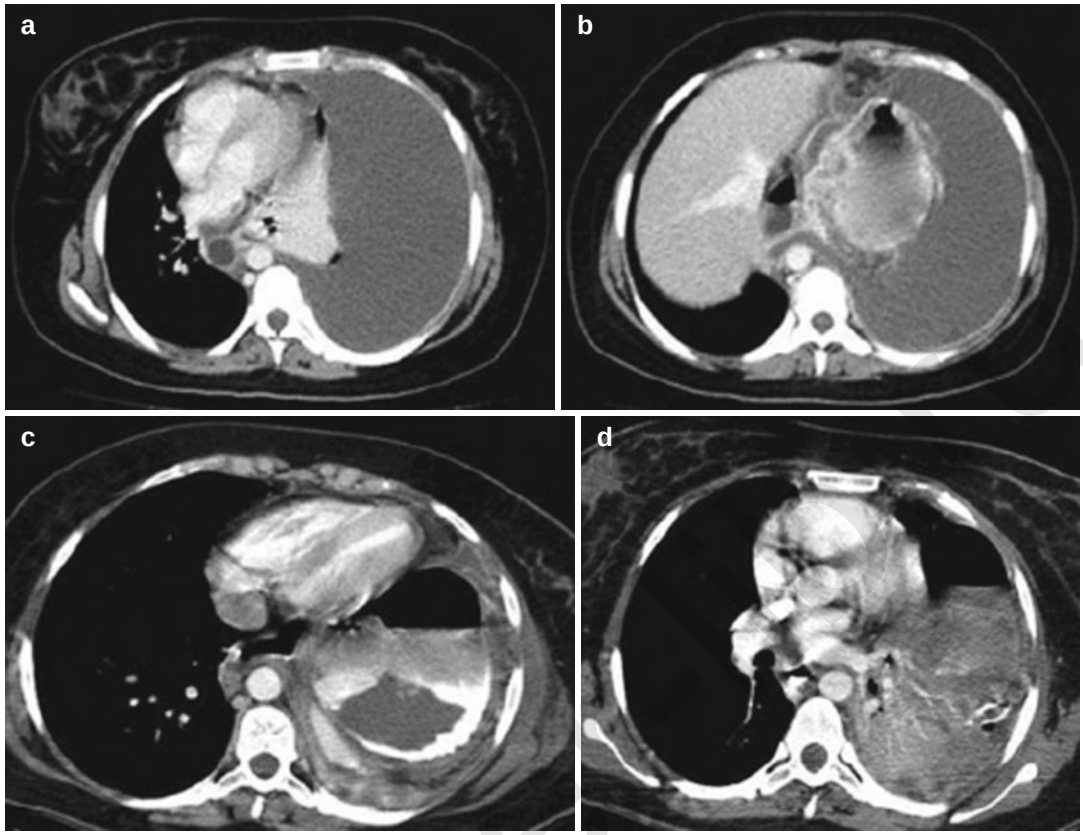

Fig. 6.4 First CT scan performed at admission in emergency department showed a massive left pleural effusion associated with severe contralateral mediastinal shift (**a**) and a complete intrathoracic gastric herniation (**b**). A second CT scan performed after chest tube placement and during water-soluble contrast examination demonstrated the leak at the level of the stomach (**c**) and documented only a partial re-expansion of the pulmonary parenchyma (**d**) [50]

pressure [67]. In emergent presentation there is no indication for conservative therapy.

6.4.2 Surgical Treatment

6.4.2.1 Indications for the Operation

Asymptomatic Patients

For asymptomatic patients Kurzel et al. recommended Cesarean delivery after fetal lung maturity with simultaneous hernia repair always before the onset of labor. The authors based their recommendation on 17 cases reported in the English literature with maternal and fetal morbidity being 55 and 27 %, respectively, when vaginal delivery was attempted before the DH was repaired [9]. The fact that the majority of women who present have had previous uneventful pregnancies with the hernia present opens the question as to whether exposing an asymptomatic mother and fetus to the morbidity of antenatal repair is justified. Therefore, others recommend vaginal delivery if certain precautions are taken; these include planned induction of labor (to avoid precipitous labor at a remote site), regional anesthesia to help prevent the urge to bear down, and the use of instrumentation to assist the second stage [6]. There are cases of symptomatic DH in previous pregnancies. Due to severe and prolonged vomiting and weight loss or even hematemesis, there are cases of fetal loss. In such cases elective repair should be undertaken to prevent similar presentations in further pregnancies [51].

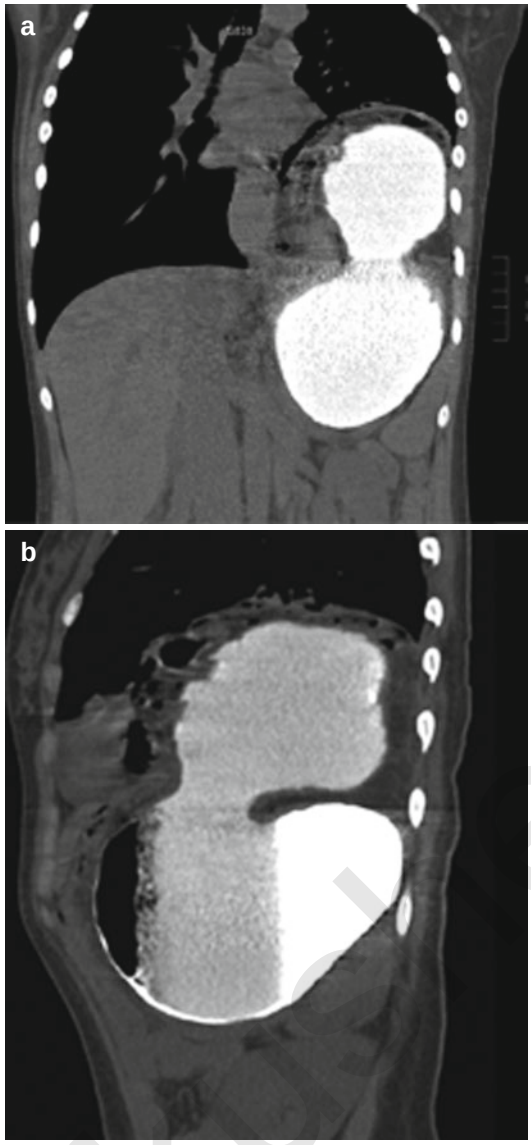

Fig. 6.5 Front view (**a**) and lateral view (**b**) of the CT scan showing the left diaphragmatic rupture and the typical aspect of the stomach, in form of hourglass (*the Collar sign*) [66]

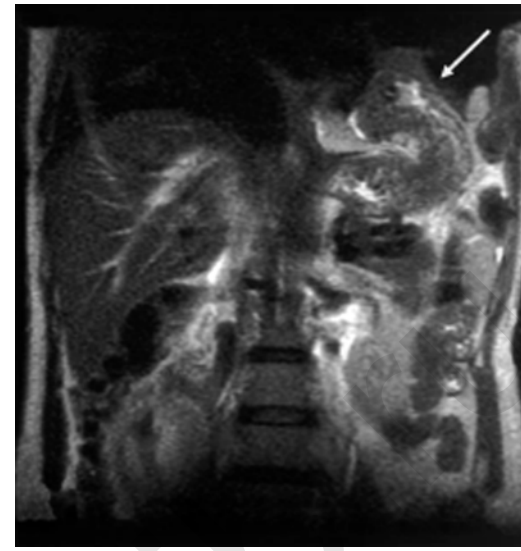

Fig. 6.6 Magnetic resonance image demonstrating Bochdalek's hernia with associated abdominal organs in the left chest. The *arrow* indicates the herniated portion of colon [6]

Symptomatic Patients

Symptomatic DH should be managed without delay because of the associated high maternal and fetal mortality rates if left uncorrected [6, 9, 48]. Even if the pregnancy is normal, there is a possibility of puerperal symptomatology. One recommendation is that if the diagnosis is made in the first trimester, in the absence of complications, the patient should be carefully monitored and observed. Surgery is delayed until the second trimester when organogenesis is complete, before the increasing bulk of the gravid uterus risks further herniation. Other authors suggest repair shortly after diagnosis, regardless of gestation because the condition is associated with a poor or complicated outcome, particularly if early surgical intervention is not undertaken [9]. Genc et al. suggested that gastric decompression lowers intra-abdominal pressure and could improve the clinical condition of the pregnant patient with a diaphragmatic hernia who presents with symptoms and signs of obstruction. Such an improvement can allow surgery to be delayed until the patient is transferred to a tertiary care center or until antenatal corticosteroids are administered [6]. Even in non-emergent situations, treatment of nausea and vomiting with drugs or by nasogastric suction is therapeutic because it ameliorates symptoms [67]. Only one laparoscopic repair of symptomatic DH (Bochdalek type) has been made to date [68].

Emergent Presentation

A patient presenting with signs of visceral strangulation and infarction presents a surgical

emergency and immediate operation is indicated, irrespective of fetal maturity. This condition is associated with a high maternal and fetal mortality. If surgery (left thoracoabdominal or midline incision) demonstrates strangulation and gangrene of the herniated viscera, segmental resection of the involved portion of large intestine with reestablishment of bowel continuity is indicated. The diaphragmatic defect should be closed with interrupted sutures. If the defect is large, mesh should be used. The pregnancy is allowed to continue until 39 weeks of gestation, at which time elective Cesarean delivery is performed.

6.4.2.2 Anesthetic Considerations

During anesthesia, the fetal heart rate, blood pressure, and central venous pressure and maternal oxygenation during the patient's change of position must be watched. To avoid hypotension during induction, uterus displacement with a wedge is indicated [69]. If the hernia is approached through a thoracotomy incision [24], the affected side is placed uppermost. Mediastinal shift, which compromises venous return and collapse of the lower lung, may be worsened by positional compression from the herniated dilated viscera. A rapid-sequence induction is indicated because the patient is at risk of pulmonary aspiration.

Lung ventilation must be undertaken with low tidal volume or low airway pressure until the abdominal contents have been removed from the chest or until thoracotomy has been performed. Cardiovascular collapse might occur during positive-pressure ventilation. The re-expanded lung previously compressed by herniated viscera may shift mediastinal structures, and venous return may be impeded [70, 71]. Increased pleural pressure from mechanical ventilation is transmitted to the abdomen. It results in increased upward displacement of the viscera toward the diaphragm and may worsen cardiovascular collapse [71]. A surgeon must be ready to operate before ventilation is begun [70]. Inappropriate insertion of a chest drain may potentially lead to perforation of bowel [22], therefore

> Chest drains should always be inserted using blunt dissection.

6.4.2.3 Obstetric Considerations

The indication for delivery and mode of delivery is trimester dependent. If the hernia manifests in the third trimester, once fetal maturity is documented, the baby should be delivered by Cesarean section with simultaneous repair of the hernia [9, 49, 62]. Standard vaginal delivery should be avoided in these cases because the increase in intra-abdominal pressure may further displace the viscera and result in strangulation of the herniated viscus or disruption of diaphragmatic hernia repair. On the contrary, Genc et al. state that uterine contractions, unlike the Valsalva maneuver, do not increase the intra-abdominal pressure and are unlikely to cause rupture at the repaired site. Thus, a patient with a repaired diaphragmatic hernia can labor and deliver vaginally [6]. Unfortunately it is impossible that labor can be completed without contractions of abdominal wall musculature and probably the Valsalva maneuver; therefore, it is safer to perform Cesarean section.

Corticosteroids for fetal maturity should be administered to the mother before surgery if the gestational age is between 24 and 34 weeks because of the risk of preterm delivery during or after surgery.

There is no data on the minimum time that should elapse from hernia repair to delivery.

6.4.2.4 Open Technique

History

In 1834, Laennec [72] suggested that the diagnosis of DH could easily be made by auscultation of the chest and that a laparotomy could be used to withdraw intestine from the thorax. The first recorded attempt of reduction of a DH in general population by laparotomy was made by Naumann [73] in 1888 but was unsuccessful. Two years later, O'Dwyer [74] reported an unsuccessful attempt of repairing a strangulated CDH. Others state that Riolfi performed the first successful

Fig. 6.7 Greatly dilated gangrenous stomach, filling a large portion of the left thorax. The incision was a thoracic one in the eighth interspace, subsequently prolonged across the costal margin into the abdomen [56]

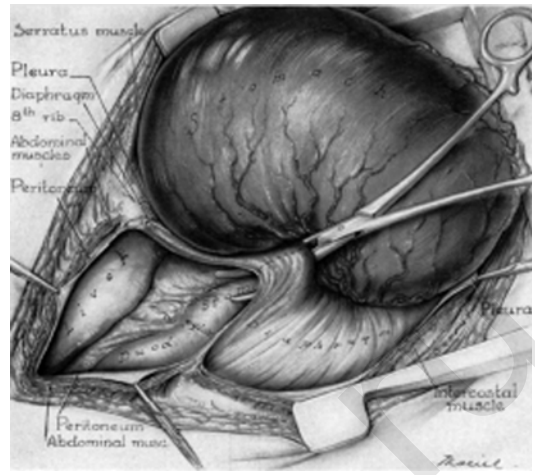

Fig. 6.8 Diagrammatic illustration indicating the extent of the gangrenous area of the stomach. Note the thrombosed vessels along both curvatures and the gangrene of the omentum [56]

repair in 1886. In 1905 Heidenhain [75] reported a successful operation performed in 1902 for CDH in a 9-year-old patient when he reduced the hernia and closed the diaphragmatic defect through a midline laparotomy incision. The first available report with operative treatment in pregnancy is that of Crump in 1911, who successfully operated upon a woman with DH complication 3 months pregnancy [76].

Transthoracic Approach

Under normal circumstances, the best surgical approach is through the chest, at the level of the eighth rib, but if strangulation has occurred, the incision should be planned as a thoracoabdominal one for more adequate exposure and for easier access to the bowel, particularly if the colon is involved. Even though this condition has been successfully managed through an abdominal incision in the past, authors are now almost unanimous in advocating an eighth rib transthoracic approach (Fig. 6.7). The repair of the diaphragm, once the adhesions are separated, is easily achieved and there is usually sufficient tissue to make a Mayo-type repair. If the tear destroys the musculature of the esophageal hiatus, this should be carefully reconstituted (Fig. 6.8). When the diaphragm is avulsed from the chest wall and there is insufficient tissue left peripherally repair should be affected by suturing the free edge to the chest wall with interrupted sutures to two adjacent intercostal muscles to obtain a wider adherence. In the opinion of the author, there is no justification for paralyzing the phrenic nerve, even by "temporary" crushing, but on rare occasions, it may be necessary to resect lengths of the lower ribs subperiosteally to allow closure of a peripheral tear. The thoracic cavity should always be drained by an underwater seal system.

In case of peptic intrathoracic perforation (Fig. 6.9a) due to NSAIDS, gastric ulcer could be found (Fig. 6.9b). A primary repair with a double-layer suture of the gastric mucosa should be performed; then, after having replaced the stomach in the abdominal cavity, a direct double-layer closure of the diaphragmatic hiatal defect is completed.

Transabdominal Approach

The transabdominal approach enables good access to herniated parenchymal organs such as liver and spleen [77, 78]. However, some authors prefer the transthoracic approach in longer-lasting hernias to treat pleuroperitoneal adhesions. On the other hand, transabdominal

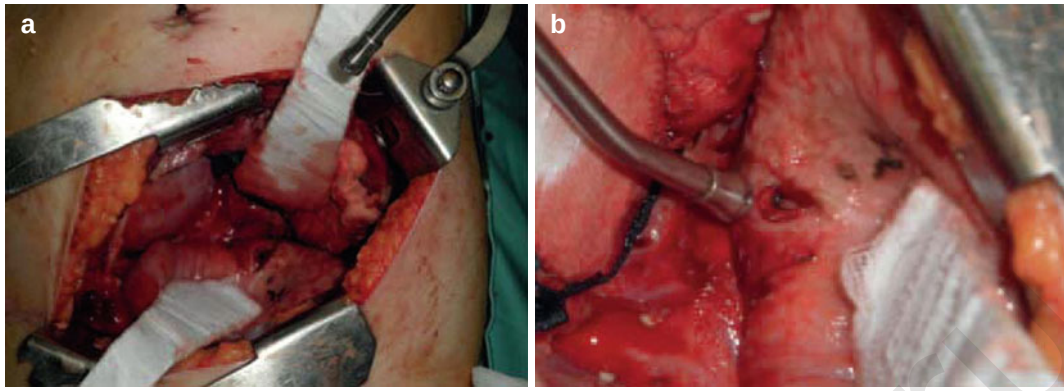

Fig. 6.9 Surgical findings during emergency thoracotomy: **a** complete intrathoracic gastric herniation through a large diaphragmatic hiatal defect without macroscopic signs of visceral strangulation, **b** a small well-defined gastric ulcer (1 cm in diameter) was found at the level of lesser curvature [50]

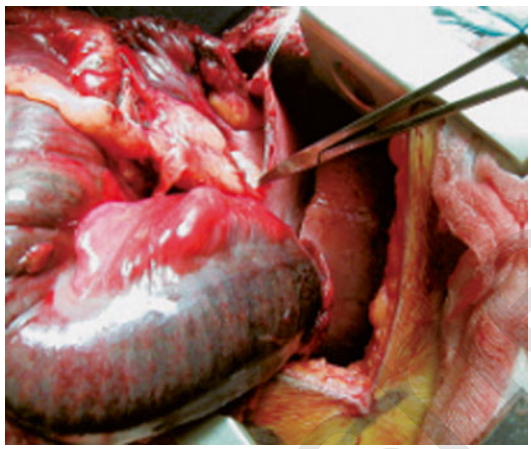

Fig. 6.10 Bochdalek's hernia (defect) in the left hemidiaphragm with the gangrene of a large part of the herniated transverse colon [8]

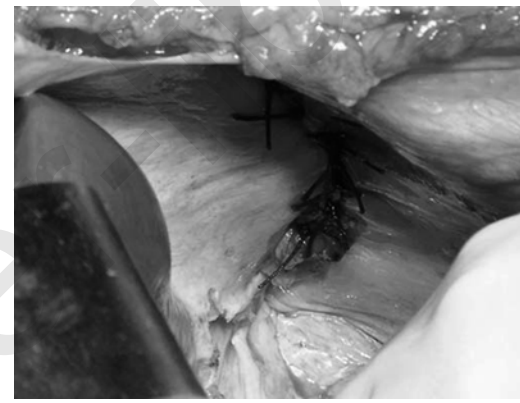

Fig. 6.11 Intraoperative photographs showing the completed hernia repair. The hernia hilum was repaired with interrupted sutures [80]

approach is better in pregnancy if Cesarean section is indicated which can be performed through the same laparotomy.

The patients who had undergone repair of hernia during their first or second trimester can be allowed to deliver vaginally. Uterine contractions do not increase intra-abdominal pressure and are unlikely to cause rupture at repair site [6].

Thoracoabdominal Approach

Extended approach is when abdominal incision is extended into thoracotomy. Abdominal incision is necessary if wide resections of gangrenous organs are present (Fig. 6.10)

6.4.2.5 Laparoscopic Repair

Recently even laparoscopic repair was performed in one pregnant patient. It was a 27-week pregnant woman having diaphragmatic rupture and intrathoracic ruptured spleen. The patient was managed by laparoscopic reduction of the intrathoracic viscus, with repair of the defect and splenectomy [79]. Another two cases were operated laparoscopically in puerperium (see next section *Puerperium*).

6.4.2.6 Method of Closure of Diaphragmatic Defect

The best method of closure of the diaphragmatic defect in general population is still unclear.

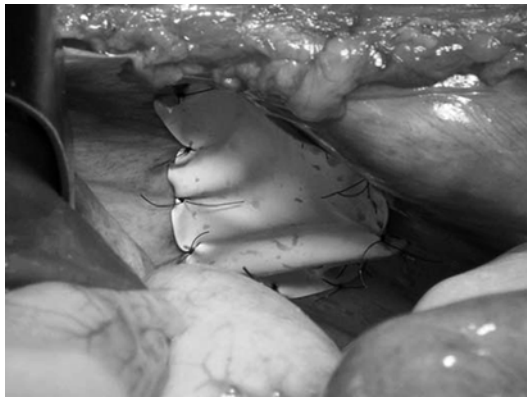

Fig. 6.12 Intraoperative photographs of the same patients after the hernia hilum repaired with interrupted sutures. Final appearance of the repair with the Gore-Tex sheet (Gore-Preclude dura substitute) [80]

Primary repair is done for most defects, unless they are very large (Fig. 6.11). When the edges can be easily opposed, primary closure is certainly the preferred method. If the defect is large and difficult to suture, a prosthetic patch is recommended (Fig. 6.12) [81].

Some authors described using Marlex mesh to close wide diaphragmatic holes and then covered the defect with a pedunculated flap, using the falciform ligament in one case and the peritoneum in another case [82]. Others described closing a large diaphragmatic gap with Gore-Tex mesh covered by the falciform ligament [83]. The polytetrafluoroethylene patch is characterized by two different surfaces: one that promotes fibrous ingrowth into the patch and another that is relatively resistant to adhesion formation and placed adjacent to the abdominal viscera [84].

Generally, a prosthetic patch should not be used if intestinal strangulation has occurred because of the high risk of postoperative infection. Jezupors and Mihelsons reported in 2006 that deep prosthesis infection occurred in 0.94 % of patients who underwent mesh repair of various abdominal wall hernias in general population [85]. In clean-contaminated and contaminated conditions, wound and mesh-related infections occurred in 7–21 % of patients but did not usually require mesh excision [86]. Some authors advocate placing a prosthetic patch for abdominal wall reconstruction in clean-contaminated conditions [85–89]. There is extremely small numbers of cases in pregnancy (less than 40) therefore specific indications for different procedures are not defined in pregnancy. Therefore, it is recommended to perform the procedure that is indicated in general population.

6.4.2.7 Puerperium

There are two cases of DH (one rupture, one left-sided posterolateral (Bochdalek) hernia) occurring in the puerperium. In one case the right colon was in the right chest causing pulmonary embarrassment [58], and in another stomach, transverse colon, and spleen were in the sac [90].

6.5 Prognosis

6.5.1 Maternal Outcome

Prognosis depends on the type of presentation, duration of symptoms and if strangulation with/without perforation is present. The mortality rate of chronic incarcerated diaphragmatic hernia can be as high as 20 %, whereas that of strangulated hernias may approach 85 % [10]. The main life-threatening complications are acute respiratory distress caused by compression atelectasis, mediastinal shift, and strangulation and gangrene of the herniated viscera [9, 19, 24, 31, 58, 60]. In these cases, the maternal mortality rate ranges 42–58.3 % [32, 60, 91, 92].

Complications due to acute herniation are more frequent during the third trimester, during delivery, and in the postpartum hours, and result in maternal deaths in 50 % of cases [9].

6.5.2 Fetal Outcome

Fetal mortality and morbidity result from premature labor and compromise maternal oxygen delivery [93]. Fetal deaths occur in 50 % of cases, and premature birth has been reported in approximately 24 % of cases [9]. In only 30 % of the cases reported, delivery was by Cesarean section [49].

6.5.3 Recurrent Hernia

The recurrence rate of diaphragmatic hernia following repair in general population depends upon the severity of the original defect (ranging from minor to diaphragmatic agenesis) and the nature of the repair. Moss et al. reported that about half their prosthetic patch repairs of CDHs showed evidence of re-herniation and required revision within 3 years [94]. This observation has two important issues. First, the prepregnancy repair is a risk factor for (recurrent) diaphragmatic hernia during pregnancy and also it is the risk factor for recurrent diaphragmatic hernia after the repair during pregnancy, labor, or puerperium.

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Intestinal Obstruction 7

7.1 Intestinal Obstruction in General

Women in a state of pregnancy may be purged, if there be any urgent necessity (or, if the humors be in a state of orgasm?), from the fourth to the seventh month, but less so in the latter case. In the first and last periods it must be avoided.

Hippocrates

Let an abdominal scar on a pregnant woman be a line of evidence denoting potential obstruction.

Mathews and Mitchell

Intestinal obstruction in pregnancy is a consequence of broad spectrum of etiological factors as in nonpregnant population. According to the cause of obstruction, there is wide variety of therapeutic options available. Therefore, depending on the cause and the type and of surgical intervention, the prognosis for the mother and the fetus is also variable.

7.1.1 Historical Perspective

The first published case of bowel obstruction in pregnancy was by Houston in 1841 [1]. Ludwig [2] in 1913 and Mikulicz-Radecki in 1926 suggested periods of increased incidence of obstruction during pregnancy. Ludwig in 1913 collected 95 cases. Ley-Klotz et al. found tense band on the left flank of the gravid uterus causing mechanical obstruction with cecum was extremely distended and the rectum and sigmoid empty. A cecostomy was done, with recovery [3]. The first English language series was presented by Eliason and Erb in 1937 [4]. Two other major reviews included report of 150 cases by Goldthorp in 1966 [5] and an analysis of 64 cases by Perdue et al. [6]. The latter review included all cases published in the English literature from 1966 through 1991.

7.1.2 Incidence

Intestinal obstruction in both general and pregnant population includes small bowel and large bowel obstruction. Incidence varies from 1:1,500 to 1:66,431. Incidence started to increase after 1940 because more and more elective and emergent abdominal operations were performed and postoperative mortality decreased. In 1940, Smith and Bartlett reported incidence of 1/66,431 deliveries [7]. In 1948, Mathews and Mitchell reported 1/12,000 deliveries and Morris, in 1965, described 1/3,161 deliveries [8]. Isolated small bowel obstruction in the pregnant population is rare (1/17,000) [9]. This large range reflects the general failure to report this complication in the literature or some cases are published in the journals that are not indexed in the most searched medical databases. Major causes of intestinal obstruction in the pregnant women include adhesions, volvulus, and intussusceptions [10]. Mathews and Mitchell's statement *let an abdominal scar on a pregnant woman be a line of evidence denoting potential obstruction* should always be remembered by obstetricians and surgeons alike. Around 50 % had a previous

G. Augustin, *Acute Abdomen During Pregnancy*,
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Table 7.1 Incidence of intestinal obstruction during pregnancy in Queen Charlotte's Hospital and District, 1930–1964 [8]

Year	Cases	Rate
1930–1934	1	1/19,940
1935–1939	2	1/8,919
1940–1944	1	1/12,214
1945–1949	1	1/18,445
1950–1954	5	1/3,494
1955–1959	6	1/2,888
1960–1964	5	1/3,161

appendectomy. Obstruction most commonly appears during the first pregnancy after surgery. Volvulus of the small bowel is responsible in 25 % of the cases, which is the most common precipitating factor [10]. Intestinal volvulus is responsible for 25 % of acute bowel obstructions in pregnant women but only 3–5 % in nonpregnant patients. The malrotation of the bowel makes it susceptible for volvulus [11]. There is increasing incidence during last century. This is due to:

- Older population getting pregnant
- Higher incidence of pregnant patients having previous abdominal operations
- Decreased postoperative mortality
- World population significantly increased during last 40 years

Table 7.1 shows increasing incidence in 5-year intervals in Queen Charlotte's Hospital and District [8].

There has been considerable controversy regarding the period in pregnancy when obstruction is most likely to occur. Both Ludwig (1913) and Mikulicz-Radecki (1926) suggested the following periods of increased incidence:

- During the fourth and fifth months when the uterus ascends from the pelvis
- During the eighth and ninth months when the fetal head descends into the pelvis
- During delivery and early puerperium when rapid involution uterine size occurs

Current reports show that most cases of intestinal obstruction in pregnancy present during the 3rd trimester [12–14].

7.1.3 Clinical Presentation

The problem with intestinal obstruction is a large scale of severity of obstructive symptoms and signs which depend upon:

- Location of the obstruction
- The degree of obstruction
- Rate of progression of obstruction

In the two largest reviews, the average length from the onset of symptoms to hospital admission ranged 48–84 h. Once admitted, an average of 48–60 h passed before definitive surgery was performed. An average delay of 4 days, reported in the more recent study, continues to remain a significant contributing factor to the high morbidity and mortality observed in the pregnant patient population. It is vital to remember that all colicky pain in pregnancy is not necessarily uterine in origin and, moreover, that premature labor can complicate intestinal obstruction and vice versa [15]. The difficulties in diagnosis and the penalties for improper conservatism are so great that laparotomy should be considered for any unusual pain.

7.1.4 Differential Diagnosis

In further text are listed the most common differential diagnoses in pregnancy that are managed conservatively. In sections with specific surgical causes of obstruction, important differential diagnosis is also analyzed.

7.1.4.1 Constipation

Disorders of the gastrointestinal tract are common in pregnancy. Constipation is one of the most common medical conditions affecting the general population with a prevalence of up to 30 % [16]. Constipation is second only to nausea as the most common gastrointestinal complaint in pregnancy. Patients with no history of bowel problems may develop constipation for the first time during pregnancy and, in addition, women

Table 7.2 *Rome 3 criteria* for the diagnosis of irritable bowel syndrome (criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis) [19]

1. Must include two or more of the following:
Straining during at least 25 % of defecations
Lumpy or hard stools in at least 25 % of defecations
Sensation of incomplete evacuation for at least 25 % of defecations
Sensation of anorectal obstruction/blockage for at least 25 % of defecations
Manual maneuvers to facilitate at least 25 % of defecations (e.g., digital evacuation, support of the pelvic floor)
<3 defecations per week
2. Loose stools are rarely present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome

who suffer with constipation prior to pregnancy will often find their symptoms are worse when pregnant. Anderson et al. reported that 38 and 20 % of women experienced constipation in the second and third trimesters, respectively [17]. More recent data from Marshall et al. reported that 35 % of women suffered from constipation during pregnancy [18]. This Irish study involving over 7,000 patients found that fewer primiparous women (35 %) suffered from constipation during pregnancy compared to multiparous women (39–42 %). A UK study prospectively evaluated 94 subjects using symptom diaries throughout pregnancy. Subjects were defined as functionally constipated when they exhibited two or more symptoms from the Rome diagnostic criteria (Table 7.2). The prevalence of functional constipation was 35, 39, 21, and 17 % in the first, second, third trimester, and postpartum period, respectively [20]. The same authors performed a separate prospective analysis of bowel habit during pregnancy [21]. Symptoms of incomplete evacuation were the highest in the first trimester (21 % decreasing to 12.5 % in the puerperium). Overall, the sensation of incomplete evacuation and the time spent defecating were higher in all three trimesters of pregnancy than in the puerperium. It was interesting to note that in this same group of subjects, sensations of urgency decreased as pregnancy proceeded and leveled off in the third trimester. Urgency increased by 24 % in the postpartum period compared with levels during gestation. There were no differences between lactating and non-lactating mothers. The causes of constipation in pregnancy are likely multifactorial. Dietary factors and lifestyle issues play a role, but factors such as hormonal and mechanical changes are also important. Investigations are aimed at excluding treatable disorders such as hypothyroidism or hypercalcemia. A full blood count, thyroid-stimulating hormone (TSH), serum calcium, and glucose should be performed in all patients presenting with constipation.

Constipation refers to difficulty in passing stool and infrequency of bowel motions, which is not secondary to an underlying cause [22]. The Rome criteria are a standard clinical measure of assessing chronic constipation but were not formulated with pregnancy-related constipation in mind (Table 7.2) [19]. Patients report symptoms relating to the frequency and difficulty in passage of stool that may not conform to strict diagnostic criteria. Patients may focus on symptoms such as straining, stools that are excessively hard, unproductive urges, and a feeling of incomplete evacuation. It is therefore possible that a patient may report constipation even when they pass a daily bowel motion. A simplified set of criteria for the diagnosis of constipation includes low frequency of stools (<3 per week), hard stools, and/or difficulties on evacuation of feces. These criteria are easier to use in routine clinical practice and are a good indicator of constipation in the pregnant woman.

As with any medication in pregnancy, laxatives should be used with caution (Table 7.3).

Anthraquinone laxatives such as dantron are associated with congenital malformations [23, 24]. Saline osmotic laxatives (magnesium citrate and sodium phosphate) can cause maternal sodium retention, while castor oil can initiate premature uterine contractions [25]. Mineral oils can theoretically affect maternal absorption of fat-soluble vitamins. In the case of vitamin K, this can lead to hypoprothrombinemia and hemorrhage [26]. Some laxatives can even produce neonatal diarrhea [25]. Stimulant laxatives such as senna should be used with caution in pregnancy because senna can be excreted in breast

Table 7.3 Laxatives in pregnancy

Safe	Caution	Unsafe
Lactulose	Saline osmotic laxatives	Anthraquinones (dantron)
Glycerin	Castor oil	Tegaserod
Polyethylene glycol (PEG)	Senna	
Bulking agents	Docusate sodium	

milk [27]. In general, the short-term use of stimulant laxatives is considered safe in pregnancy. However, as with the general population, long-term use should be avoided.

The American Gastroenterology Association (AGA) Position Statement considers polyethylene glycol (PEG) to be low risk in pregnancy and the preferred treatment for chronic constipation in pregnant women.

PEG acts as an osmotic laxative by opposing the dehydration of bowel contents that would ordinarily lead to increased stool bulk. The increased retention of water in the colon lubricates and softens the stools. There are data suggesting some absorption of PEG 3,350 in humans [28]. However, the small amounts (1–4 %) that are absorbed are excreted unchanged in the urine. Lactulose, glycerin, and sorbitol are generally considered safe. Animal studies of these agents have shown no evidence of teratogenicity.

Fiber-containing bulking agents such as Metamucil, Citrucel, and Perdiem are probably the safest laxatives to be used in pregnancy, as they are not systemically absorbed.

These agents take several days to exert their effects and are therefore not suitable for acute symptom relief. They are also contraindicated in fecal impaction. They can be used over long periods of time in patients with uncomplicated constipation. Adverse events related to bulking agents include excessive gas, cramps, and abdominal bloating.

7.1.4.2 Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a functional bowel disorder, i.e., a disorder of gastrointestinal (GI) function in the absence of any known abnormality of structure. IBS is common, affecting 9–12 % of the general population, and is a common cause of work absenteeism. The Rome 3 criteria define IBS as the presence of abdominal pain associated with a change in either the frequency or form of stool [19]. These symptoms must be present on at least three occasions per month over a 3-month period. When the patient has hard or difficult to pass stools greater than 25 % of the time, with loose or watery stools less than 25 % of the time, the diagnosis is constipation-predominant IBS (IBS-C). IBS is more common in females and is most frequently diagnosed between 30 and 45 years (i.e., the main reproductive years). It is therefore easy to see how constipation-predominant IBS can overlap with gestational constipation.

Tegaserod is a $5HT_4$ agonist that has shown considerable promise as a treatment for constipation-predominant IBS. AGA initially considered tegaserod to be low risk in pregnancy [29]. However, recent evidence of an increased incidence of ischemic cardiac and cerebral events in patients using this medication has led to the US Food and Drug Administration (FDA) to request that sale of tegaserod be suspended. Safe drugs used for idiopathic constipation can be used in constipation-predominant IBS.

7.1.4.3 Postpartum Acute Intestinal Pseudo-obstruction (Ogilvie's Syndrome)

Incidence and Risk Factors

Ogilvie's syndrome (OS) was first described in 1948 [30] and is an acute colonic pseudo-obstruction without a mechanical cause. Acute colonic pseudo-obstruction (ACPO) is rare and has been reported as isolated case reports or small case series. It has most commonly been reported

after pregnancy or Cesarean section [31], although has also been reported to occur after trauma, severe burns, abdominal and/or pelvic surgery, sepsis, electrolyte imbalance, spinal trauma/surgery, renal trauma/surgery/transplant, malignancy, congestive cardiac failure, and hip replacement and bed rest [32–36].

Pathophysiology

The pathophysiology of the condition is still unclear although one explanation is that an imbalance between sympathetic and parasympathetic innervations to the colon results in an overall excess in sympathetic activity [37]. Delgado-Aros and Camilleri [38] have summarized the pathophysiology of ACPO as follows: reflex motor inhibition through splanchnic afferents in response to noxious stimuli, excess sympathetic motor input to the gut (intestine does not contract), excess parasympathetic motor input to the gut (intestine does not relax), decreased parasympathetic motor input to the gut (intestine does not contract), excess stimulation of peripheral micro-opioid receptors by endogenous or exogenous opioids, and inhibition of nitric oxide release from inhibitory motoneurons. The mechanism of the condition is thought to involve loss of tone in the parasympathetic nerves S2 to S4. This, in turn, results in an atonic distal colon and pseudo-obstruction [39]. This explanation is given credence by the location of autonomic nerves close to structures at risk during Cesarean section, including the cervix and the vagina. Various sources report a cutoff sign relating to an area of dilated and collapsed bowel around the splenic flexure corresponding to the transition zone between the vagal and sacral parasympathetic nerve supplies [36, 40]. The cutoff sign is used to support the hypothesis of parasympathetic inhibition causing Ogilvie's syndrome [36, 40]. However, it is likely that the true pathogenesis is multifactorial. Strecker et al. reported that the association between Ogilvie's syndrome and vaginal delivery may be due to the declining serum estrogen levels in the postpartum period [41]. In the only other reported case of Ogilvie's syndrome following normal vaginal delivery in the English literature, the histological findings of the cecum after right hemicolectomy showed no specific pathology [42].

Clinical Presentation

The diagnosis of Ogilvie's syndrome is widely reported to be troublesome due to the nonspecific clinical features [42]. The common clinical feature is significant abdominal distention, and Jetmore et al. report no known cases of Ogilvie's syndrome to have presented without distension of the abdomen [36]. Progressive abdominal distension is often painless at first. Importantly, bowel sounds are usually present and may be normal. Although patients may continue to pass small amounts of flatus or stool, colonic function is generally inadequate. Abdominal pain, tenderness, and low-grade fevers are also common, while nausea and vomiting are rare [38, 43, 44].

Diagnosis

As with any case of suspected ileus or obstruction, electrolyte levels are an essential investigation, and in the 48 cases of Ogilvie's syndrome reported by Jetmore et al., 83 % demonstrated at least one electrolyte disturbance with hypocalcaemia being the most common [36]. Plain abdominal radiographs are generally diagnostic with significant colonic distention (cecal diameter ≥7 cm), with minimal or no distention of the small intestine [38, 43–46]. Abdominal radiography is a standard first-line investigation, and Keswani et al. reported that a cecal diameter ≥9 cm (Fig. 7.1) is the "only definitive sign of imminent perforation" [42]. Serial plain abdominal X-ray is important for the definition of the progression along with WBC and CRP. CT can be used in doubtful cases to exclude other etiologies of obstruction (Fig. 7.2).

Conservative (Medical) Management

Initial management should include intravenous fluid therapy and nasogastric suction. Patients should be fasting; if possible, all narcotic analgesics should be stopped. Colonoscopic decompression is successful in the majority of cases, unless signs of peritonism are evident, although recurrence is common [36]. Pharmacological treatment includes naloxone, cholinergic stimulation

with neostigmine or erythromycin, and cisapride although the benefit in cases of idiopathic Ogilvie's syndrome is not certain [40]. With regard to postpartum patients, Strecker et al. support the use of laxatives in the postpartum period and stress the importance of early diagnosis [41].

The most important potential complication of the condition is large bowel perforation with subsequent fecal peritonitis and associated high mortality [48]. Several cases of colonic perforation secondary to Ogilvie's syndrome have been reported following Caesarian section [47, 49], but only two reports in the English literature describing the condition after "normal" vaginal delivery [42]. One of these patients had third-degree tear during delivery, which requires suturing in the operating room. The patient had been commenced on laxatives following the repair of the perineal tear and showed no symptoms of perineal sepsis. She presented with Ogilvie's syndrome 5 days after vaginal delivery [50].

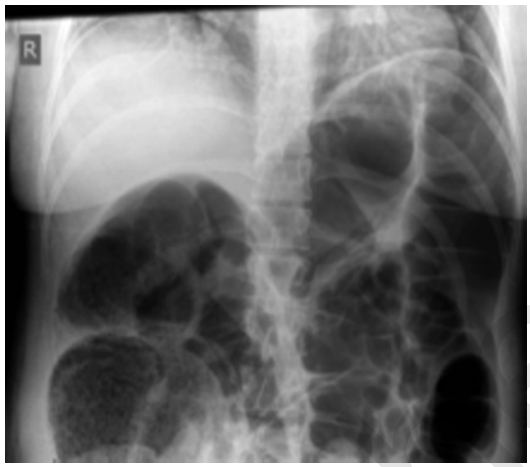

Fig. 7.1 Plain supine abdominal radiograph showing widespread colonic dilatation with no free air [47]

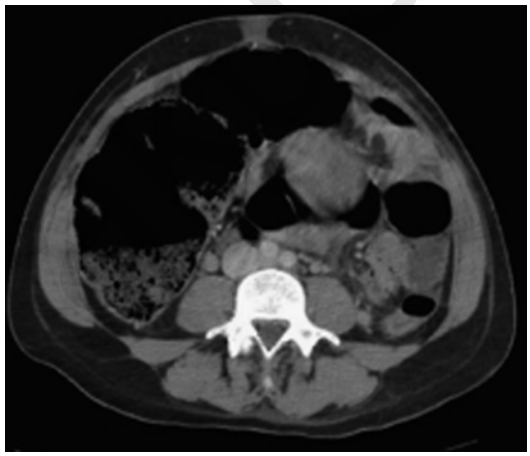

Fig. 7.2 Abdominal computed tomography image showing widespread colonic dilatation with maximum cecal diameter of 8 cm [47]

Surgical Treatment

Surgical treatment is indicated when:

- Cecal diameter >9 cm
- Progression of cecal distention or failure of resolution after several days
- Evidence of perforation
- Unsuccessful colonoscopy
- Recurrence after successful colonoscopy

Mostly, perforation occurs at the right colon and cecum according to Laplace's law. Surgical treatment comprises either cecostomy (preferred with appendectomy) or, if ischemic bowel is present, limited right hemicolectomy with or without primary anastomosis (Fig. 7.3).

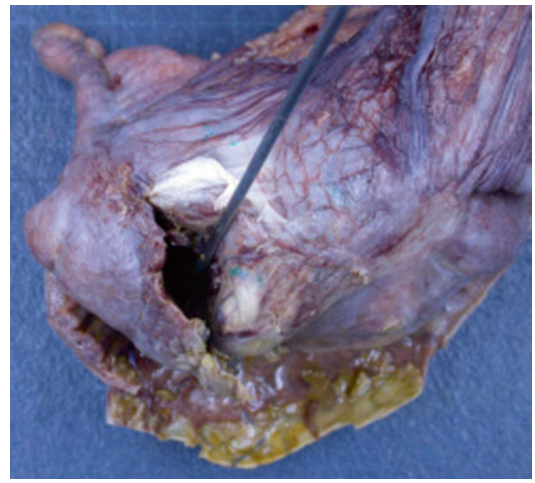

Fig. 7.3 Cecum with 4×4 cm perforation (with no evidence of acute appendicitis or colitis) with surrounding exudate [50]

7.1.5 Therapy

Conservative and surgical therapy for intestinal obstruction during pregnancy is discussed for every disease specifically throughout the chapter. One of the modalities of conservative strategy is described here because if inadequately administered could cause many side effects.

7.1.5.1 Total Parenteral Nutrition and Refeeding Syndrome

Refeeding syndrome was first recognized during World War II, when returning prisoners of the Japanese who had been starved rapidly developed neurological and cardiovascular abnormalities after the institution of a normal diet [51].

Pathophysiology

The pathophysiology of refeeding syndrome relates to the rapid rise in insulin production following a carbohydrate or protein shock, when protein calories are administered at a rate above which the patient can tolerate. This can occur in those receiving even moderate dietary intake depending on their underlying nutritional, metabolic, or physical condition and may arise with administration of glucose alone. This insulin release, associated with possible increased insulin sensitivity, leads to increased cellular uptake of glucose, fluid, and electrolytes with associated altered plasma availability of electrolytes. Refeeding syndrome can manifest as either metabolic changes (hypokalemia, hypophosphatemia, hypomagnesemia, altered glucose metabolism, and fluid balance abnormalities) or physiological changes (i.e., arrhythmias, altered level of consciousness, seizures, cardiac or respiratory depression) and potentially death [52].

Total Parenteral Nutrition in Pregnancy

Total parenteral nutrition has been used successfully in pregnant women with hyperemesis gravidarum, postintestinal surgery, and acute pancreatitis [6]. In 1988, Levine and Esser reported that maternal and neonatal outcomes measured by adequate maternal weight gain and fetal growth were not compromised by total parenteral nutrition [53]. In pregnant women, Lee et al. stated that the average daily intake through total parenteral nutrition should be 2,430 kcal [54]. However, it is better to increase daily calories to avoid the refeeding syndrome.

Two algorithms are presented for initial management (Table 7.4) and for monitoring (Table 7.5) of refeeding syndrome from the *Drug Therapy Guideline No: 46.00 Issued: 10.10.07 Refeeding Syndrome Guideline (NHS trust)*:

Table 7.4 Initial management of refeeding syndrome

1. Identification and treatment of sepsis
May not be clinically apparent but may explain an acute deterioration
Low threshold for septic screen
Low threshold for broad-spectrum antibiotics (orally or via NG tube if possible)
2. Fluid resuscitation and monitoring fluid balance
Assess and carefully restore circulatory volume, monitor pulse rate, fluid intake, and output
Malnourished patients have a reduced tolerance of intravenous fluids in moderate to high intakes (>2 L/24 h) that can lead to heart failure
Administration of intravenous fluids may be necessary in the initial 72 h until sufficient oral intake is achieved
If evidence of dehydration, for careful rehydration, i.e., 1–2 l in the first 24 h depending on response. Greater volumes only if severely dehydrated
Total fluid intake (including intravenous, enteral, and oral) should aim for a maximum of 30 ml/kg per day (≤1.5 L)
At least 6 hourly monitoring of blood pressure, pulse, and respiratory rate is necessary to detect evidence of heart failure or inadequate intravascular volume
3. Correction of electrolyte abnormalities
Ensure recent (last 48 h) electrolyte levels are available. These should include urea and electrolytes, phosphate, calcium, magnesium (add to standard blood profile), liver function tests, full blood count
If electrolytes are deranged consider and treat possible causes
Perform ECG if: potassium is less than 3.5 mmol/l or phosphate is less than 0.80 mmol/l
Organize supplementation if: phosphate <0.8 mmol/l, K <3.5 mmol/l, Mg <0.5 mmol/l, or adjusted Ca <2.0 mmol/l
Caution should be used in renal patients due to the reduced excretion of these electrolytes
If very low plasma electrolyte values are demonstrated, e.g., phosphate <0.32 mmol/l,

(continued)

Table 7.4 (continued)

K <2.5 mmol/l, Mg <0.5 mmol/l, then the institution of feeding or nutritional support may result in a further drop of these electrolytes to possibly critical levels. Electrolyte correction with oral or intravenous supplementation is required to achieve levels above these thresholds before the institution of feeding
4. Correction of hypoglycemia/blood sugar control
Monitor blood glucose once to twice daily unless more frequent tests are indicated (i.e., for those patients with known diabetes or IGT)
If hypoglycemic replace intravenous fluids with 5 % glucose
5. Management of hypothermia
Monitor body, and if necessary core, temperature at least daily
Hypothermia is commonly associated with malnutrition. Its correction should be simultaneous with fluid rehydration and can include provision of heated drinks and blankets
6. Correction/prevention of micronutrient deficiencies
Administer thiamine 100 mg orally or crushed via feeding tube three times daily for 10 days or until recommended feeding rate reached with the first dose being administered at least 30 min before instituting feeding
If enteral route not available, patient has anorexia nervosa or has chronic alcoholism; administer Pabrinex IVHP – one pair of ampoules 30 min before instituting feeding and then daily until recommended feeding rate reached
Administer vitamin B compound strong (one tablet three times daily) and Sanatogen Gold (one tablet daily) orally or crushed via feeding tube

7.1.6 Prognosis

7.1.6.1 Maternal and Fetal Outcome

In a review on intestinal obstruction during pregnancy in 1937, maternal mortality rate was 21 % and fetal mortality rate 50 % [6]. It should be noted that intestinal obstruction includes broad spectrum of etiological factors and not only obstruction but primary cause of the obstruction determinate prognosis. Because of the delay in diagnosis and the reluctance to operate on pregnant women, maternal mortality rate was high. Bellingham et al. [55] reported premature labor with subsequent neonatal death in 33 % (2/6) of their patients with second trimester obstruction, whereas Harer and Harer [56] reported 47 % perinatal loss in the third trimester obstruction. Hypoxia and hypotension during anesthesia should be prevented as these are the most common causes of fetal death. Morris in 1965 reported a mortality rate of 11.5 % among 26 patients [8]. There are few data of the fetal outcome in the collected series during the first half of the twentieth century.

Table 7.5 Monitoring of patients with suspected or proven refeeding syndrome (minimum 72 h)

Monitor until levels in reference range or patient on stable feeding regimen
Serum urea and electrolytes, adjusted calcium, phosphate, liver function tests at least daily
Serum magnesium baseline, every 3 days, and then weekly once stable
Fluid balance daily
Blood glucose once to twice daily unless more frequent tests are indicated
Temperature, pulse, respiration, heart rate; daily
Blood pressure 6 hourly
ECG if abnormal heart rate or pulse. If evidence of cardiac abnormalities on assessment or during refeeding patient will require cardiac monitoring. If necessary transfer to appropriate ward

Clinical deterioration may reflect over rapid feeding, too little is always safer than too much, halve rate of feeding and observe

7.2 Intussusception

7.2.1 General Considerations

Intussusception was usually fatal until early twentieth century. John Hunter described the clinicopathological characteristics. Sir Fredrick Treves, an eminent nineteenth-century surgeon described the plan of treatment, which by and large remains valid to date [57]. Adult intussusception is rare. It is expected to be found in 1/30,000 of all hospital admissions [58], 1/1,300 of all abdominal operations [58], 1/30–1/100 of all cases operated for intestinal obstruction [58, 59], and one case of adult intussusception for every 20 childhood ones. The mean age at

presentation tends to be in the sixth decade of life [58–62]. Higher age at intussusception may point to underlying malignancy since the mean age for benign cases is 44 years as opposed to 60 years for the malignant [60]. It may be acute or chronic (persistent or intermittent) in addition to being "silent" [63, 64]. The chronic intussusception may have lasted in some instances for a year before the diagnosis. The male-to-female ratio is 1:1–1.3 [65]. This entity can be classified into four distinct categories [60]:

- *Enteric*, in which the intussusception is confined to the small bowel
- *Ileocolic*, in which the ileum invaginates through a fixed ileocecal valve
- *Ileocecal*, in which the ileocecal valve itself is the lead point for the intussusception
- *Colocolic*, in which the lead point is restricted to the colon

Intussusception (invagination of one part of the bowel into another) is largely a disease of children with only about 5 % of all cases of intussusception occurring in adults. About 80–90 % of intussusceptions in adults are secondary to an underlying pathology typically associated with tumors, granuloma formation, a foreign body, or an anatomic defect. Small bowel intussusceptions in adults are secondary to benign lesions in most cases, with malignant lesions causing 15 % of cases and idiopathic intussusceptions accounting for approximately 10–20 % [66]. Although in small bowel intussusception in adults surgical intervention is considered necessary when patients are symptomatic, many asymptomatic and likely transient intussusceptions may be incidentally detected on CT. When self-limited, they do not require surgical therapy [67].

7.2.2 History

First known cases described are intussusception of the rectum in pregnancy by Berthold Ernest Hadra (Fig. 7.7) and another from 1914 by Williamson. The second case is a 26-year-old woman in 34th week of her second pregnancy. Before first pregnancy, she was twice operated due to peptic ulcer, and one of the operations was gastroenterostomy. She died during diagnostic workup, 2 days after expelling stillbirth [68].

7.2.3 Incidence

7.2.3.1 Pregnancy

The incidence of intussusception is not different between pregnant women and the nonpregnant adult population [69]. The rate of intussusception as a cause of intestinal obstruction averages as high as 6 % [70]. The most common type of intussusception occurring in pregnancy or the puerperium is ileocecal [69], and Meckel's diverticulum is the most common precipitating factor of intussusception in pregnant women. Chaffen, Mason, and Slemons collected 20 cases which were associated with pregnancy either before labor, at labor, or in the puerperium [71]. In the study by Chiedozie et al., 30 % (3/10) of cases of intestinal obstruction were caused by intussusception [12]. In pregnancy the most common precipitating factor of intussusception is a Meckel's diverticulum [72]. There are only several cases of primary intussusception in pregnancy published. Probably this is due to bimodal incidence of intussusception – in the childhood and with increasing incidence during life with second peak in the sixth decade of life.

Postoperative invaginations should also be mentioned, one of the first published by Williamson (see Sect. 7.2.2) [68].

7.2.3.2 Puerperium

Even a case of idiopathic intussusception in puerperium after normal vaginal delivery is published [73]. Another two cases of post-Cesarean section intussusception are published. One case is secondary to colonic adenocarcinoma and another of idiopathic intussusception of 27-year-old women with preeclampsia with ileoileal invagination 80 cm proximal to the ileocecal valve which was manually reduced [74].

7.2.4 Etiology

Currently, it is not known how does pregnancy contribute to the development of intussusception or is it just a coincidence. There are several more cases published on PubMed but without abstract and important data for further analysis are therefore missing. It should be noted that most of these patients were in advanced pregnancy.

The cause of intussusceptions in adults varies by location. Large bowel lead points are more frequently malignant than small bowel lead points. The small bowel leading points are hamartomas, lipomas, leiomyomas, neurofibromas, adenomas, inflammatory polyps, Peutz-Jeghers syndrome, Meckel's diverticulum, parasitic infestation, and adhesions [75–77]. One patient in 34 weeks' gestation underwent a right hemicolectomy, and no pathologic or anatomically anomalous lead point was identified intraoperatively or on final pathology [78]. Another patient in 33 weeks of gestation had an ileoileal intussusception without a lead point. Histology of the resected bowel segment showed hemorrhagic infarction without evidence of malignancy [14]. Third case is [79]. Fourth patient in 20th week pregnancy had jejunojejunal intussusception with resection and anastomosis [80]. Fifth patient was diagnosed in 19th week but had previously two attacks that were unrecognized [81]. Sixth is patient in 30th week of pregnancy with jejunojejunal intussusception due to hamartomatous polyp [72] and another with benign neurilemmoma in 35th week of pregnancy [82]. The earliest patient was in 17th week of pregnancy [83]. There are two cases of heterotopic pancreas causing intussusception during pregnancy. It is postulated that there is relationship of the enlargement of a heterotopic pancreas with the hormonal changes in gestation [84]. The first case described gastric outlet obstruction [84] and other ileoileal intussusception (Figs. 7.4 and 7.5) caused by a heterotopic pancreas in a pregnant woman [85].

There are two cases of primary non-Hodgkin's lymphoma as intussuscipiens [86], one with the definitive diagnosis made at the time of Cesarean section [87].

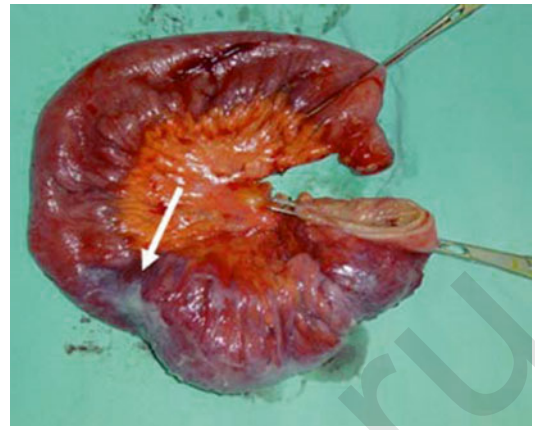

Fig. 7.4 The resected necrotic specimen of the intussusception. The *white arrow* shows the invagination point [85]

7.2.5 Pathophysiology

It is generally believed that masses in the bowel or lumen act as an irritant and provoke abnormal peristaltic movement, which may lead to the telescoping of one bowel segment over the adjacent segment. Intussusception appears as a complex soft tissue mass consisting of the outer intussuscipiens and the central intussusceptum (Fig. 7.6). Any tumor acting as the lead point of an intussusception may be outlined distal to the tapered lumen of the intussusceptum.

Intussusception of the rectum in pregnancy is a malady to which Berthold Ernest Hadra (Fig. 7.7) calls attention in *The Richmond and Louisville Medical Journal* of December 1876. The long-standing obstipation, common in pregnancy, as well as the direct pressure exerted by the gravid womb upon the rectum in the direction of the sacrum, tends to produce this entity.

7.2.6 Clinical Presentation

The clinical presentation of adult intussusception varies considerably. Presentation depends on the location of intussusception, rapidity of obstruction, and additional symptoms and signs especially if the process is malignant. The most

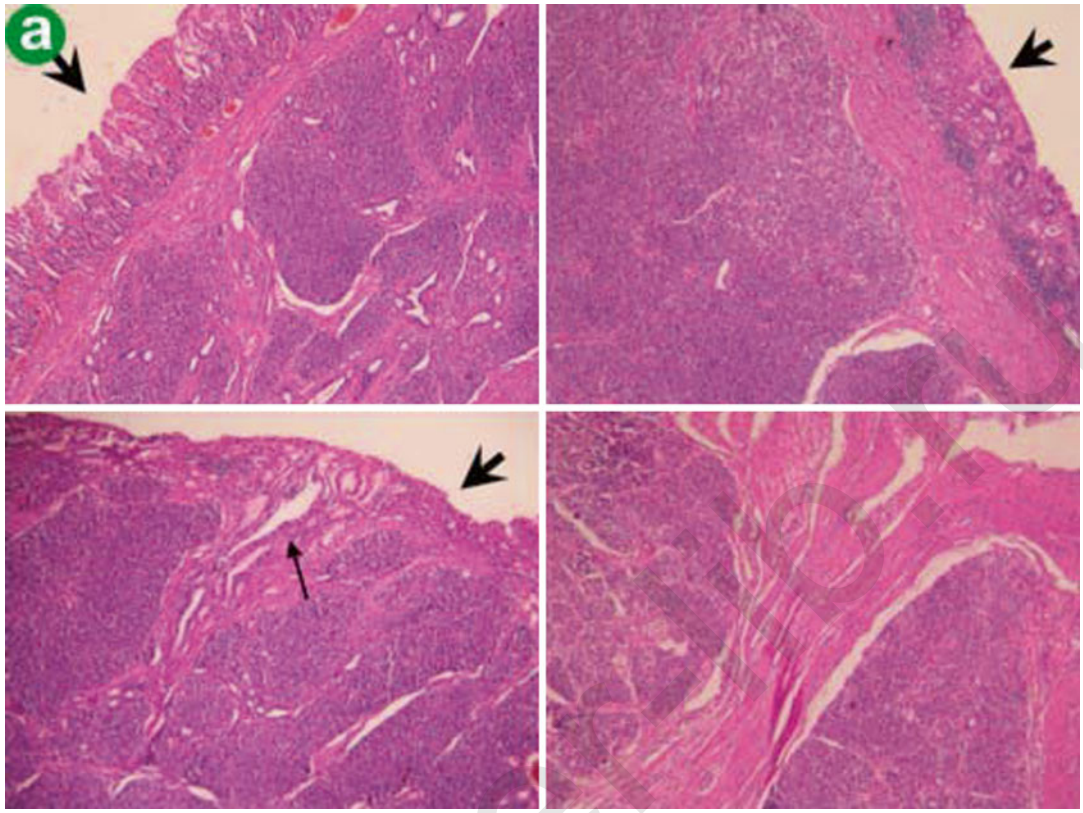

Fig. 7.5 Mature exocrine pancreatic tissue within the intestinal wall with atrophic overlying mucosa (*arrowheads*) and a duct draining into the intestinal lumen (*arrow*) (H&E, original magnification 40×) [85]

common symptoms of intussusception are abdominal pain, nausea, and vomiting; less frequent symptoms are melena, weight loss, fever, and constipation [66]. Symptoms are usually of long duration (several weeks to several months), although the patient may occasionally present with an acute abdomen [66]. Common physical findings include abdominal distention, decreased or absent bowel sounds, and abdominal mass [60, 89, 90]. Specifically, making a diagnosis of intussusception in adults is equally tasking because the classical pediatric triad of intussusception (acute abdominal pain, palpable sausage-shaped mass, and "red currant jelly" stools) is seldom observed in adults. However, in a woman with a gravid uterus and especially at advanced stage of gestation, it may not be possible to palpate a mass [14]. Palpable mass can be found especially during early gestation [91]. A malignant cause of intussusception is more likely to present with a shorter duration of symptoms [92]. The implication of these is that there is often a delay in making a diagnosis of intestinal obstruction in pregnancy and such delay is even worse making a diagnosis of intussusception in pregnancy [93]. Sometimes the symptoms can resolve but can recur during same pregnancy [14].

Symptoms of the intussusception of the rectum are very frequent stools, small, slimy and more or less mixed with blood, and uncontrolled by internal medication, tenesmus, and absence of fever. Examination by the rectum (anoscopy or rectoscopy) easily reveals the intussuscepted fold.

Additional diagnostic problem is when obstructive symptoms present in the puerperium. Symptomatology is the same as in general or pregnant population after normal vaginal delivery [73] or Cesarean section [74]. Suspicion should

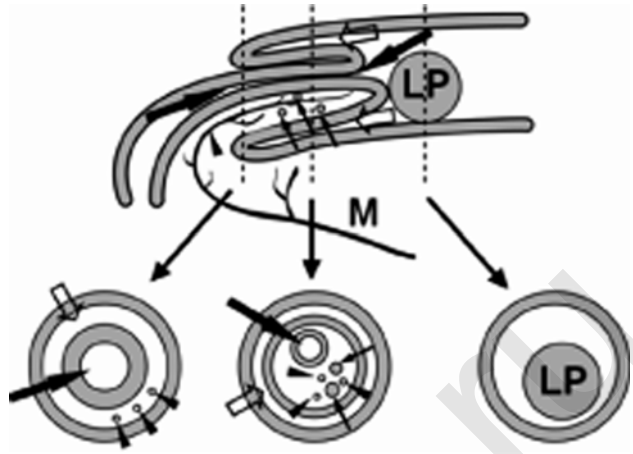

Fig. 7.6 Schematic drawings of intussusception. Longitudinal and serial cross-sectional diagrams of intussusception show invagination of one segment of gastrointestinal tract (intussusceptum) (*thick solid arrows*) into adjacent segment (intussuscipiens) (*open arrows*). Proximal cross-sectional diagram of intussusception (*bottom right*) shows two layers, although classic appearance of three layers (*middle bottom*) is shown in midportion of intussusception. Note invagination of mesentery, mesenteric vessels (*arrowheads*), and hyperplasic mesenteric lymph nodes (*thin solid arrows*). *LP* lead point, *M* mesentery [88]

be raised if abdominal pain or distension occurs after a period of normal post-Cesarean section course or normal vaginal delivery. Difficulties after Cesarean section are encountered because (1) symptoms are attributed to incisional pain and (2) ileus is attributed to early postoperative ileus [94]. It should be kept in mind that idiopathic postoperative intussusception is more common after abdominal operations and usually occurs within 2 weeks following surgery.

7.2.7 Diagnosis

In the 11 reported cases of intussusception in pregnancy in the past 25 years, 55 % (6/11) were diagnosed preoperatively. Three cases were diagnosed by abdominal ultrasound [83], one by plain abdominal X-ray postdelivery, and one by abdominal MRI [70, 72, 81, 83].

Abdominal sonography can make the diagnosis of an intussusception in an adult when the characteristic sign of a "target-like" lesion or "bull's eye" lesion is shown, similar to the CT findings, and is sometimes enough for the definitive diagnosis [83]. The classic features of intussusception include "target," "doughnut," or "crescent-in-doughnut" signs on a transverse view and the "pseudokidney" sign in the longitudinal view (Fig. 7.8), or multiple concentric rings of intussusceptum (Fig. 7.9) or multiple concentric vascular signals in thickened intussuscipiens (Fig. 7.10) [72, 73, 95–97]. The central echogenic area is produced by the mucosa of the intussusception, which is surrounded by a hypoechoic ring representing the walls of both the intussusceptum and the intussuscipiens [98]. This variability in appearance is largely due to the scanning level, the amount of intussuscepted mesentery, the degree of bowel wall edema, and the presence of a pathologic lead point and lymph nodes. Ultrasound is an operator-dependent technique whose utility may be limited by obesity and air in distended bowel loops.

Intussusception is well diagnosed on abdominal CT, which shows a pathognomonic bowel-within-bowel configuration with or without contained fat and mesenteric vessels [99]. Intussusception appears as a sausage-shaped mass when the CT beam is parallel to its longitudinal axis but as a target-like mass when the beam is perpendicular to the longitudinal axis [66]. With the increasing use of ultrasound, CT, and improved methods for examining the small bowel, intussusception is currently diagnosed more frequently before

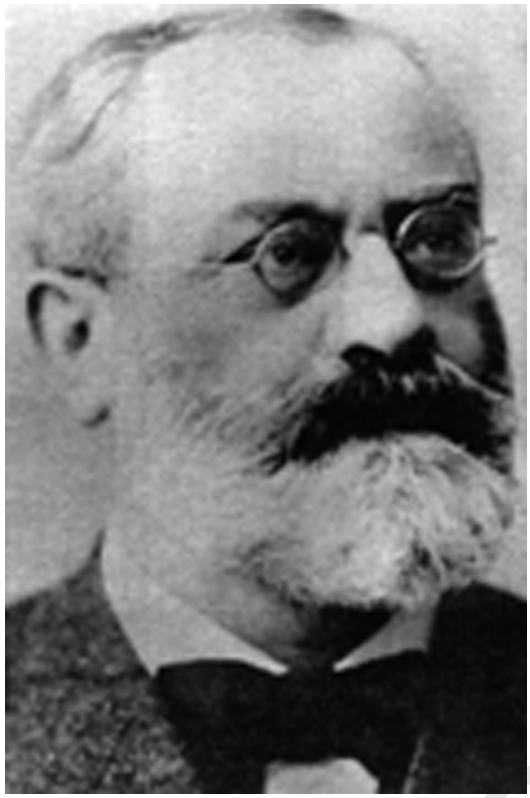

Fig. 7.7 Berthold Ernest Hadra (1842–1903), physician and surgeon, was born near Breslau, Prussia (now Wroclaw, Poland). He obtained his medical education from the universities of Breslau and Berlin. He was appointed chairman of Surgery at Texas Medical College at Galveston in 1888 and helped to transform that institution into what is now known as the University of Texas Medical Branch at Galveston. He received international respect for his pioneer work in the fields of surgery and gynecology (Courtesy of *American Association of Neurological Surgeons*, 2004)

operations (Fig. 7.11). Currently, instead of CT scan, MRI is used to eliminate ionizing radiation (Figs. 7.12 and 7.13).

Barium reflux in the lumen of the space between the intussusceptum and intussuscipiens allows the coiled spring to be visualized.

Abdominal MRI was first used to define intussusception during pregnancy in 1992 [70]. In the study by Chiedozie et al. [12], two of the three patients that had intussusception did not have any leading point, and in the case by Osime et al. the leading point was not found (patient had previous appendectomy) [14].

In the puerperium, all imaging diagnostic modalities could be used for the diagnosis. Plain abdominal X-rays, abdominal ultrasound, and abdominal CT were used in all three patients presented after delivery [73, 74, 94].

7.2.8 Therapy

Therapeutic principles for intussusception are the same as in nonpregnant population. There are two important principles of treatment. First is to solve the intussusception itself and second to treat the cause of the intussusception if indicated. Most adults with intussusception require surgery to clarify the etiology of the lead point. Treatment usually requires resection of the involved bowel segment [73]. Reduction can be attempted in small-bowel intussusception if the segment involved is viable and if malignancy is not suspected [74]. If the leading point is present, it should always be resected because further therapy depends on the pathohistological diagnosis (Fig. 7.14). Recently, laparoscopic exploration is used to minimize abdominal wall trauma and shorten postoperative hospital stay [74]. This is important to facilitate earlier return to normal life and maternal care about newborn baby.

In colonic intussusception, malignancy and resection are more likely. Therapeutic barium enema can be tried in a few selected cases where the underlying pathology is known [101]. In some patients, small-bowel intussusception may be an incidental finding. Careful observation may be indicated if imaging does not reveal an identifiable lead point, vascular compromise, or bowel obstruction [102]. Almost all patients were explored by laparotomy but laparoscopy could also be performed with all its advantages [103].

Rectal intussusception treatment in 1879 (see Sect. 7.2.5) consisted in copious injections of

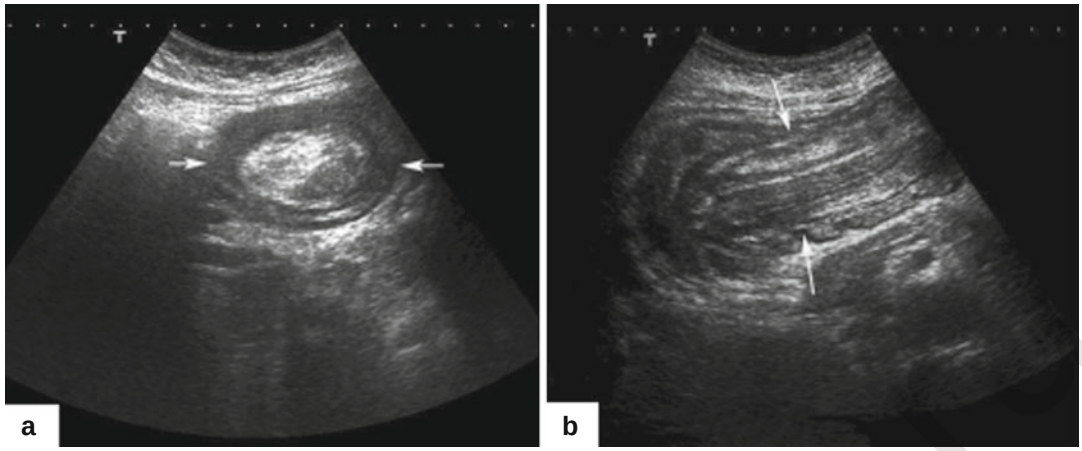

Fig. 7.8 (**a**) Transverse abdominal sonography: in the left lower quadrant, a "bull's eye" or "doughnut" image with an echogenic center and a translucent rim (*arrows*) is visible. (**b**) Longitudinal ultrasound scan showing the "pseudokidney" sign, representing the appearance of the intussusceptum and intussuscipiens (*arrows*) [73]

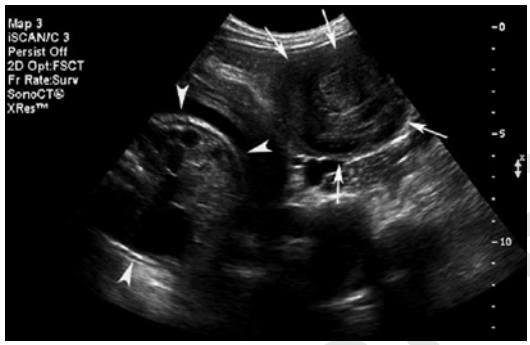

Fig. 7.9 Jejunojejunal intussusception during late pregnancy in a 33-year-old woman. Transverse gray-scale sonogram showing multiple concentric rings (*arrows*) representing multiple layers of the innermost intussusceptum, intervening mesenteric fat, and vessels and outer intussuscipiens at the left of the fetal abdomen (*arrowheads*) [72]

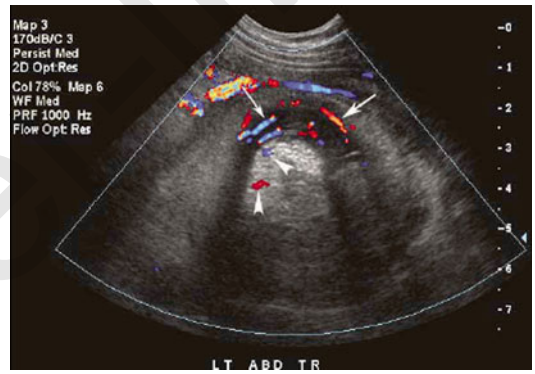

Fig. 7.10 Jejunojejunal intussusception during late pregnancy in a 33-year-old woman. Transverse color Doppler sonogram showing multiple concentric vascular signals in thickened intussuscipiens (*arrows*) and some vascular spots in the hypoechoic intussusceptum (*arrowheads*) and echogenic mesentery [72]

cold water made with considerable force. These unfolded the invagination and produced natural dejections.

7.2.9 Prognosis

As early as 1937, it was stated that the mortality was definitely higher in all stages of pregnancy [71]. Prognosis depends on the state of the bowel. If the resection is not necessary (viable bowel without the lead point), the prognosis is excellent. If resection due to ischemic bowel is necessary, prognosis is still excellent. Higher rates of spontaneous abortion and preterm labor are present if perforation with peritonitis occurs.

If intussusception presents during puerperium, clinicians easily indicate diagnostic imaging modalities such as plain abdominal X-rays or abdominal CT scan; therefore, diagnosis is

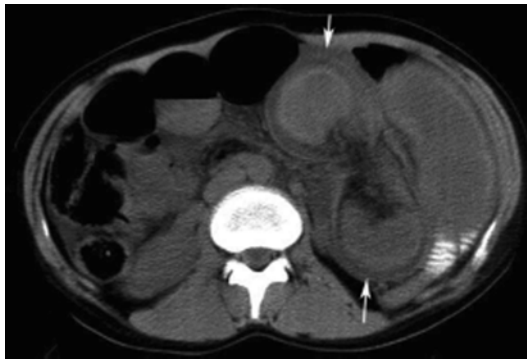

Fig. 7.11 Oral contrast-enhanced CT showing a round "target-shaped" mass in the *left* mid-abdomen consisting of different densities with distended fluid-filled small bowel loops (*arrows*) [73]

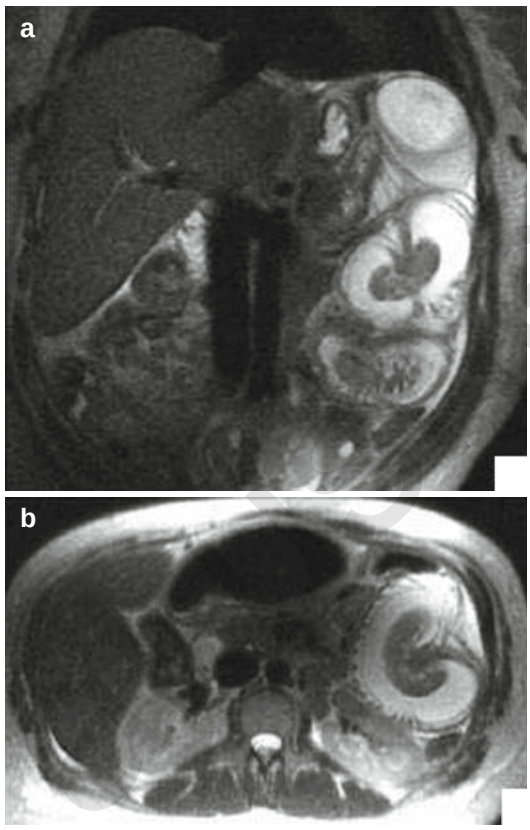

Fig. 7.12 A 31-year-old woman at 23 weeks' gestation with severe left-sided abdominal pain. Sagittal (**a**) and transverse (**b**) images show intussusception of small bowel in the left upper quadrant. Note dilated loops of small bowel and free fluid [100]

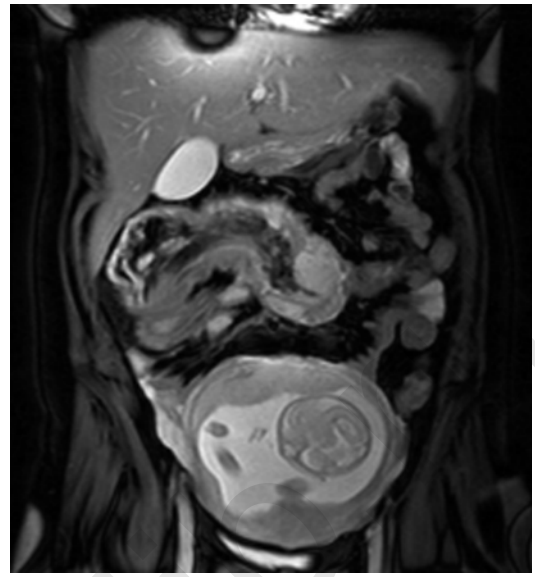

Fig. 7.13 Magnetic resonance image of intussusception in the epigastric region, with the gravid uterus inferior to and separate from the mass [81]

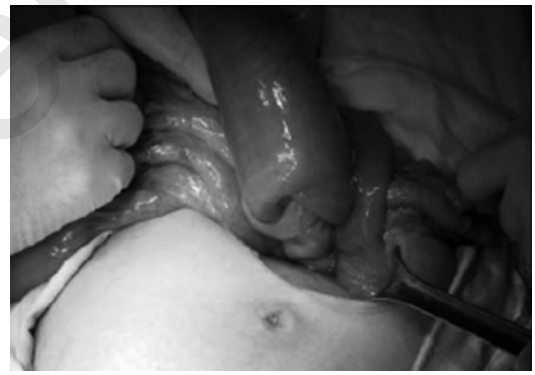

Fig. 7.14 Jejunojejunal intussusception during late pregnancy in a 33-year-old woman. Jejunojejunal intussusception of about 80 cm in length shown as a sausage-shaped mass comprising the swollen intussuscipiens with an invaginating intussusceptum of more proximal loops. Pedunculated polypoid mass was hamartomatous polyp [72]

made earlier and more accurately. Two patients with ileoileal intussusception (one with small bowel resection [73] and another with manual reduction [74]) and one patient with malignant colonic intussusception [94] were alive after the operation.

7.3 Uterine Perforation After Surgical Abortion

7.3.1 Introduction

Let alone the fact that abortion is an extremely sensitive topic everywhere, it is perhaps unreasonable to expect reliable data about abortion practices in a country such as India where even vital registration – the recording of births, deaths, and marriages – is far from complete and accurate [104]. Most illegal abortions are conducted in the rural areas of developing nations without adequate facilities and by persons with no knowledge of anatomy who operate with non-sterile instruments with increased percentage of mortality and morbidity [105–109]. One important, although rare, complication is small bowel obstruction through uterine wall perforation. Obstructions of the large intestine are rare due to its fixed position; therefore, complications with large bowel mostly include instrumental perforations.

One of the first published cases of small bowel obstruction in the form of evisceration through vaginal introitus is from 1949 by Haddad [110], and several more similar cases were published up to 1967 [111, 112]. The most data in this section are from the most recent review article by Augustin et al. published in 2013 with most cases from 1907 to 2012 [113].

7.3.2 Incidence

First trimester surgical abortion (as opposed to prostaglandin medical abortion) is one of the most frequently performed procedures in the United States: 853,485 procedures were performed in 2001 [114]. In a large study evaluating morbidity secondary to first trimester surgical abortion, Hakim-Elahi et al. reported minor complications managed as an outpatient procedures (0.846 %), including mild infection, resuctioning on the day of procedure or subsequent resuction, cervical stenosis, cervical tear, underestimation of gestational age, and convulsive seizure after local anesthesia [115]. Major complications requiring hospitalization after a first trimester surgical abortion (0.071 %) included incomplete abortion, sepsis, uterine perforation, vaginal bleeding, inability to complete abortion, and combined (heterotopic) pregnancy. Uterine perforation during abortion is rare, with a reported rate of 0.05–1.9 % [116–119].

There are, fortunately, around 30 case reports of small bowel obstruction through uterine perforation after vacuum abortion, surgical abortion, or unsafe abortion published. All cases were during the first trimester except one which occurred in the second trimester [120]. The distribution through the trimesters is contrary to the fact that second trimester abortion has a higher rate of complications than abortions performed in the first trimester [117, 119, 121].

Extremely rare incidence of small bowel obstruction after uterine perforation due to surgical abortion is due to:

- Rare occurrence of instrumental uterine perforation
- Spontaneous healing of most (recognized and unrecognized) uterine perforations without further complications [122]
- Immediate laparotomy/laparoscopy in 47–84 % of cases with recognized complicated uterine perforation [118]
- Unknown number of cases not published in the medical literature
- Prehospital mortality, especially in undeveloped countries [123]

7.3.3 Risk Factors

In an attempt to identify factors potentially leading to uterine perforation, several authors determined that the level of training was the strongest statistically significant risk factor for perforation [124, 125]. Other factors were advanced

maternal age, greater parity, retroverted uterus, history of prior abortion or Cesarean section, history of previous cone biopsy, failure to use ultrasound, and underestimation of the duration of pregnancy [116, 117, 119, 126, 127]. Amarin and Badria concluded that uterine perforations were mostly located at the uterine fundus, presumably caused by the introduction of cervical dilators [128]. Hence, difficulty during cervical dilatation also has been associated with a higher perforation rate, and some authors recommend prostaglandin use to aid in dilatation of the cervix [117, 119]. Additionally, prostaglandins have the benefit of contracting the uterus, which may help decrease the perforation rate [118]. Currently, there are no known risk factors for small bowel obstruction after uterine perforation. Unfortunately, there are insufficient data for the conclusions, but three factors could cause the increase of the incidence [113]:

- Failed medical abortion [126, 129]
- Curettage for retained parts of the placenta after previous pregnancy [130]
- Diameter of uterine perforation
- Multiple pregnancies

7.3.4 Mechanisms of Small Bowel Obstruction

There are several mechanisms of small bowel obstruction after uterine perforation. Most common is due to small bowel prolapse (Fig. 7.15) through uterine perforation mostly due to inadvertent aspiration [120, 131–135] with the most extensive type when the small bowel loops are pulled out of vaginal introitus (Fig. 7.16) [123, 124, 129, 136–140].

Second mechanism is where uterine perforation contains incarcerated herniated omentum and a band attached to the omentum strangulates a segment of the extrauterine small bowel, producing obstruction (Fig. 7.17) [116].

The third mechanism is when the small bowel is entrapped in adhesions at the site of uterine perforation [142]. Fourth mechanism is Richter hernia-type obstruction when the antimesenteric wall of the intestine protrudes through a defect in the uterine wall [134]. Explanation for symptomless Richter type of small bowel obstruction follows. During the first pregnancy (2 years previously), a dilatation and curettage had been performed 4 weeks after delivery to remove the retained placenta. During instrumentation, the uterine wall perforation occurred with formation of Richter type of hernia but without ischemia of

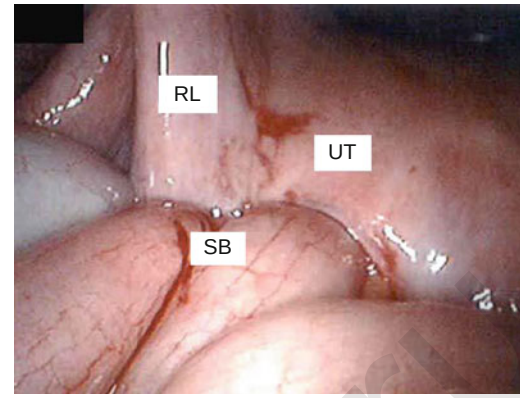

Fig. 7.15 Intraoperative photograph demonstrates a defect in the anterior myometrium of the uterus (*UT*) at the level of the left round ligament (*RL*), through which the small bowel (*SB*) has become incarcerated [131]

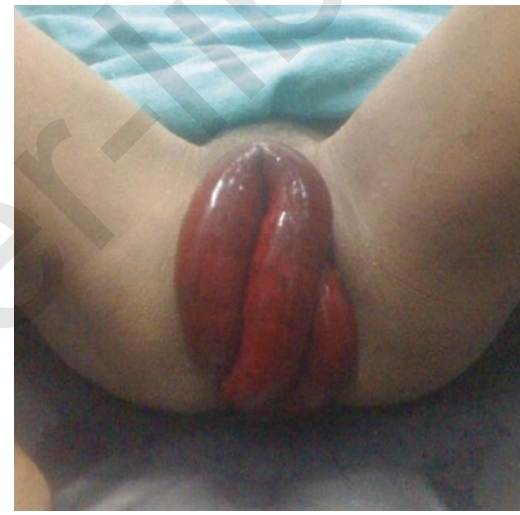

Fig. 7.16 Congested and edematous intestinal loops pulled out of vaginal introitus 2 h following evacuation of the uterus done for an incomplete abortion [136]

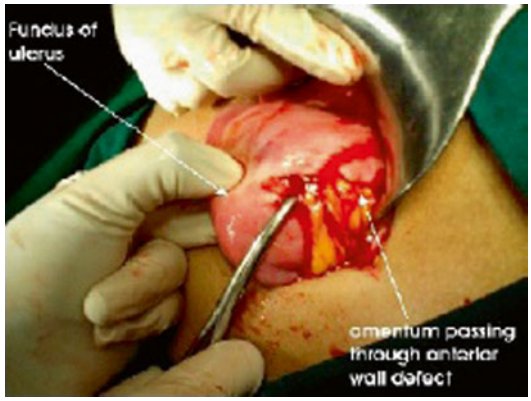

Fig. 7.17 Intraoperative photographs showing greater omentum incarcerated through the anterior wall defect of the uterus [141]

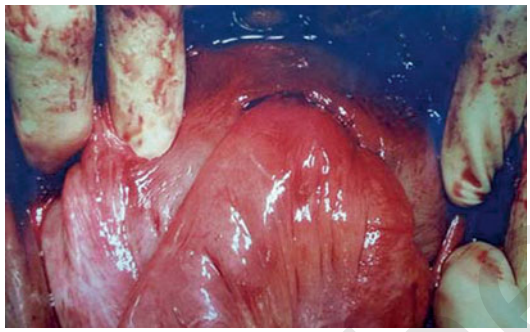

Fig. 7.18 Richter type of hernia when the antimesenteric wall of the intestine protrudes through a defect in the uterine wall causing partial obstruction which evolves to complete obstruction during subsequent pregnancy [130]

the small bowel wall. In this second pregnancy at advanced stage, growing uterus that made compression and occlusion of the small bowel that was fixated to the uterus previously as Richter type of hernia (Fig. 7.18) [130].

It is important to note that most (83 %) large-bowel injuries were associated with posterior uterine wall perforation, whereas 60 % of the small-bowel injuries were associated with anterior wall or uterine fundus perforation [109].

7.3.5 Clinical Presentation

The uterine perforations are usually recognized at the time of the dilatation and curettage. If unrecognized, majority of patients have uncomplicated course with spontaneous healing of uterine perforations (see Sect. 7.3.2). The type and time of presentation depend on two pathophysiologic processes that could coexist (iatrogenic bowel perforation is excluded):

1. Mechanism of small bowel obstruction
2. (Associated) bleeding
   (a) From the uterine wall around perforation
   (b) From the mesentery detached from its bowel [143]

Ad 1. The mechanism of small bowel obstruction dictates the severity, intensity, and time of presentation of obstruction. If adhesions are the cause of partial or progressive small bowel obstruction than nonspecific symptoms including abdominal pain with/without distension, vomiting, (paradoxical) diarrhea, or absence of flatus and/or stool is present. Fever and chills are present in the advanced stage when small bowel gangrene ensues. A serious consideration of this possibility is necessary, as the intrauterine location of strangulated bowel may mask the characteristic peritoneal signs [116]. Ischemic bowel perforation should be pathopysiologically differentiated from the direct bowel injury during instrumental uterine perforation. Such injuries develop clinical picture mostly within few hours after the procedure [144]. In the study by Augustin et al., duration of symptoms due to adhesions was from 4 days to 4 months in four patients [113]. These symptoms cause the delay in diagnosis because the patients with partial obstruction are commonly managed conservatively [135]. Presentation after 2 years was due to Richter type of hernia. Presentation of Richter hernia is not predictable. It can incarcerate initially with early presentation or other pathophysiologic event should be present for initiation of obstruction. Probably it depends partly on the size of uterine perforation. Such mechanism of delayed presentation was present in one patient [130]. If the incarceration of the bowel through uterine wall is present and not recognized during abortion and if complete obstruction due to bowel prolapse through the uterine wall is the cause, then all patients presented 1–48 h after uterine instrumentation [113]. If the small bowel is

prolapsed in a form of vaginal evisceration, the diagnosis is evident clinically due to the vaginal small bowel prolapse.

Ad 2. Any mechanism of small bowel obstruction could be accompanied by hemorrhage from either uterine wall perforation or detached mesentery from its bowel. Clinically, hemorrhage from uterine wall perforation is evident due to transvaginal bleeding, but mesenteric bleeding can present either with transvaginal or intra-abdominal bleeding or both. An intra-abdominal bleeding presents as abdominal pain and should be always looked for because the pain can be attributed to abdominal pain caused by coexisting small bowel obstruction with abdominal distension. It is difficult to conclude is hemorrhage or small bowel obstruction dominant in these patients because variations in severity of developing obstruction and variations in severity of bleeding could be present. In the study by Augustin et al., 39 % (7/18) of patients were hypotensive [113].

7.3.6 Diagnosis

The diagnosis should be suspected when air-liquid levels of small bowel are evident on plain abdominal X-ray. Knowledge of the typical appearance of the uterus after a first trimester surgical abortion is clearly helpful in recognizing an abnormal pelvic ultrasound. In the emergently presenting patient, ultrasound is the preferred diagnostic modality, but it should be recognized that the normal appearance of the uterus after a first trimester surgical abortion can be quite variable. A small number of imaging studies have documented the appearance of the uterus after a first trimester surgical abortion [145–147]. Dillon et al. [145] performed short-term follow-up with ultrasound to qualitatively evaluate the uterine cavity after a first trimester surgical abortion in 19 asymptomatic patients. In this study, 59 % of patients had a varying amount of intrauterine material, initially appearing hyperechoic and then later iso- or hypoechoic. No material seen resembled retained fetal parts or placental material. The time for the return of the endometrial stripe to baseline appearance was variable, ranging 1–14 days. Similarly, another larger study by Bar-Hava et al. [146] examined the appearance of the uterus of 74 women who had undergone a first trimester surgical abortion within 1 week of the procedure. Only 23 % of patients demonstrated reversion to a thin endometrial stripe, 50 % displayed a thick endometrial stripe (7–19 mm), and 27 % an endometrial stripe >20 mm or with very irregular echogenicity >14 mm. These investigators also described a trend toward hyperechoic endometrial contents earlier in the week versus hypoechoic contents later in the week, presumably due to liquefying endometrial contents. The appearance of endometrium after the first menstrual period reverted to normal in all patients. Patient demographics such as gravidity or date of first trimester abortion did not correlate with the appearance of the uterus.

Ultrasound appearance of uterine perforation with suspected bowel entrapment was first reported in 1983 by Dunner et al. [133]. Defect in the uterine wall could be detected with the transabdominal ultrasound. Tubular-shaped irregular tissue could be seen within the endometrial cavity, with a small echoic focus suggesting the presence of air (Fig. 7.19). An abnormally increased amount of echogenic free fluid could be seen in the cul-de-sac [131].

Transvaginal sonography is a convenient tool in aiding in the diagnosis. Image findings of free fluid in the pelvis, loops of bowel within the myometrial wall, extrauterine fetal parts, or intraoperative presence of the curette within the myometrium have all been used to confirm uterine perforation [148]. Ultrasound of the pelvis could delineate bright, serpiginous, fluid-filled tubular structures within the endometrial cavity (Fig. 7.20). Adjacent material of increased echogenicity could be suggestive of fat. Color Doppler would not show blood flow in these structures, and no peristalsis would be seen in the intrauterine contents [131].

The first reported CT diagnosis of incarcerated bowel in a uterine perforation was by Dignac et al. (incarcerated appendix) and Chang et al. in 2008 [126, 127]. Evaluation with CT has an important diagnostic role in cases where ultrasound is ambiguous or if non-gynecologic

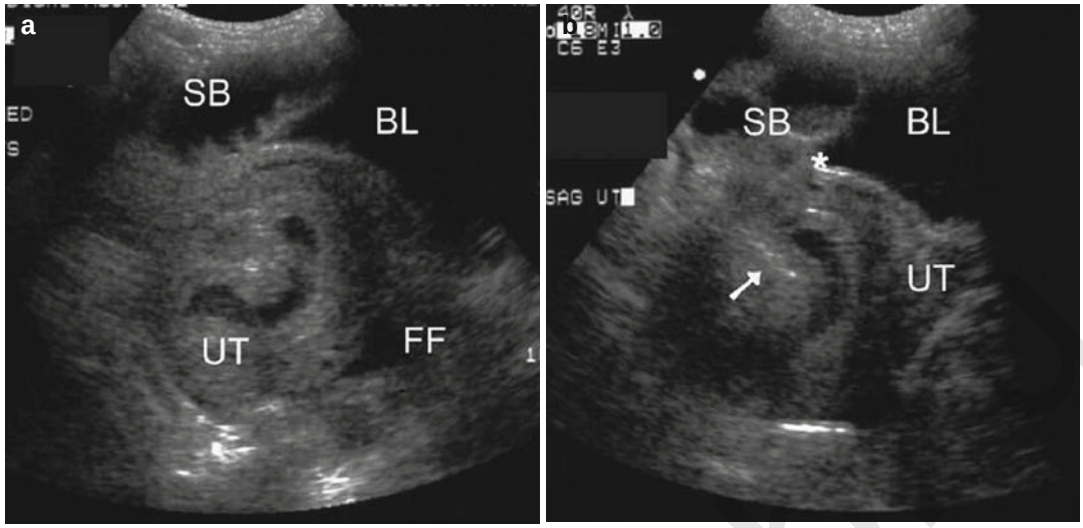

Fig. 7.19 (**a, b**) Transabdominal pelvic ultrasound images demonstrate a retroverted uterus (*UT*) adjacent to the urinary bladder (*BL*) with adjacent fluid-filled small bowel (*SB*) closely apposed to an interrupted uterine wall (*asterisk*). A tubular structure is seen within the uterus. A small amount of anechoic free fluid (*FF*) is seen in the cul-de-sac. Linear echogenicity (*arrow*), consistent with the appearance of gas, is adjacent to the abnormal intrauterine tubular structure [131]

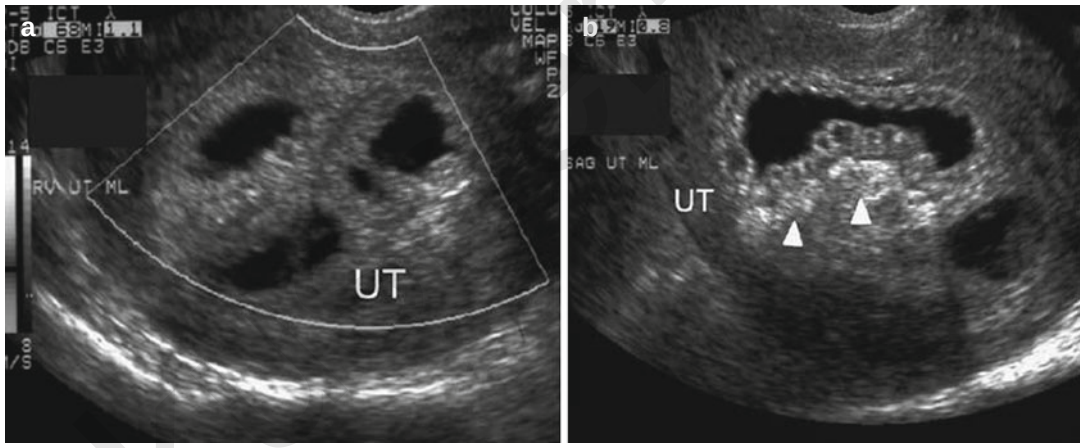

Fig. 7.20 (**a**) Transvaginal pelvic ultrasound transversely demonstrates multiple tubular structures containing anechoic fluid within the uterine cavity (*UT*); (**b**) sagittally, echogenic material (*arrowheads*), suggesting the presence of fat, is adjacent to the intrauterine tubular structure [131]

pathology is suspected. Although the uterine wall can hinder visualization of intrauterine bowel loops, Dignac et al. emphasize that the bowel's mesentery can be well visualized on CT scan due to its fatty nature and should be a red flag for intrauterine bowel [127]. CT scan can delineate bowel loops within the uterus (Fig. 7.21).

Finally, MRI has been utilized to assess the endometrial cavity after a first trimester surgical abortion [147], but this is not routinely performed on an emergent basis. There is only one case showing incarceration of the greater omentum in the uterine perforation without bowel obstruction [149].

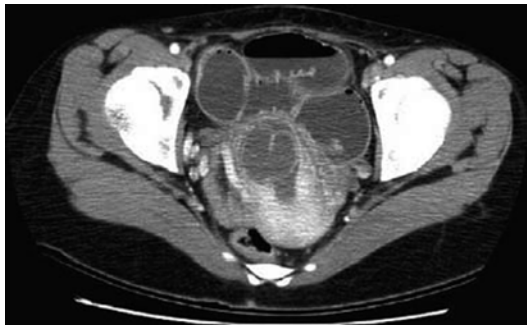

Fig. 7.21 Pelvic computed tomography scan taken after failure of conservative treatment. Intrauterine mass was later shown to be an incarcerated bowel [126]

7.3.7 Therapy

7.3.7.1 Conservative Therapy

Uterine perforations should be divided into uncomplicated and complicated ones. Most uterine perforations recognized during abortion without complications could be managed conservatively [118, 119]. Kaali et al. [122] managed conservatively 22 perforations after 7,114 elective abortions, with a significant number of these perforations detected during combined laparoscopy. This implies that the true perforation rate may be underreported and under-recognized without severe consequences to patients, suggesting that conservative management of uncomplicated uterine perforations with close observation is typically adequate [118, 127, 134].

7.3.7.2 Surgical Therapy

The diagnosis or even suspicion of intrauterine bowel/bowel injury (complicated uterine perforation), however, mandates emergency laparotomy or laparoscopy. Emergency laparotomy/laparoscopy is necessary to prevent the progressive bowel distention with ensuing ischemic necrosis and/or subsequent perforation of the bowel. During laparotomy/laparoscopy, the bowel should be reduced into the peritoneal cavity and evaluated for vitality. The involved herniated bowel may be strangulated, have direct bowel wall trauma, or may be devascularized by coexistent injury or incarceration of the mesentery [135]. In the study by Augustin et al., in all cases of vaginal evisceration, resection was necessary. In 14 of 18 patients, the length of resected small bowel was measured. In only one patient, the resected length was 30 cm, and in all others, the minimal resected length was 100 cm. In 56 % of patients, more than 200 cm was resected. In the subgroup of patients with ileal adhesion (three patients), the resection of ischemic bowel was necessary in two patients (67 %). The question is whether the bowel could be saved with earlier diagnosis and operation earlier in the course of the disease, but the answer cannot be made because of the lack of all necessary data.

Diversion in form of a stoma was made in only one patient with complete small bowel resection. It should be performed in patients with hemorrhagic shock or in sepsis due to late presentation with gross purulent and/or fecal contamination of the peritoneal cavity. Study by Augustin et al. shows that if isolated small bowel obstruction is present, resection with anastomosis is preferred treatment in patients without peritonitis.

7.3.7.3 Gynecologic/Obstetric Procedures

Uterine perforation/laceration should be repaired after treatment of small bowel injury. Sometimes uterine perforation should be enlarged for easier pulling of the bowel into peritoneal cavity minimizing the possibility of further bowel and mesenteric damage (two patients) [132, 143]. Rarely, a hysterectomy is required if the uterus is necrotic or irreparable [144, 148]. Hysterectomy was performed in four of the seven patients from the first half of the century and none after 1966. Conclusion by Augustin et al. is that uterine debridement with suture repair is the procedure of choice [113] despite description of one patient without repair of uterine perforation where perforation size was 1 cm [116].

Preoperative consultation with the patient for permanent sterilization should be done because during operation short additional procedure could prevent repeating of complications of further abortions. During surgical exploration, a search for mutilated fetus should be done [139] with definitive curettage if necessary. Perioperative

antibiotics should be administered as in bowel obstruction in general. During follow-up, ultrasonogram of the uterus and βHCG measurement should be performed to eliminate the possibility of retained products of conception [139].

7.3.8 Prognosis

Worldwide, there are 30–50 million induced abortions that result in the death of 80,000–110,000 women of which an estimated 34,000 are in sub-Saharan Africa [125]. Appropriately timed surgical intervention in complicated uterine perforation is crucial to decrease morbidity and mortality rates. Available data in a study by Jhobta et al. show the survival rate of 93 % (two deaths) during the whole century (1907–2012). One patient died due to massive small bowel necrosis where resection with high jejunostomy was made. The girl left the hospital against medical advice for social and family reasons and died [109]. Assumption is that high jejunal stoma with high output caused dehydration and electrolyte imbalance, finally causing death. The second patient had additional sigmoid colon laceration treated during initial operation with resection and anastomosis. The authors write that the patient became febrile and deteriorated on the fourth postoperative day. Assumption is that dehiscence of colorectal anastomosis with diffuse stercoral peritonitis and subsequent septic shock with multiorgan failure ensued [129]. The results of this study show that excellent prognosis is present throughout the whole century due to several reasons:

1. The population of these patients is young, mostly without comorbidities, and can compensate significant pathophysiologic stress such as small bowel obstruction and/or perforation sometimes accompanied by various degrees of hemorrhage. Such conditions could be deleterious for old people especially with significant comorbidities.
2. Most patients present with evident small bowel obstruction either clinically as vaginal evisceration (60 %) or during first 48 h with small bowel in uterine wall (23 %) mostly diagnosed quickly and accurately with pelvic sonography. Small bowel obstruction in remaining patients was confirmed with plain abdominal X-ray before perforation ensued.
3. Complications of small bowel resection in young, healthy patients without advanced atherosclerosis are rare and even long segmental resections have good long-term prognosis.

7.4 Adhesions

7.4.1 Incidence

Adhesions are associated with more than 60 % of intestinal obstruction in pregnancy [150, 151]. In one study, 77 % of the 66 cases presented with known obstruction due to adhesions from previous abdominal surgery, pelvic surgery, or pelvic inflammatory conditions [6]. Incidence of intestinal obstruction caused by adhesions during stages of pregnancy is [69]:

- First trimester: 6 %
- Second trimester: 27 %
- Third trimester: 44 %
- Postpartum: 21 %

7.4.2 Pathophysiology

7.4.2.1 Uterine Enlargement During Pregnancy

As the uterine fundus arises out of the pelvis, intraperitoneal adhesions may produce initially a partial bowel obstruction, which may become complete as the uterine bulk increases [152].

7.4.2.2 Adhesive Small Bowel Obstruction After Appendectomy

Around 50 % of patients with adhesive obstruction had previous appendectomy. Obstruction most commonly appears during the first pregnancy after surgery. The none of these cases reports was the description of neither the technique of appendectomy nor the stage of appendiceal inflammation. In three cases, appendectomy was performed more than 9 years before presentation of adhesive obstruction in pregnancy. In two patients, terminal ileum was the site of

obstruction [153, 154]. The third case is obstruction of the long loop of the sigmoid colon [155].

7.4.3 Diagnosis

Diagnostic workup is the same as for every patient presenting with symptoms and signs of bowel obstruction no matter the cause and is described previously (see Sect. 7.1).

7.4.4 Therapy

7.4.4.1 Conservative (Medical Treatment)

Unlike other causes of obstruction, if adhesions of small bowel are suspected and other causes excluded the conservative therapy could be initiated. It consists of bowel rest, intravenous fluids, and NG tube placement. In nonpregnant patients, plain abdominal X-ray is indicated every 6–12 h, but in pregnant population, clinical evaluation every 6 h can indicate further diagnostic workup.

7.4.4.2 Surgical Treatment

Emergent surgical treatment is indicated if:

- Clinical deterioration
- Unsuccessful conservative therapy (48 h)
- Strangulation suspected initially or during conservative treatment (clinical deterioration, elevation of WBC and CRP)

7.5 Small Bowel Volvulus and Congenital Intestinal Malrotation

7.5.1 Small Bowel Volvulus

7.5.1.1 Incidence

Primary small bowel volvulus occurs without any predisposing cause. It is rare in Western countries but common in Africa, India, Nepal, and the Middle East [156–158]. Although volvulus is a very rare condition in pregnancy, most cases of obstruction secondary to small bowel volvulus occur in the third trimester or puerperium [6, 156, 159, 160], but a case in first trimester was described when 4 days after the operation, sonography revealed a dead fetus with 10 weeks age [161].

7.5.1.2 Pathophysiology

Volvulus is a consequence of the intestine rotating about its mesenteric axis, eventually resulting in a closed-loop obstruction. The major sites of volvulus are the sigmoid colon and the small bowel [162, 163]. Conditions implicated in the development of volvulus include adhesions, congenital bands, Meckel's diverticulum, and hernias. The uterus enlarges most rapidly between 16 and 20 weeks and again between 32 and 36 weeks, and obstruction occurs most frequently at these times [164, 165].

7.5.1.3 Clinical Presentation

Clinical presentation of small bowel volvulus is due to both the mechanical obstruction and the vascular compromise with resultant ischemic bowel. Initial symptoms are similar to those common in pregnancy, including crampy abdominal pain, nausea, vomiting, and constipation, frequently delaying definitive diagnosis. Classical findings of bowel obstruction in the nonpregnant patient, including constipation, altered bowel sounds, and peritoneal signs, are frequently obscured by the gravid uterus [163–165].

7.5.1.4 Treatment

Treatment is always surgical and type of operation depends on the stage of ischemia caused by volvulus. If the bowel is vital, then the cause of the volvulus is eliminated. If the bowel is necrotic, then it should be resected and decision of performing the anastomosis made.

7.5.1.5 Prognosis

Early diagnosis and management is essential to avoid infarction of bowel. The condition may result in a maternal mortality rate of 6–20 % and a fetal loss in 26–50 % of the cases even with a delay of 24 h [166].

7.5.2 Congenital Intestinal Malrotation

Congenital small bowel malrotation in pregnancy is extremely rare cause of ischemic bowel. There are only a few case reports highlighting this condition in gravid patients [10, 167–169]. The problem with this entity is that volvulus of the complete small bowel could ensue with bowel necrosis which is incompatible with life which was found in case by Scheuermeyer in 27th week of pregnancy [170]. Even a more complex case was described with volvulus of the small intestine, cecum, and ascending colon [171]. Therefore, emergency laparotomy is indicated if the condition is suspected.

7.6 Carcinoma of the Colon and Rectum

7.6.1 General Considerations of Colorectal Cancer in Pregnancy

Due to the extremely rare occurrence of emergent presentation of colorectal cancer (CRC) in pregnancy, here is the current knowledge about CRC in pregnancy in general. It could help in decision making in elective and emergent settings.

7.6.1.1 Incidence

CRC is common in elderly population, but 2–6 % of tumors are found before the age of 40 [172]. However, CRC presenting in pregnancy is an uncommon disease with a reported incidence of 0.002 %. Others reported 0.028/1,000 births [173] or 1/13,000 pregnancies in 1992 [174]. Cruveilhier reported the first case of rectal carcinoma in pregnancy in 1842 [175]. The first case of colon cancer above peritoneal reflection was reported by Evers in 1928 [176]. Up to 1993, Shioda et al. found 25 such cases [177]. Other study from the same year with mailed questionnaire of the *American Society of Colon and Rectal Surgeons* and review of the literature included 41 cases of women with large bowel cancer who presented during pregnancy or the immediate postpartum period. The mean age at presentation was 31 years (range, 16–41 years). Tumor distribution was as follows: right colon (7.3 %), transverse colon (4.9 %), left colon (4.9 %), sigmoid colon (19.5 %), and rectum (63 %). Dukes' stage at presentation was A, 0 %; B, 39 %; C, 41 %; and D, 15 % (two patients were unstaged). Up to 2005, there have been over 275 cases in the literature; most of these have been case reports [178–180]. In the study by Dahling et al. of 134 patients, 103 were diagnosed postpartum, whereas only 28 cases were diagnosed before delivery and three cases at delivery [173]. This study shows that parity is neither positively or negatively associated with CRC.

7.6.1.2 Carcinogenesis and Predisposing Factors

The carcinogenesis of CRC is not fully understood. The hypothesis that estrogen receptors (ER) and progesterone receptors (PgR) may be involved in the pathogenesis of CRC during pregnancy has been studied. Several studies have reported the presence of ERs in colon cancer [181–183]. It has been suggested that as many as 20–54 % of colon tumors have ERs [184]. Studies have also demonstrated the presence of PgRs in colon cancer [185] with up to 42.8 % of colon tumors being PgR + [186]. These findings suggest that increased levels of estrogen and progesterone found in pregnant women could stimulate the growth of CRCs that have these receptors. Stimulation of these receptors could also help to explain the advanced stages found in the majority of patients at the time of diagnosis. However, it is important to note that the data to support the role of these receptors in the pathogenesis of CRC are scarce and that conflicting data exist in the literature regarding ERs and PgRs in CRC. In a study by Slattery et al., only one PgR + tumor and no ER + tumors were found in an analysis of 156 women diagnosed with CRC [184]. The role of Cox-2 enzymes in CRC and pregnancy has also been studied and was that these enzymes are vital for each stage of pregnancy [187]. Cox-2 products appear to be essential for the early sequences of

pregnancy, including ovulation, fertilization, implantation, and decidualization [188]. The early events of pregnancy and the pathogenesis of tumor spread have important similarities: both events require cells to migrate from the site of origin to another site at which these cells must establish new vasculature to grow and mature [188]. Cox-2 enzymes are found in high levels in many CRC cells [189]. Studies have also demonstrated that Cox-2 inhibitors such as aspirin can alter the course of colon cancer [190]. Increased levels of Cox-2 enzymes in pregnant patients could play a role in the pathogenesis and prognosis of CRC in pregnancy. However, no studies have been performed to date to explore this potential relationship [179].

CRC is a rare event in young patients. This implies that colon cancer in pregnancy among this population of patients is likely caused by the presence of predisposing factors compared with the general population of patients with colon cancer [191]. Predisposing factors for colon cancer include hereditary nonpolyposis CRC (i.e., Lynch syndrome), familial adenomatous polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, and prolonged history of inflammatory bowel disease [179]. However, these increased-risk groups represent only a small portion of CRCs diagnosed in pregnancy [180]. Girard et al., in a review of 19 pregnant patients, demonstrated that four of 19 patients had one of these strong predisposing factors for colon cancer [192]. The presence of genetic abnormalities is not known. A family history must be recorded in all these patients, and an evaluation by cancer genetic clinics should be considered [179].

In countries fortifying flour with folic acid, a steady decrease in incidence of neural tube defects (NTDs) has been documented, in parallel to the doubling of plasma and RBC folate levels [193]. The main criticism against flour fortification has been that this strategy exposes large segments of the population, such as those who never become pregnant, to levels of folate beyond what may be necessary [194]. During the last decades, in parallel to the reports on a dramatic decrease in rates of NTDs in jurisdictions where fortification took place, concerns have been raised that heightened folate status may increase the risk of cancer in general, with CRC being cited more commonly than others [195]. The results of the largest meta-analyses suggest that there is an inverse association between folate intake and CRC incidence [196, 197]. High folate level decreases the risk by 8–15 % in one study [197] and 19–25 % in the other [196]. Women of reproductive age should not be discouraged from adequate intake of folate based on a wrongly perceived risk of CRC.

7.6.1.3 Clinical Presentation

The most common clinical manifestations of colon cancer include abdominal pain, change in bowel habits, anemia, nausea, vomiting, and rectal bleeding. These symptoms are commonly found in pregnant patients and, as a result, are usually considered by physicians and patients to be the usual manifestations of pregnancy, without an appropriate evaluation [179, 198]. The delay in initiating the workup for the symptoms related to CRC is one of the major contributing factors to the poor prognosis associated with this disease [199]. In general, pregnant women gain weight. However, women can experience weight loss in the first trimester. Pregnancy can obscure weight loss secondary to cancer in second and third trimesters. Rectal bleeding is a common finding during pregnancy and is usually secondary to the high incidence of hemorrhoids among pregnant patients; however, rectal bleeding is a particularly ominous sign and should never be attributed solely to pregnancy itself without a proper evaluation. Nausea and vomiting are very common symptoms of pregnancy, particularly during the first trimester. Nausea or vomiting can occur as a result of synchronous colon cancer, but they are often attributed to pregnancy itself. Constipation is another common complication of pregnancy, which, again, can delay workup for CRC. Abdominal mass constitutes a natural process in pregnancy. Potential palpable masses secondary to colon cancer are often missed secondary to changes of pregnancy. Anemia is a physiological finding in pregnancy. Anemia associated with pregnancy can mask blood loss from cancer.

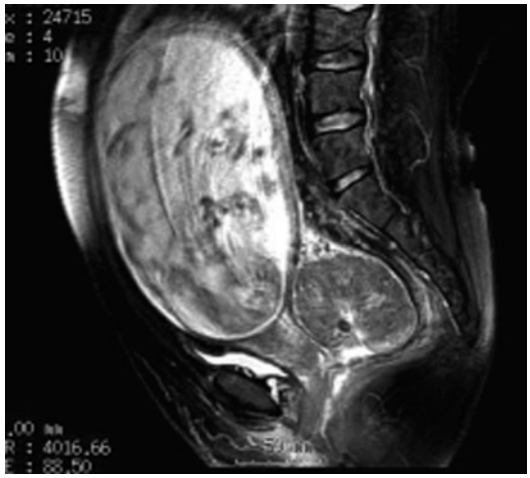

Fig. 7.22 MRI of the pelvis (T2 weighted) showing metastatic left ovarian tumor at 23 weeks' gestation from the primary carcinoma of the sigmoid colon [202]

7.6.1.4 Diagnosis

Ovarian metastatic disease from CRC poses another challenge to the treating physician. The incidence of ovarian metastases from CRC is higher in pregnant (25 %) than in nonpregnant (3–8 %) patients [200–202]. It could mislead the clinician to make the diagnosis of primary ovarian tumor preoperatively. Unfortunately, there are two cases of Krukenberg tumor from the primary colon carcinoma: one was unilateral (Fig. 7.22) and another bilateral (Fig. 7.23). The working diagnosis was external colon obstruction from ovarian tumors, and histopathology revealed primary colon carcinoma.

7.6.1.5 Therapy

Surgical Therapy

Surgery could be performed safely before 20 weeks of gestation when appropriate [204]. After this gestational age, it is recommended that surgery be delayed to have a reasonable maturation of the fetus. Delivery of a viable infant can occur at 32 weeks of gestation if the lungs are properly stimulated to mature. It has been proposed that CRC surgery can be done right after an uncomplicated Cesarean section [198]. Intraoperatively, the patient should be placed in the slight left lateral position to prevent uterine compression of the inferior vena cava and left iliac vein. Maternal blood gases should be monitored, as carbon dioxide insufflation can induce maternal hypercapnia, which can lead to fetal hypercapnia, tachycardia, and hypertension.

When faced with clearly malignant bilateral ovarian tumors, the ideal surgical approach is total hysterectomy, bilateral salpingo-oophorectomy, pelvic and abdominal washings, omentectomy, and para-aortic lymph node biopsies. However, even in the event of bilateral malignant disease, it is possible to omit hysterectomy if the uterus is not grossly involved, thus allowing the preservation of an existing pregnancy.

Conservative or Bridge Therapy

Other approaches to bowel obstruction can be considered. Retrograde insertion of a colonic stent in general population has been widely used for the relief of a colonic obstruction caused by malignancy [205, 206]. Colonic stent decompression can provide palliation in patients with widespread metastatic disease or serve as a bridge to surgery but at the risk of greatly increased maternal and fetal morbidity [6].

Mode of Delivery

The mode of delivery is not affected by cancer, with the exception of a Cesarean section owing to a distal tumor obstructing the birth canal or anterior rectal wall carcinoma. The placenta should be carefully examined for metastases [207]. Adjuvant chemotherapy with 5-fluorouracil (5-FU) is suggested for stage III tumors; however, the risk and benefits should be discussed with the patient [198]. The most serious complications occur when the chemotherapy is given during 3–12 weeks of gestation [208]. In animal models, this agent is highly teratogenic. Mechanisms by which 5-FU may lead to fetal abnormalities include interrupting DNA synthesis and cell development through inhibition of embryonic thymidylate synthase [209]. In several case reports, 5-FU during the first trimester has been associated with spontaneous abortion as well as normal-term births [210–214]. In one case, a patient who had 5-FU administered in high doses over 5 months of the second and third trimesters gave birth to a healthy but small baby [215]. Moreover, no congenital anomalies or other clinically significant adverse effects

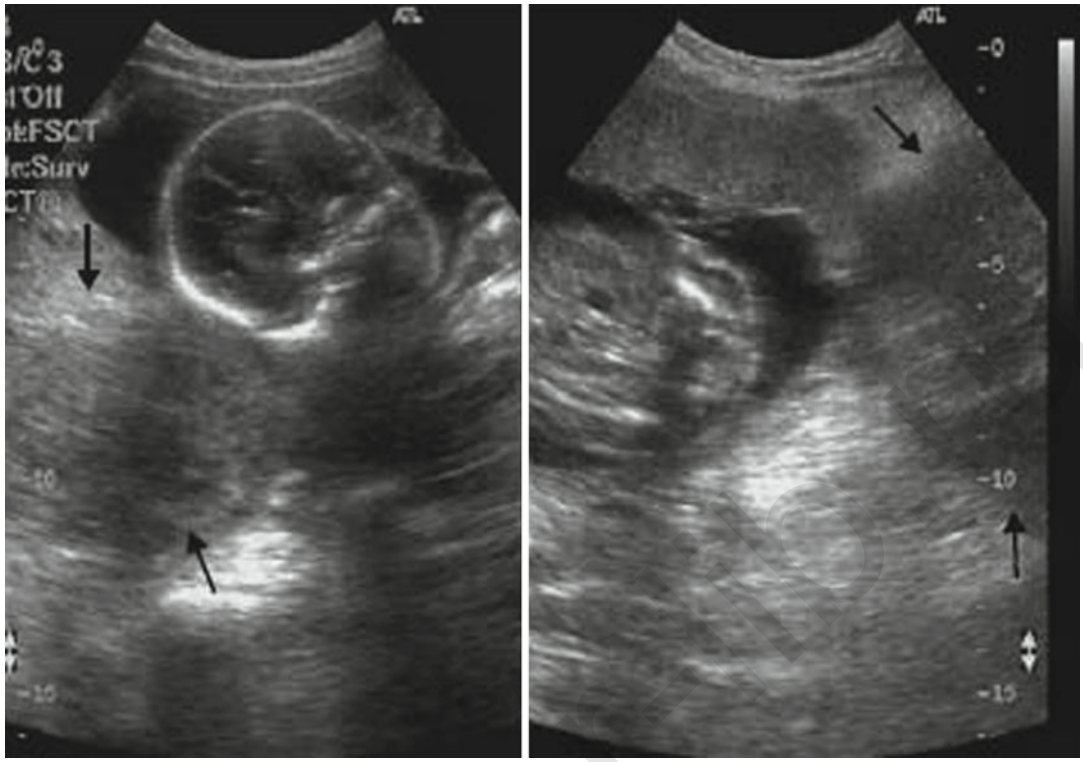

Fig. 7.23 Ultrasonogram showing the fetus and two ovarian masses (*arrows*) [203]

were observed in 40 infants whose mothers were treated for breast cancer during the second and third trimesters of pregnancy with intravenous 5-FU in combination with doxorubicin, cyclophosphamide, and other chemotherapeutic agents [216–218]. Transient cyanosis and jerky movements were reported in a newborn whose mother received 5-FU during the third trimester [219]. There are no reports on the use of 5-FU during lactation. Cisplatin and other platinum-based chemotherapy drugs are also used in CRC, but they are not recommended during pregnancy or breastfeeding [220]. Oxaliplatin has not been studied in pregnant women. However, studies in animals have shown that oxaliplatin causes miscarriages, decreased weight or death of the fetus, and problems with bone formation [221]. Patients should use some kind of birth control while receiving oxaliplatin, and a pregnancy test should be performed before initiation of chemotherapy. It is not known whether this drug passes into breast milk. Irinotecan may cause harm to the fetus when given during pregnancy [222]. No human data are available. Women of childbearing age should use some kind of birth control during treatment with irinotecan. Before administering this agent, the physician must rule out pregnancy. Chemotherapy is safer during the second and third trimester of pregnancy, although there is an increase in the incidence of intrauterine growth retardation and prematurity [223]. Although a few cancer chemotherapy studies have failed to show adverse effects in treatment in the third trimester, the possible neurocognitive effect of chemotherapy cannot be totally excluded because brain development is not completed during pregnancy or even early in life [224]. Adjuvant radiotherapy is used in the management of rectal cancer. Radiation therapy to the pelvis is not recommended during pregnancy because of the potential harm to the fetus. Fetal radiation exposure should be measured by a medical physicist in any radiation during pregnancy [225]. Future fertility should be considered before proceeding with treatment because radiotherapy can cause permanent damage to ovaries

and lead to infertility [226]. If a woman of childbearing age is considering radiotherapy, she must be informed of this possible outcome, and consent must be documented.

7.6.1.6 Prognosis

Maternal Outcome

Pregnant women with CRC generally have a poor prognosis. In a review of 42 patients with CRC above the peritoneal reflection, Chan et al. noted that 56 % (23/42) of these patients died by the time the cases were reported in the literature [227]. Most died within 1 year of being diagnosed, and the median survival for the group was less than 5 months. One patient survived for 3.5 years after bowel resection but had multiple recurrences. No patient with CRC in pregnancy reported in the literature has survived longer than 5 years. No data are available for obstruction CRC in pregnancy because it is extremely rare condition. One case of intussusception of colon carcinoma in pregnancy is described in the separate section (see Sect. 7.7.1). Other study with mailed questionnaire of the *American Society of Colon and Rectal Surgeons* and review of the literature included 41 cases of women with large bowel cancer who presented during pregnancy or the immediate postpartum period. The mean age at presentation was 31 years (range, 16–41 years). Average follow-up was 41 months. Stage for stage, survival was found to be similar to patients with CRC in the general population. Large bowel cancer coexistent with pregnancy presents in a distal distribution (64 % of tumors in the current series and 86 % of those reported in the literature were located in the rectum) and presents at an advanced stage (60 % were stage C or more advanced at the time of diagnosis). While patient survival is poor, it is no different stage for stage from the general population with CRC [178].

The survival of patients with metastasis involvement of the ovaries is poor, in the range of 3–12 months [201]. Prophylactic bilateral salpingo-oophorectomy simultaneous with CRC surgery is recommended by some physicians [228, 229]. However, it is prudent to take into consideration the desire of the patient for future pregnancies. Also, bilateral salpingo-oophorectomy at the time of resection has been linked to an increased incidence of spontaneous abortion, especially if performed during the first trimester [199]. Nesbitt et al. recommend obtaining bilateral wedge biopsies of the ovaries during surgery for pathologic examination of the frozen sections with subsequent removal if the ovaries are involved [199].

Fetal Outcome

There are no reports of adverse fetal outcomes due to the malignancy itself, even in widespread metastatic disease [230]. Metastasis to the placenta was reported once in maternal colorectal malignancy [231]. Although a complete evaluation of the placenta is recommended, there is no evidence to support periodic follow-up of the baby.

Maternal obstetrical outcomes were good overall, though pregnancy-associated cases of CRC did have higher rates of Cesarean sections and preterm deliveries. Preterm deliveries were not only secondary to scheduled inductions and Cesarean sections, likely related to the woman's cancer diagnosis, but also to higher rates of preterm labor. Authors also noted that pregnant women with CRC had larger number of major puerperal infections. It is possible that women with CRC are more prone to infections that may be subclinical before delivery but predispose them to have preterm labor. This could be secondary to malignancy-related immune suppression or some other unknown cause. Another explanation is that CRC initiates an inflammatory reaction that then starts the preterm labor cascade secondary to the close proximity to the uterus. Despite the higher rates of preterm delivery, neonatal outcomes were excellent, which is in agreement with several other studies [172, 232, 233]. When CRC is diagnosed before delivery, several reports recommend Cesarean section after documentation of fetal lung maturity with concomitant tumor resection [173, 174]. Women with pregnancy-associated CRC were less likely to receive chemotherapy, but more likely to receive radiation than age-matched, nonpregnant women though the differences in rates of

adjuvant radiotherapy were not statistically significant [173]. Because most women were diagnosed after delivery, this phenomenon cannot be fully explained by a concern for the fetus, unless it represents a breastfeeding concern. This finding is even more surprising given that authors did not find a difference in stage of disease between the populations. Study does not elaborate on timing of radiation and chemotherapy relative to surgery, and so no conclusions can be made. Prognosis in CRC is largely based on the stage at diagnosis. The literature is predominated by the belief that pregnant women with CRC are diagnosed at a more advanced stage secondary to delay in diagnosis, and this leads a worse prognosis [232, 234]. However, study by Dahling et al. shows that stage at initial diagnosis in women with pregnancy-associated CRC is no different than the age-matched, nonpregnant population of women with CRC [173]. Another controversy in the literature regards histological subtype, with some reports of pregnant women having higher rates of an aggressive, mucinous subtype [232]. Report by Dahling et al. shows similar histological subtypes between the two populations of women. Ultimately, survival was no different among women with pregnancy-associated CRC and nonpregnant women with CRC [173]. This is in agreement with other reports [174, 178, 232, 234, 235]. Although differences exist between the biology and clinical behavior of anal and colon cancers, all were analyzed together. A separate analysis done after omission of the ten patients with anal cancer yielded perinatal and cancer outcomes virtually identical to those of the group as a whole [173].

7.7 Stomal Obstruction

Various forms of stomal obstruction occur in general population. These forms include stomal prolapse, stomal stenosis, obstruction due to surrounding tumor progression, and intussusception. These causes are extremely rare in pregnant patients due to the rarity of stomas in this population and because most of these stomas are temporary.

7.7.1 Intussusception

7.7.1.1 Incidence

Intussusception in stoma is rare [236–238], and only three cases have been reported previously in the literature reviewed since 1950 [239–241].

7.7.1.2 Risk Factors

There are too few cases for analysis but in one case there was a 21 weeks twin pregnancy. She had had total colectomy and ileostomy 8 years previously for ulcerative colitis. Ileostomy was refashioned three times for parastomal hernia, parastomal abscess, and retraction [241]. In cases with intussusception in ileostomy in a pregnant woman described by Priest et al. [239] and with loop colostomy described by Keane and Whittaker [240], there were no etiological factors.

7.7.1.3 Clinical Presentation

Clinical presentation of intestinal obstruction is the same as for any other cause (see Sect. 7.1).

7.7.1.4 Diagnosis

It is important to stress that in a patient with a stoma it should be evaluated for possible local obstruction. The diagnosis is easily confused with prolapse [240], which is easily reducible and for which local revision is usually adequate [236–238]. If the stoma is the cause of obstruction ionizing diagnostic modalities could be excluded from the diagnostic algorithm.

7.7.1.5 Therapy

Surgical management was different in all three cases. In the case described by Priest et al., the patient was managed by revision of her ileostomy [239] and in the case of Keane and Whittaker by resection and refashioning of the colostomy [240]. In the third case, at laparotomy, herniation of one wall of the ileum through a defect in the abdominal wall next to the stoma was found. This part of the ileum went on to prolapse through the spout and was followed by more ileum to form the intussusceptum. Reduction was achieved by gentle traction, the lateral space to the stoma was closed, and the ileum was attached to the anterior abdominal wall with absorbable sutures [241].

7.7.1.6 Prognosis

In all three cases, the mothers survived [239–241]. In the case by Adedeji and McAdam [241], both twins survived and were normal after Cesarean section in 35th week when fetal distress occurred.

7.7.2 Stomal Obstruction

7.7.2.1 Incidence

In one study, 10 % of patients with ileostomies had an intestinal obstruction during pregnancy. Increased abdominal pressure may occasionally cause a stomal ileal prolapse. This usually occurs in patients who have had an ileostomy placed less than a year before becoming pregnant [15].

7.7.2.2 Diagnosis

Plain abdominal X-rays lack sensitivity and specificity in the gravid patient, while abdominal CT scanning exposes the fetus to ionizing radiation. Although no definitive study regarding absolute safety has been performed (or indeed will probably ever be), abdominal MRI is increasingly used [242, 243].

7.7.2.3 Treatment and Prognosis

Gestational intestinal obstruction has previously been associated with very significant maternal and fetal mortality and morbidity, and so the prevailing consensus in the (limited) literature strongly favors aggressive management by urgent surgical intervention [242, 244].

7.8 Sigmoid Volvulus

7.8.1 Incidence

Sigmoid volvulus is the most common cause of bowel obstruction complicating pregnancy, accounting for 25–44 % of published cases [69, 162, 245, 246]. In endemic regions for Chagas disease, in South America, digestive manifestations are common and sigmoid volvulus is a possible complication during pregnancy [247].

Since the initial report by Braun in 1885, it is estimated that around 84 cases of sigmoid volvulus have been reported occurring in the pregnancy and puerperium. Lambert [248] reported 29 cases of sigmoid volvulus before 1931, followed by another 12 cases reported by Kohn et al. [249] between 1931 and 1944. Subsequently, all the previously reported cases were reviewed by Harer et al. [56] in 1958, who reported an additional 11 cases between 1994 and 1958. Later on, Lazaro et al. [250] compiled another 13 cases occurring between 1558 and 1969. Another 19 cases have identified reported till 2009 and one from 2012 added [251]. In the study by Ballantyne et al., sigmoid volvulus in pregnancy accounted for 2 % of all sigmoid volvulus in the Mayo Clinic between 1960 and 1980 [162].

7.8.2 Pathophysiology

Pregnancy itself is considered to be the precipitating factor for sigmoid volvulus. The occurrence of sigmoid volvulus in pregnancy is due to displacement, compression, and partial obstruction of a redundant or abnormally elongated sigmoid colon by the gravid uterus [56]. This could probably explain the increased incidence of sigmoid volvulus in the third trimester [6]. Sigmoid volvulus is most frequent between 22 and 38 weeks of gestation [252]. Despite this higher propensity in the third trimester, there have been reports of this complication developing in the early pregnancy as well as the puerperium [56, 253–255]. An increase in uterine volume is implicated in the formation of the volvulus [256].

7.8.3 Clinical Presentation

The diagnosis of sigmoid volvulus is suspected when a pregnant female presents with a clinical triad of abdominal pain, distention, and absolute constipation. The average time from the onset of obstructive symptoms until presentation has been reported to be 48 h [6]. This is largely because pregnancy itself masks the clinical picture since abdominal pain, nausea, and leukocytosis can occur in an otherwise normal course of pregnancy [257]. In the review of the last 20 cases, the mean delay between the onset of symptoms and

presentation was 2 days, with a range from few hours to as many as 6 days. Six patients presented more than 48 h after the onset of symptoms [251]. Harer et al. [56] also noted similar delay in presentation in their review and concluded that such a delay in diagnosis and surgical intervention had a significant impact on the ultimate outcome of the mother and fetus.

7.8.4 Diagnosis

Plain abdominal X-ray is often necessary for the diagnosis of volvulus (Fig. 7.24). It involves a radiation dose of 0.001 Gy, which is a dose significantly lower than the doses with the risk of congenital malformation.

7.8.5 Therapy

7.8.5.1 Surgical Treatment

The management of volvulus with or without perforation in pregnant women is pretty much similar to that of nonpregnant women. The aim of surgical treatment is to remove the obstruction without a risk of recurrence. The basis of therapy is early surgical intervention [259]. In the absence of peritonitis and during the second trimester of gestation, Utpal and Kamal preferred detorsion by minilaparotomy [260]. Such algorithm was found in 1950 to shorten the operation while the sigmoid resection with anastomosis was performed after puerperium [261]. Diallo et al. justified the choice of intestinal resection by elimination of the risk of recurrence and reduction of morbidity and mortality [262]. Given the impossibility of nonoperative detorsion in Mali and the high risk of recurrence (13.5 % in 30 days after intervention) [262], the recommendation is to perform a sigmoidectomy with anastomosis. This approach has also been recommended in the second trimester of gestation by other authors [263]. In the third trimester, if sufficient intestinal exposure cannot be obtained due to the enlarged uterus, a Cesarean section must be carried out [259]. After detorsion, the deflated loop could be on the left side of the abdomen and should be replaced without even treating the uterus. This could be done by slipping the loop of bowel over the fundus of the uterus (Fig. 7.25). Probably, compression of the uterus could be contributing factor in obstruction when volvulus is partial.

The entire bowel should be examined for other areas of obstruction. Intestinal viability should be assessed cautiously and segmental resection

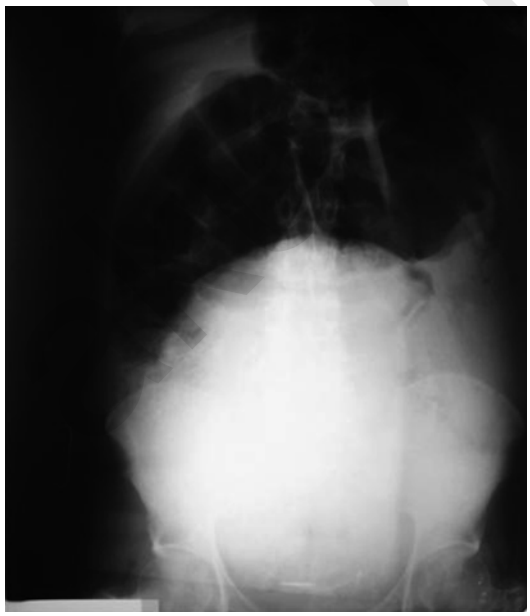

Fig. 7.24 Plain abdominal radiograph showing sigmoid volvulus in pregnancy [258]. The characteristics of the sigmoid volvulus are distorted due to the enlarged uterus

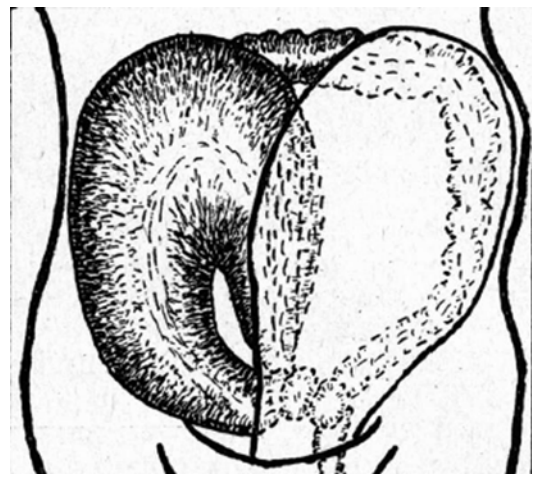

Fig. 7.25 Diagram showing relative positions of the uterus on the right and sigmoid volvulus on the left and behind the uterus [261]

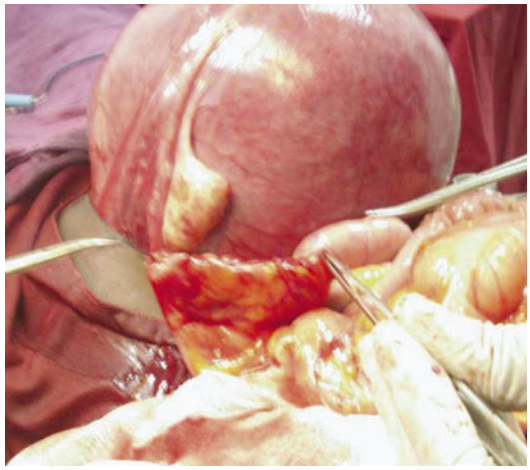

Fig. 7.26 Sigmoid volvulus in pregnancy, followed by resection and primary anastomosis [258]

with or without anastomosis is often necessary (Fig. 7.26) [259].

7.8.5.2 Conservative Treatment

There is one case of successful decompression by Malecot catheter during pregnancy of a patient with recurrent sigmoid volvulus [264].

7.8.6 Prognosis

The maternal and fetal outcome in sigmoid volvulus has been directly related to the degree of bowel ischemia and subsequent systemic sepsis. In analysis of recent 20 cases, maternal and fetal mortality were 20 and 40 %, respectively, including one ectopic pregnancy. It is important to note that all the maternal deaths occurred in the group of patients where delay in presentation and surgical intervention was more than 2 days [253, 265, 266]. Similarly, five fetal deaths were seen in patients who presented after 48 h of onset of symptoms, as compared to two fetal deaths in patients presenting early in the course of the disease. This observation highlights the fact that high index of clinical suspicion is vital in cases of intestinal obstruction in pregnant patients. This fact needs to be emphasized among the general practitioners and community obstetricians primarily responsible for taking care of these patients especially those treating their constipation.

7.9 Cecal Volvulus

During pregnancy and the puerperium there should not be much delay in performing laparotomy in doubtful cases.

Spence JH, 1937

7.9.1 General Considerations

Volvulus of the cecum is torsion of the bowel around its own mesentery that results in a closed-loop obstruction. Cecal volvulus can occur in 11–25 % of the population who has hypermobility of the proximal colon because of inadequate lateral peritoneal fixation during development [1, 8–11]. Furthermore, the distal ascending colon must be fixed, resulting in a pivot point around which the cecal rotation may occur. While this point of fixation is typically the normal congenital peritoneal attachments, other possibilities include postoperative adhesions or an abdominal mass. In pregnancy, the enlarged uterus may displace any redundant or abnormally mobile cecum out of the pelvis. Partial obstruction may occur from uterine pressure or from kinking of the colon at a fixed point. The ensuing distension raises the colon even higher, producing torsion at this fixed point [56, 267]. Fixed cecum due to adhesion from the previous operations is a predisposing factor for volvulus [268].

7.9.2 History

The first published case found was by White in 1914. The 26-year-old in her 33-week second pregnancy was constipated for 6 years after the drainage of the abscess of appendiceal origin with the incisional hernia (presumably midline incision). The patient then expelled the stillbirth, and after several days indication for the operation was made. The cecal and ascending colon gangrene due to volvulus was found. Resection was performed

but the patient died [269]. Basden in 1934 reported the case of a woman in labor in whom laparotomy (and Cesarean section) was done for a suspected intra-abdominal condition and a volvulus of the cecum was found [270]. Spence in 1937 quoted a case of volvulus shortly after delivery in which too much attention was paid to the associated uterine infection. He stated that "during pregnancy and the puerperium there should not be much delay in performing laparotomy in doubtful cases" [271]. Another case from 1941 was of a patient that presented 17 h after delivering stillborn by forceps. During extensive diagnostic workup, the patient died and at necropsy volvulus of the cecum and part of ascending colon was found [272]. Kohn et al., in 1944, reviewed the literature and reported 79 cases of volvulus in pregnancy, 19 of which were of the right colon [249].

7.9.3 Incidence

Cecal volvulus occurs approximately 1/500,000 pregnancies but may be as low as 1/1,000,000 [273]. In the study by Ballantyne et al., cecal volvulus in pregnancy accounted for 2 % of all sigmoid volvulus in the Mayo Clinic between 1960 and 1980 [162].

7.9.4 Clinical Presentation

The symptoms and findings at clinical examination are often vague and indistinguishable from the usual symptoms attributed to late pregnancy or other causes of an acute abdomen. In a survey of volvulus complicating pregnancy, the condition was diagnosed before laparotomy in only 25 % of the cases [56, 267]. In one case, the diagnosis was more difficult because a 38-year-old woman, gravida 3, para 2, presented at 31 weeks of gestation. The patient had undergone a sigmoid colectomy for Dukes' B adenocarcinoma 11 years previously. She had a subsequent balloon dilatation of a colonic anastomotic stenosis but had otherwise recovered well and was free of recurrence [268].

7.9.5 Differential Diagnosis

In pregnancy, cecal volvulus may be mistaken for placental abruption, degenerating fibroids, a ruptured uterus, hyperemesis, and torsion of the ovary, extrauterine pregnancy, acute polyhydramnios, cholecystitis, appendicitis, urinary tract infections with or without urolithiaisis, and other causes of bowel obstruction [274, 275].

7.9.6 Diagnosis

Classically, cecal volvulus presents as bowel obstruction, but often the signs and symptoms are vague. Abdominal radiographs usually demonstrate obstruction, but the findings are not always specific for cecal volvulus (Figs. 7.27 and 7.28). The diagnosis may be obscured if the closed loop is filled with fluid, oriented in an anteroposterior plane, or overlain by loops of air-distended bowel [276]. The intermittent abdominal pain may be misinterpreted as uterine contractions, and emergency Cesarean section for intestinal volvulus has been described [267].

When CT is considered appropriate, a senior radiologist should always be involved in the decision-making process to avoid overutilization of a potentially harmful test (Fig. 7.29). Radiology

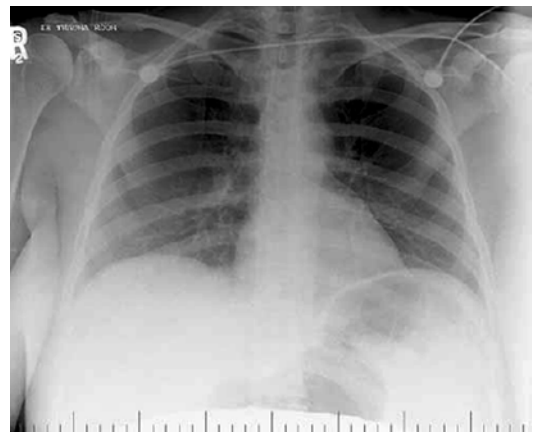

Fig. 7.27 Erect chest radiograph showing dilated air-filled bowel loops under the left hemidiaphragm. Shielding of the lower abdomen is present [268]

departments should have specific low-dose CT protocols in place for imaging the acute abdomen in pregnancy so as to avoid confusion when such cases arise. MRI is increasingly used in pregnant patients. MRI has been used extensively in the characterization and staging of neoplastic disease in pregnant women, but its usefulness in the evaluation of the acute abdomen is not yet clear [277]. Abdominal MRI has been shown to be accurate for the diagnosis of acute appendicitis [278, 279] (see Chap. 3) and has been used in the setting of pregnancy [280]. However, this has not yet been thoroughly evaluated. Abdominal MRI may potentially be of benefit in demonstrating the site of transition in bowel obstruction and identifying areas of inflammation, abscess formation, or hemorrhage within the abdomen and pelvis [281].

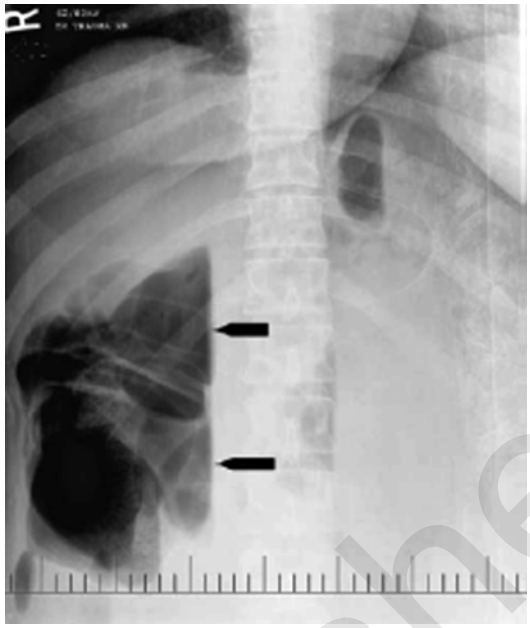

Fig. 7.28 Right lateral decubitus radiograph showing dilated loops of bowel with air-fluid levels (*arrows*) [268]

Surgical options in the treatment of cecal volvulus include colonic detorsion open or laparoscopic [282] with or without appendectomy, colonic detorsion and either cecopexy or cecostomy, and right hemicolectomy. Evidence from several retrospective studies in general and pregnant population suggests that recurrence of cecal volvulus with either detorsion, cecopexy, or cecostomy is unacceptably high; thus, right hemicolectomy is the treatment of choice for this disease [275, 283]. In pregnancy, resection of the hypermobile cecum is justified to avoid recurrence.

7.9.7 Prognosis

7.9.7.1 Maternal and Fetal Outcome

It is obvious (see Sect. 7.9.2) that in the early twentieth century, up to 1940, due to complex clinical picture and limited diagnostic modalities,

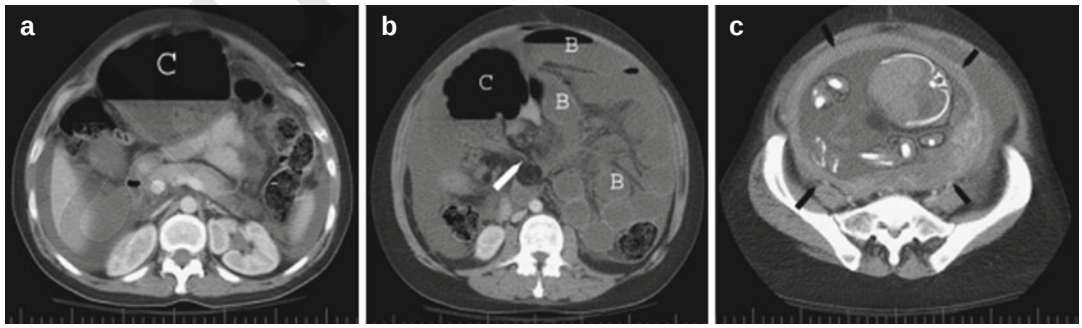

Fig. 7.29 (**a**) Axial dynamic CT showing a dilated cecum with an air/feces level in the mid-upper abdomen; (**b**) The dilated cecum (*C*) shows progressive tapering terminating at the site of torsion (*white arrow*) resulting in the appearance of a bird's beak. Dilated fluid-filled loops of small bowel are shown (*B*). The lack of normal mural enhancement of the cecum on CT, compared with the normally enhancing small bowel loops, is suggestive of ischemia. The cecum was subsequently found to be necrotic at surgery. (**c**) Axial views of the *lower* abdomen show the gravid uterus (*black arrows*) [268]

the prognosis for mother and the newborn was extremely poor.

7.10 Incarcerated Internal Hernia

7.10.1 Post-Bariatric Surgery

7.10.1.1 Introduction

During the last two decades, there has been a dramatic increase in the number of bariatric surgeries performed for the management of morbid obesity [284], with Roux-en-Y gastric bypass (RYGB) comprising the most frequent such surgery performed in the United States [285, 286]. Laparoscopic RYGB is becoming one of the most commonly performed weight loss surgeries in the United States, especially in females of childbearing age. Weight loss is likely to reduce infertility and increase sexual activity, leading to increase pregnancy rates in such females. The health risks experienced by obese women during pregnancy can be reduced by the weight loss induced by bariatric surgery [287–289], but these patients are at risk of bariatric surgical complications during their pregnancies. Women who have undergone Roux-en-Y gastric bypass for morbid obesity are at risk of internal hernias, intussusception, and small bowel obstruction during pregnancy, which can lead to maternal and/or fetal death [290]. The most common site of herniation following laparoscopic RYGB is through a surgical defect in the transverse mesocolon, which is created when using a retrocolic approach in forming the anastomosis between the Roux limb and gastric pouch. Although some surgeons may opt to use an antecolic approach to avoid the creation of such a defect, it remains possible for small bowel to herniate through a surgical defect in the small bowel mesentery or through a defect between the Roux limb mesentery and the transverse mesocolon, constituting a so-called Petersen's hernia (Fig. 7.30) [292].

Although an internal hernia in this setting is challenging to diagnose clinically given the

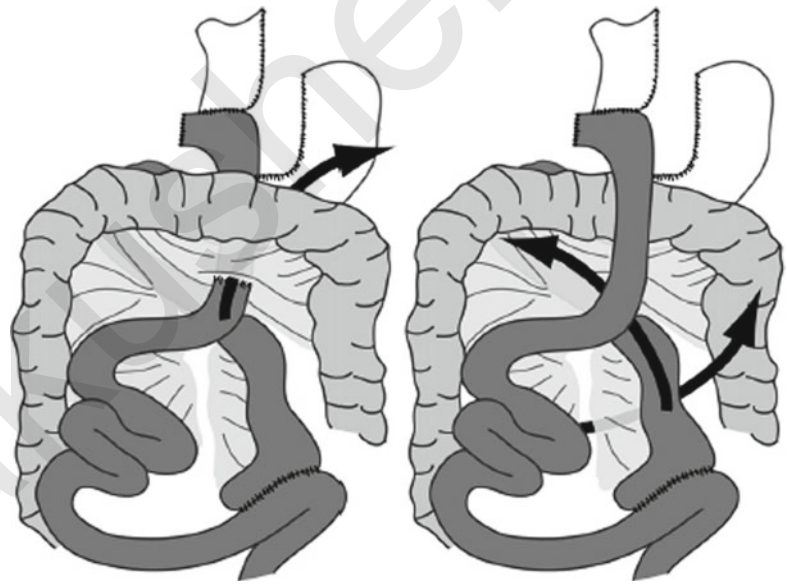

Fig. 7.30 Diagram of the internal hernias that may occur following laparoscopic RYGB. The hernia through the transverse mesocolon defect is the most common hernia that occurs following laparoscopic RYGB but is only possible when a retrocolic approach is used. When an antecolic approach is used, it is possible for small bowel to herniate through the space between the Roux limb mesentery and the transverse mesocolon (Petersen's hernia) or through the surgically created small bowel mesenteric defect. Note that these later two hernias may uncommonly occur in the setting of a retrocolic approach as well [291]

nonspecific and often subtle presentation, a delay in diagnosis and operative treatment may result in dire consequences, including bowel incarceration, ischemia, gangrene, sepsis, and possibly death [285, 293, 294]. There has been increasing awareness by the radiology community of the risk of internal hernia following gastric bypass surgery, as well as of the critical nature of establishing the diagnosis, with numerous recent studies in the radiology literature demonstrating the ability of abdominal CT to diagnose an internal hernia following RYGB [284, 295–298]. A number of recent reports have described internal hernia following RYGB that occurred in a female patient during pregnancy. Indeed, over 80 % of gastric bypass surgeries in the United States are performed in female patients [299], frequently of childbearing age [286, 294]. The significant weight loss that results from the surgery has been found to improve fertility and increase sexual activity, such that pregnancy commonly occurs in patients with a history of RYGB [286, 290, 294, 300].

7.10.1.2 Incidence

Internal hernia has been estimated to occur in up to 5 % of patients following laparoscopic RYGB for morbid obesity [301]. This rate is higher than when this surgery is performed using an open approach, attributed to greater adhesion formation with the open approach that serves to tether and immobilize small bowel loops, preventing their passage through surgically created mesenteric defects [284, 294, 300]. Modifications of the initial bypass procedure to lower the risk of subsequent internal hernia are not fully effective in this aim. For instance, although it has become common to suture all mesenteric defects at the time of initial surgery, the rapid weight loss that occurs postoperatively predisposes to a widening of suture lines and reopening of these defects [285, 286, 300–302].

In 2004, Moore et al. provided the first report of a transmesenteric internal hernia following RYGB occurring in a pregnant patient [290]. The diagnosis was delayed resulting in extensive bowel infarction by the time of eventual emergency laparotomy. The mother and fetus ultimately died. Following this initial case, nine further reports have been identified representing a total of 11 additional patients with internal hernia following RYGB in pregnant patients [285, 286, 293, 294, 299, 300, 303–306]. It is suggested in these reports that pregnancy may contribute to the development of internal hernia secondary to increased abdominal pressure and superior displacement of small bowel loops by the enlarged gravid uterus [285, 286, 294, 300, 303].

The maternal age was in the range of 23–41 years. There was a wide spectrum of intervals between RYGB and the time of internal hernia, ranging from 6 months to 9 years [285, 286, 290, 294]. The possibility of developing an internal hernia following gastric bypass surgery is a lifelong risk [286]. It is notable that almost 50 % of the cases [285, 294, 303–305] occurred within a year of RYGB, in view of the recommendation that women avoid pregnancy for at least 1 year following the procedure to allow for complete wound healing and stabilization of weight [285, 286, 294]. Petersen's hernia occurred in four patients [293, 296, 298, 300], and mostly it occurs in the third trimester and equally in the first and second trimesters.

7.10.1.3 Clinical Presentation

One of the most important aspects in the long-term postoperative care of gastric bypass patients is the prompt diagnosis and treatment of the patient who presents with abdominal pain and obstructive symptoms. In patients who have undergone gastric bypass for morbid obesity, internal hernias of the small bowel, with or without bowel obstruction, can develop and can be catastrophic. Patients can present with severe epigastric pain or periumbilcal pain, initially cramping, and seek to find a position of comfort, either leaning forward or on their side. Patients typically have nausea and retching. The laboratory evaluation is often relatively normal at presentation; this can delay appropriate care if physicians are not experienced in the care of these patients. Plain abdominal X-rays often do not show typical signs of obstruction such as air-fluid levels or dilated loops of bowel, and the findings can be misleading.

Once internal hernias occur, the obstructed afferent limb of duodenum presents no typical

symptomatology suggestive of intestine obstruction [305]; therefore, progression from obstruction to strangulation and ischemia develop. Laboratory findings provide no help in differentiation. Instead, the impression could initially be the diagnosis of conditions such as gastritis, perforation of peptic ulcer, or acute pancreatitis.

7.10.1.4 Diagnosis

In six of 12 (50 %) reports [286, 294, 299, 300, 303], the CT appearance of the internal hernia is demonstrated. In an additional three reports, the CT findings assisted in the diagnosis [285, 305]. The CT findings noted in these cases match the characteristic CT findings of internal hernia following RYGB described in the radiology literature, including an abnormal cluster of small bowel loops and displacement, engorgement, and stretching of the mesenteric vessels [295, 307]. Four of the articles maintain that CT should be obtained promptly, even in the pregnant patient, given increased recognition of the appearance of internal hernia using this method [286, 290, 299, 300].

Abdominal CT scan with oral and intravenous contrast is the best radiological tool for evaluation in gastric bypass patients who present with obstructive symptoms of internal hernias. Radiologists with little experience in the care of these patients can miss the subtle signs of an internal hernia without obvious obstruction. The interpretation of the CT scan by an experienced bariatric surgeon and radiologist experienced in bariatric patients can often make the diagnosis of altered anatomy of an internal hernia [284, 308]. The risk of radiological imaging of the pregnant patient using CT is a major concern, but the benefit is these scenarios need to be considered to avoid catastrophe [309]. The policy for gastric bypass patients presenting with obstructive symptoms of internal hernia typically includes rapid evaluation by abdominal CT scan; however, we have a low threshold to proceed to diagnostic laparoscopy on the basis of clinical symptoms alone.

The various findings identified on MRI in this case match the previously reported CT findings of an internal hernia [295, 297, 298, 302, 307, 310]. It is noted that the mesenteric vessels were not optimally assessed as intravenous gadolinium chelate was not administered; however, such an assessment was not ultimately required for making the diagnosis in this particular case. Previous reports have shown the utility of MRI in the pregnant patient for diagnosing other small bowel abnormalities, including obstruction from postoperative adhesions [311] and ventral hernia [312]. It seems reasonable that MRI could have utility in establishing the diagnosis of an internal hernia in future patients with a similar operative history and presentation. However, MRI cannot replace CT for this diagnosis in all cases. For instance, the only suggestive findings in some cases may involve changes in the mesenteric vasculature, which would not be optimally assessed by unenhanced MRI (Fig. 7.31). Furthermore, MRI may not be available on an emergent basis in all institutions. CT remains an option in cases in which MRI cannot be performed or in which the diagnosis remains equivocal following MRI. Based upon this report, MRI should at least be considered during the evaluation of a pregnant patient with a history of RYGB who presents with abdominal pain, as this approach may enable a confident diagnosis without the use of ionizing radiation [291].

7.10.1.5 Therapy

Treatment depends on the vitality of the bowel. If gangrenous changes are present, then segmental resection with anastomosis is indicated (Fig. 7.32). Since the three cases (27 %) were diagnosed in the third trimester and had exploratory surgeries performed within 2 days of admission, the conclusion drawn is that the cases of the third trimester had serious bowel strangulation due to high pressure. Moreover, due to high fetal survival rate in the third trimester, the decision to perform an exploratory laparotomy is made more easily without hesitation than in other trimesters.

7.10.1.6 Prognosis

Maternal Outcome

Mother survived in all (11) cases making mortality rate 0 %, although endometritis and deep venous thrombosis occurred in 1 case [285].

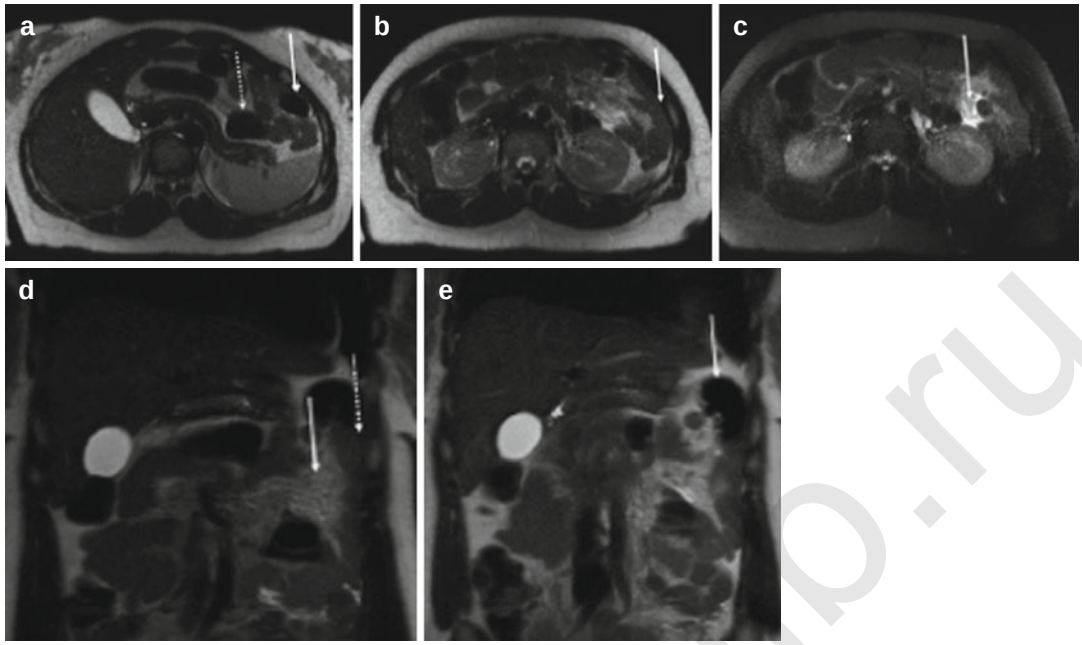

Fig. 7.31 Axial, single-shot, fast spin-echo, MR images (**a**) and (**b**) demonstrate a cluster of small bowel loops in the left upper quadrant, including a dilated loop (*solid arrow*, **a**), that overlie a centrally displaced segment of the transverse colon (*dotted arrow*) and show no overlying omental fat (*solid arrow*, **b**). Axial, fat-suppressed, single-shot, fast spin-echo, MR image (**c**) better demonstrates the presence of mesenteric edema in this region (*solid arrow*). Coronal, single-shot, fast spin-echo, MR image (**d**) demonstrates herniation of fat with prominent vessels through a mesenteric defect (*solid arrow*) as well as the abnormally positioned loops of the small bowel within the far *left lateral* aspect of the abdominal cavity with an absence of overlying omental fat (*dotted arrow*). An additional coronal, single-shot, fast spin-echo, MR image (**e**) confirms the presence of the dilated loop of the small bowel in the left upper quadrant (*solid arrow*) [291]

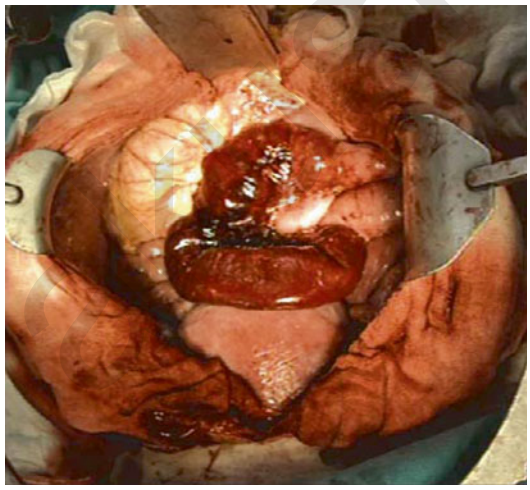

Fig. 7.32 After Cesarean delivery, an exploratory laparotomy demonstrated gangrenous change of the upper jejunum due to fibrous band involving the afferent limb near the site of the Roux anastomosis. Segmental resection of the nonviable bowel, about 20 cm in length, was performed [304]

Fetal Outcome

The fetus survived in all but 2 [286, 305] of these 11 cases making the mortality rate 18 %. Fetal morbidity is not known.

7.10.2 Spontaneous Incarcerated Internal Hernia

7.10.2.1 Sigmoid Mesocolon Hernia

Incidence

The incidence of internal hernia is estimated to account for approximately 1–6 % of intestinal obstruction [313]. Sigmoid mesocolon hernia is an uncommon type and estimated to account for approximately 6 % of internal hernia [314–317]. Up to 2005, there were 15 cases of transmesosigmoid hernias (see Sect. Classification) [318]. There are only two cases in pregnancy and postpartum published (see Sect. Etiology).

Classification

Benson and Killen in 1964 classified these hernias in general population into three types [319]:

- *Intersigmoid hernia*: Herniation into an intersigmoid fossa, situated at the attachment of the lateral aspect of the sigmoid mesocolon.
- *Transmesosigmoid hernia*: Incarceration of intestinal loops through an isolated, oval defect in the sigmoid mesocolon.
- *Intramesosigmoid hernia*: A congenital, oval defect unrelated to the intersigmoid fossa is present in the lateral peritoneal surface of the mesocolon, and herniation occurs.

Etiology

Pathologic apertures of the mesentery and visceral peritoneum are due mostly to congenital, surgical, traumatic, inflammatory, or circulatory etiologies [314]. Congenital causes of sigmoid mesocolon hernias have also been proposed as possible causes [318, 320]. However, the role of congenital factors remains obscure and theoretical. Some case reports have documented transmesosigmoid hernias developing during pregnancy or postpartum [318, 321]. The authors of these case reports proposed that dilatation and shrinkage of the uterus concomitant with pregnancy or delivery contributed to the development of transmesosigmoid hernias. The abnormal aperture could have been formed from the sigmoid mesocolon tearing by traction due to postpartum shrinkage of the enlarged uterus. One of the theories is that herniation could have occurred a few decades later through the abnormal aperture formed during the pregnant period in some cases.

Clinical Presentation

The clinical features of internal hernia are abdominal pain, distension, and vomiting. According to a review by Kaneko and Imai, more than 21 % of patients complained of left lower abdominal pain [322].

Diagnosis

Plain abdominal X-ray shows distended small bowel loops and air-liquid level formation, suggestive of a mechanical obstruction.

Abdominal CT scan demonstrated (as in all small bowel obstructions) ascites, dilated small bowel loop with a cutoff at the same level of the small bowel. The key CT findings for diagnosis of the transmesosigmoid hernia included [323]:

- A cluster of dilated fluid-filled loops of the small bowel entrapped in the left posterior and lateral aspect of the sigmoid colon through a mesosigmoid defect.
- The defect was located between the sigmoid colon and the left psoas muscle.
- The sigmoid colon showed anterior and medial displacement.
- These encapsulated loops of the small bowel showed U- or C-shaped configurations and wall thickening representing closed-loop obstruction and ischemic change.
- Attached mesentery with vessels engorgement and fat obliteration indicating strangulation.
- The proximal small bowel showing dilatation.

However, in the majority of cases, the diagnosis of transmesosigmoid hernia is confirmed only by surgical intervention [324–326].

Therapy

Patients with small bowel obstruction not responding to conservative management require operation. If an internal hernia is suspected, the operation should be prompt, as strangulation and gangrene of the bowel is likely to occur if the surgery is delayed. The role of laparoscopy in patients with intestinal obstruction is being increasingly recognized in general population, but due to small number of pregnant patients, its role in pregnancy is not defined. Kaneko and Imai reported that necrosis of the strangulated intestine occurred in up to 80 % of patients with a transmesosigmoid hernia during the course of treatment, necessitating extensive resection of the small intestine [322].

Prognosis

Maternal outcome is excellent because in both cases there were no massive bowel resections and pregnant population is mostly young and without comorbidities.

7.10.2.2 Transomental Herniation

Idiopathic transomental herniation in general population is an extremely rare cause of small bowel obstruction, accounting for just 1–4 % of all

cases of intra-abdominal herniation [327]. There is only one case published on this pathology, but with confusing intraoperative description, different to one found in the title of the article (*There was a hernia sac between the root of the mesentery and transverse mesocolon*). Her operation was uncomplicated and lasted for about 90 min. She had an uneventful postoperative course is standard term for normal postoperative course. She was discharged on the fifth postoperative day with a continuing pregnancy. She went into labor at term, had a labor epidural, and was delivered by emergency Cesarean section for suboptimal cardiotocography. A good sized healthy female baby was born. She had an uneventful postoperative course [328].

7.11 Gastric Outlet Obstruction

7.11.1 Heterotopic Pancreas

7.11.1.1 Incidence

Heterotopic pancreas (HP) in general population is often found incidentally in patients operated on for other reasons or during autopsies. The condition is relatively uncommon; it has been found in 0.6–13 % of patients in autopsy studies [329, 330] and encountered in about one of 500 operations in the upper abdomen [331–336]. A few cases of HP as a cause of gastric outlet obstruction in infant [337], child [338], and adults [329, 339–345] have been published. There is only one case of HP causing gastric outlet obstruction in pregnancy [84]. There is one case of gastric outlet obstruction in pregnancy due to active chronic peptic ulcer [346] and another of a case of HP (in the small bowel) causing small bowel intussusception (see Sect. 7.7.1) [85].

7.11.1.2 Embryology

It is possible that early in fetal life, during rotation of the foregut and fusion of the dorsal and ventral parts of the pancreas, small parts are separated from it and continue to develop in the wrong location [347]. Most often, HP is found in the stomach, duodenum, and jejunum, but it may also be found anywhere in the digestive tract, intra-abdominally, in the mediastinum, and in the lung [348].

7.11.1.3 Clinical Presentation

The symptoms can be (a) non-emergent such as epigastric pain (77 %) and abdominal fullness (30 %), (b) semi-urgent as tarry stools (24 %) due to ulceration, or (c) emergent as due to intussusception and obstruction [333, 349–351]. Gastric outlet obstrucion mostly presents first as postprandial vomiting and weight loss with progression of vomiting [342, 345].

Although HP often exists from childhood, it seldom causes symptoms. Conditions that trigger this previously asymptomatic disorder to become symptomatic include bacterial infection and pancreatitis [352, 353], and there is only one report of an ectopic pancreas becoming symptomatic due to pregnancy [84]. Authors think that symptoms developed as the enlarging uterus narrowed both the gastroduodenal canal and the peritoneal space, although the ectopic pancreas itself existed beforehand. Currently, there is no report about the relationship of enlargement of a HP with the hormonal changes in gestation.

7.11.1.4 Diagnosis

This disorder is difficult to diagnose preoperatively, despite modern diagnostic procedures such as abdominal ultrasonography, gastroduodenoscopy (Fig. 7.33), and abdominal CT [351, 354]. According to one report of patients in general population, only 6 % (1/17) of them were considered to have a HP preoperatively [351]. In the only published case in pregnancy [84], an accurate diagnosis was not able to be made from the abdominal MRI findings because of the contrast medium restrictions and the motion artifact of the fetus (Fig. 7.34). Degenerated GIST is similar to a submucosal tumor with a central cyst, although it usually grows extraluminally rather than intraluminally in the upper stomach. Contrast-enhanced CT scans may help to make a prompt diagnosis [355]. In conclusion, HP should be considered in the differential diagnosis of a potentially obstructive gastric submucosal tumor, even though it is a rare event.

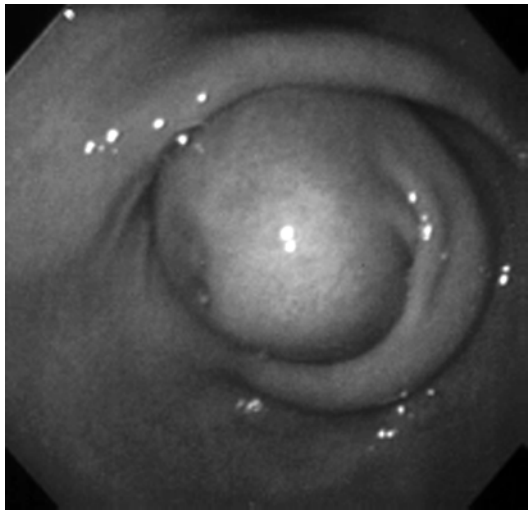

Fig. 7.33 Preoperative gastro-fiberscopic examination showed a submucosal tumor prolapsing through the pyloric ring and obstructing the gastric outlet [84]

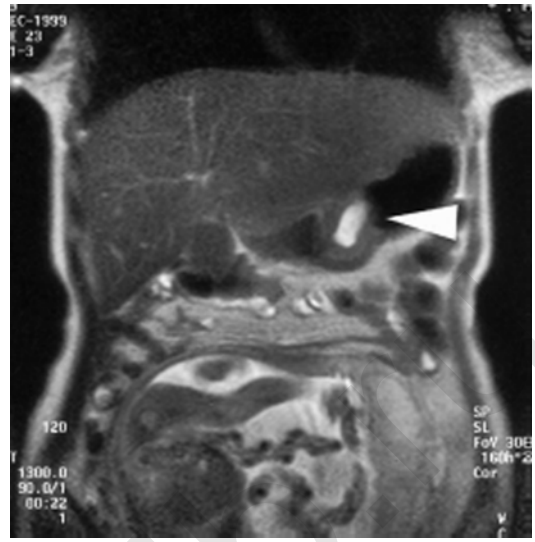

Fig. 7.34 T2-weighted magnetic resonance imaging showed a 4.7 × 3.6 × 2.4 cm target-like tumor in the posterior wall of the gastric antrum (*arrowhead*). The relatively large central portion showed a high signal intensity suggesting cystic components. The fetus can be clearly seen in the low abdomen [84]

7.11.1.5 Therapy

There are two standard procedures for gastric outlet obstruction. One is endoscopic balloon dilatation (especially suitable for peptic gastric outlet obstruction) and another is surgery. Surgery is always indicated when there is a suspicion of malignancy. Taking a full-thickness biopsy of the lesion at surgery is mandatory for establishing the diagnosis of HP from a frozen section; however, this carries the risk of scattering cells if there is malignant disease [334]. This disorder can be treated by various operative procedures, including bypass gastroenterostomy or antrectomy with gastroduodenal anastomosis [334–336]. Lymphadenectomy is not considered necessary as lymphatic spread rarely occurs from a HP or GIST [356]. Less invasive surgery can successfully be performed through a small skin incision. Antrectomy without lymph node dissection was most appropriate to avoid interruption of the pregnancy.

Histologically, HP with mucus retention of the gastric antrum needs to be differentiated from duplication and mucinous carcinoma of the stomach. Frozen sections at surgery are not enough to distinguish these three diseases without verifiable pancreatic tissue [357]. Duplication of the stomach can easily be ruled out if the lining of the cysts did not consist of normal gastric mucosa. Although extremely rare, the possibility of adenocarcinoma arising from ectopic gastric pancreas must also be considered [358].

7.12 Gynecologic Causes of Intestinal Obstruction

The cause of the intestinal obstruction is very important because apart from treating obstruction with its consequences itself, also a cause itself sometimes should be treated additionally. Gynecologic causes of acute abdomen are present in the separate chapter, and gynecologic conditions would unlikely be considered as an underlying cause of intestinal obstruction.

7.12.1 Ovarian Teratoma

7.12.1.1 Incidence

The occurrence of teratoma with pregnancy is uncommon; only about 10 % of the cases of matured cystic teratoma are diagnosed during

pregnancy [359]. The most of the cases presented in the second trimester [360, 361]. Mature cystic teratomas usually occur in young women with a peak age incidence of between the ages of 20 and 40 years [362].

7.12.1.2 Clinical Presentation

The most frequent symptom of teratoma is lower abdominal pain. Only few cases present for the first time with abdominal mass [363]. Though the complications of teratoma in pregnancy include torsion, rupture, obstruction to birth canal, there is only one reported case of its association with intestinal obstruction [361]. There was 2-week history of abdominal pain, abdominal distension, and vomiting. The pain was located around the umbilical region and was colicky in nature. There was associated constipation with signs of generalized abdominal tenderness.

7.12.1.3 Diagnosis

With respect to diagnosis, abdominal ultrasound (transabdominal and transvaginal) scan is the method of choice. In the single case report, a repeat ultrasound scan also reported a singleton intrauterine pregnancy with vague abdominal masses on both sides of the uterus and distended bowel loops. It is able to determine the dimension of the tumor [361].

7.12.1.4 Therapy

A diagnosis of intestinal obstruction in pregnancy was made, and a laparotomy was performed. Findings at surgery were those of bilateral ovarian masses (benign cystic teratoma) with the right causing kinking of the small intestine (ileum). The right mass adhered partially to the ileum, and it separated from it without difficulty (Figs. 7.35 and 7.36). The adhesion might have resulted from a response of the surrounding tissue, including intestine to the pressure effect of the tumor. On the other hand, it might have also resulted from minor leak of tumor content into the surrounding tissue. However, there was no evidence of invasion of the intestinal wall thus ruling out gross feature of malignancy. The size of both tumors was approximately 15 cm in diameter. This tumor possibly existed before the onset of pregnancy. Caspi et al. reported that

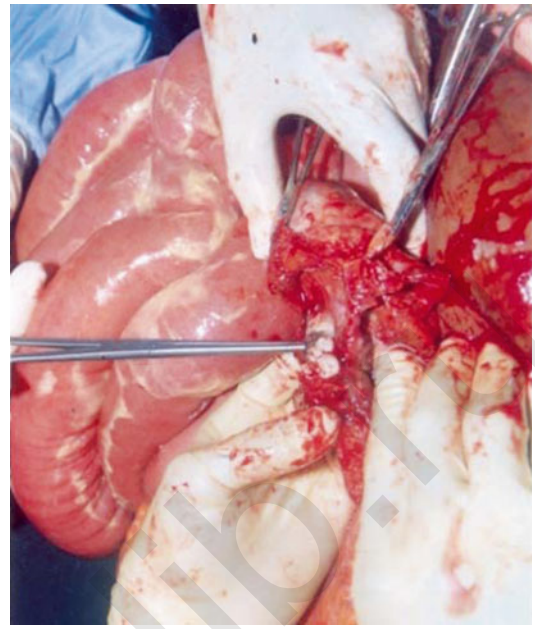

Fig. 7.35 Teeth and other structures of benign ovarian teratoma causing small bowel obstruction with dilated loops [361]

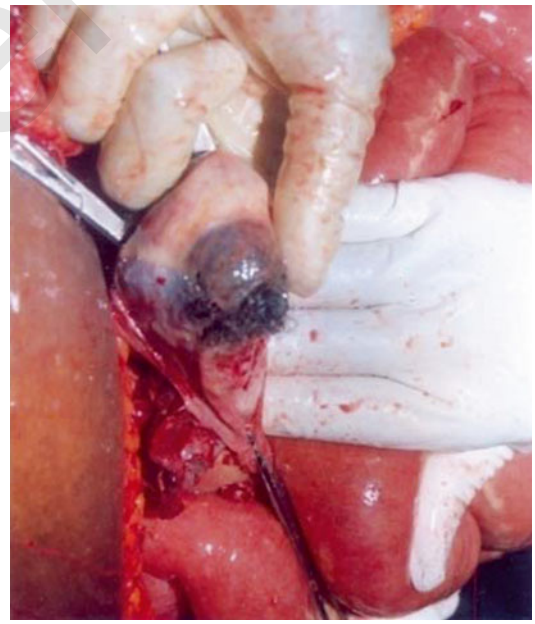

Fig. 7.36 Intra-abdominal teratoma being teased from distended bowel loops [361]

teratomas less than 6 cm occurring before pregnancy do not grow during pregnancy [364].

7.12.1.5 Prognosis

As the tumor was benign, the pregnancy was carried to term and she delivered a male baby by spontaneous vertex delivery. APGAR score of the baby at birth was 7 at 1 min and 8 at 5 min [361].

7.12.2 Ectopic Pregnancy

7.12.2.1 Incidence

Most complications of ectopic pregnancy are in the form of tubal rupture with massive hemorrhage and hemorrhagic shock. There are only three cases of intestinal obstruction due to ectopic pregnancy published. Catani et al. reported a case of intestinal obstruction due to adhesion from an ectopic pregnancy located on the mesenteric side of the ileum [365]. The other similar case of terminal ileum obstruction is presented by Singh [366]. Orawke et al. reported another case of combined intrauterine and extrauterine pregnancy diagnosed preoperatively as simple intestinal obstruction [367].

7.12.2.2 Clinical Presentation

There are two conditions that present simultaneously. The most common signs and symptoms of ectopic pregnancy include amenorrhea, abdominal pain, irregular vaginal bleeding, and pain on abdominal or pelvic examination. A pelvic adnexal mass is palpated in only 50 % of the patients. Unfortunately, the most common signs and symptoms of ectopic pregnancy are correct in predicting only 50 % of cases [368]. Abdominal pain is the single most consistent feature of ectopic pregnancy [369]. Clinicians should have a high index of suspicion for ectopic pregnancy in patients with a previous history of tubal pregnancy, tubal surgery, pelvic inflammatory disease (PID), tubal disease, endometriosis, abdominal surgery itself, intrauterine device, fertility treatment, smoking, and history of multiple sexual partners.

The presentation of bowel obstruction is described earlier in the chapter (see Sect. 7.1).

7.12.2.3 Differential Diagnosis

Possible differential diagnoses include [370]:

- Pelvic inflammatory disease
- Acute appendicitis
- Typhoid enteritis
- Incomplete septic abortion
- Uterine fibroid
- Gastroenteritis
- Peptic ulcer
- Intestinal obstruction

7.12.2.4 Diagnosis

To improve the chances of correctly diagnosing an ectopic pregnancy, admitting staff should obtain accurate menstrual and sexual history, and facilities should be able to provide serum β-human chorionic gonadotropin (βHCG) levels and transvaginal ultrasound scans [370]. Transabdominal ultrasound is of little help due to dilated bowel loops which prevent adequate visualization. The diagnosis of bowel obstruction is described earlier in the chapter, and diagnostic algorithm is standard when intestinal obstruction is suspected. These diagnostic modalities itself cannot reveal ectopic pregnancy as the cause of obstruction. First, diagnostic modality is plain abdominal X-ray showing air-liquid levels (Fig. 7.37).

Almost all ectopic pregnancies are tubal (97.7 %); therefore, obstruction develops in the lower abdomen, and two of three cases were located in the terminal ileum [365, 366].

7.12.2.5 Therapy

There are several therapeutic options for ectopic pregnancy, including medical (methotrexate), expectant, and surgical. In cases with intestinal obstruction due to ectopic pregnancy, surgery is the only modality to deal with obstruction and ectopic pregnancy simultaneously.

Surgical Therapy

The type of operation for intestinal obstruction depends on the severity of the obstruction. If simple, adhesiolysis is performed. If gangrene is

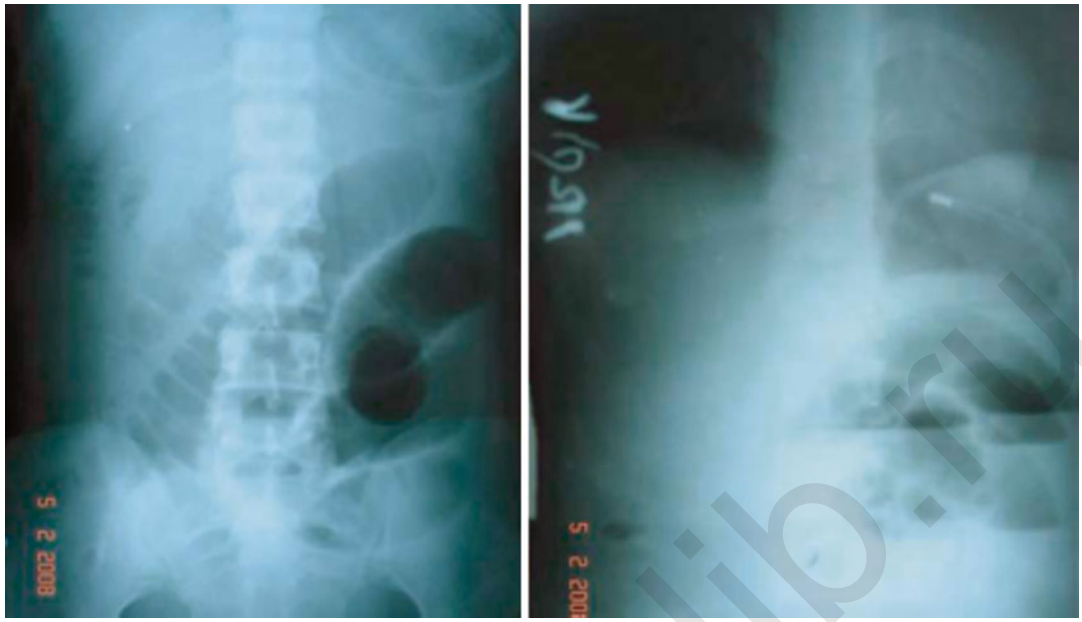

Fig. 7.37 Plain abdominal radiographs with the patient in both the upright and supine positions show multiple air-fluid levels and dilated jejunal loops [366]

present due to long-standing obstruction or strangulation, bowel resection is made. Decision on continuity or stoma is made on several factors as in other causes of intestinal obstruction.

Gynecologic Therapy

The type of operation for ectopic pregnancy depends on the location of ectopic pregnancy. Treatment of choice for unruptured ectopic pregnancy is salpingostomy, sparing the affected Fallopian tube and thereby improving future reproductive outcome. Salpingectomy is performed if Fallopian tube is morphologically changed in a way that it precludes further fertility.

7.13 Intestinal Obstruction Caused by Normal Pregnancy

7.13.1 History

Pinard in 1902 was quoted by LePage et al.: *There is no need to begin another chapter in puerperal pathology entitled 'Intestinal Occlusion of Pregnancy'. I have never seen intestinal occlusion complicate a normal pregnancy* [371]. The explanations offered by the various French and German writers varied. The French writers discuss the anatomic causes in abdomens without previous surgical intervention and so without adhesions as far as is known. Sencert and Cuneo called attention to the intestinal occlusion caused by a loop of bowel caught and held by the infundibulopelvic ligament, the latter being held taut by a gravid uterus rising into the abdomen. Vautrin, of Nancy, in 1922 presented two cases of acute intestinal obstruction caused apparently by normal pregnancy [372]. In discussing these cases Vautrin pointed out the "colic angulation" caused by the tense infundibulopelvic ligament, the stercoral accumulation adding to the trouble, and the two causing obstruction. Ludwig, in 1913, assembled 96 cases of intestinal obstruction occurring during pregnancy. He found the condition most common in the 3rd and 4th months and again in the last 3 weeks of pregnancy [2]. These cases were perhaps in part aggravated by the pregnancy, but none could be directly attributed to the pregnancy alone. In 1918, Fleischauer

[373] reported two intestinal obstructions during pregnancy – one, a woman pregnant 4 months, with severe obstruction and peritonitis. At the autopsy, a hindrance to the passage of the intestinal contents was found at a point where the possibility of compression between the uterus and pelvic brim arose. There was also dilatation of the ureters where they entered the pelvis, so that in this case the gravid uterus must be considered the cause of the obstruction, in his opinion. According to Fleischauer, this case confirmed the opinion of Van der Hoeven, in 1912, that in the 3rd and 4th months of pregnancy an occlusion of bowel is more liable to appear than at any other time, that is to say, at the time the uterus rises beyond the brim of the pelvis [374]. Der Verf was of the opinion that in the final analysis the cause of the ileus is to be found in the bowel itself owing to muscle weakness and loss of muscle tone. A second case described by Fleischauer appeared at the 6th month. The obstruction was caused by adhesions from a previous operation – the growing uterus being simply the deciding factor in the cause of the ileus. In LePage et al.'s comprehensive treatise on the subject from 1913, the patients are divided into two classes [371]:

- Without any past history of intestinal or peritoneal trouble
- With history of intestinal or peritoneal trouble and possible operation

LePage et al. say: *If we can diagnose those exceptional cases in which the presence of a gravid uterus suffices to produce obstruction, even occlusion, in an intestine non-adherent and with no bands, but simply compressed, therapeutics should immediately consist in getting rid of the uterine tumor*. This course, he adds, *raises the great question of the right of the fetus to life*. Kohler, in 1920, says the cases in which a pregnant uterus alone produces the ileus are rare [375].

7.13.2 Incidence

The incidence is extremely rare. Review of the literature up to 1926 by Bohler found only twelve cases published in a paper from 1930 [376]. Additional four cases have been collected since (see Sect. 7.13.3).

7.13.3 Pathophysiology

The concept of pathophysiologic process is simple. The enlarged uterus causes compression, on the locations where the bowel cannot move freely or where there are junctions of mobile and immobile parts of the bowel:

1. Rectosigmoid junction (pelvic brim)
2. Point where the bowel, in a form of a stoma, enters the abdominal wall
3. Ileum proximal to ileoanal pouch (J-pouch)

Ad 1. Rectosigmoid junction is the most common location because the uterus is located in the lower abdomen in all phases of uterine enlargement. Possible additional factor is long sigmoid loop predisposing to kinking and development of sharp angles [373, 374, 377].

Ad 2. Theoretically, incidence is increasing as the pregnancy advances due to enlargement of the uterus (both cases are after 32 weeks of gestation). In pregnant patients with the normal bowel anatomy, the terminal ileal loops remain relatively mobile, allowing them to move aside when abutted by the enlarging uterus and thereby maintain normal patency and function. The obstruction can have several similar mechanical mechanisms. The enlarging uterus may in addition drag on the ileostomy loop from within, causing stomal retraction. Incarceration is a theoretical risk; it can arise either from adhesions fixing the retroverted uterus in the pelvis, or possibly from the pernicious habit of rectal surgeons of using the uterus to close the pelvic floor after excision of the rectum. Stomal problems are common and are caused by displacement, enlargement, and sometimes prolapse. Fortunately, most of the stretching of the abdominal wall is in the region of the linea alba, and the stoma gets eased out of the way laterally. It should be noted that in patients

with ileostomy, additional nutritional support, as oral iron, can provoke ileostomy dysfunction.

Ad 3. Explanation could be that ileum proximal to J-pouch is more or less tensed and cannot freely move away from the enlarging uterus and therefore obstruction occurs [378].

There are some conditions that should be fulfilled for the diagnosis of *intestinal obstruction caused by normal pregnancy*:

- No obstructive symptoms before pregnancy except long-standing constipation
- No other causes of obstruction intraoperatively
- Compression of the enlarged uterus on the bowel at the site where the proximal distended bowel continues to the collapsed bowel
- No other causes of stomal obstruction (parastomal hernia, stenosis, or prolapse)

7.13.4 Diagnosis

When intestinal obstruction is suspected, of any cause, plain abdominal X-ray is most often diagnostic and sufficient for the indication for the emergent operation. MRI of the abdomen with or without contrast (oral or intravenous) can be used in unequivocal cases (Fig. 7.38). Multiplanar images could demonstrate multiple loops of the dilated small intestine. The point of transition from distended to the collapsed bowel can be identified with or without focal lesion as they likely cause of obstruction. MRI is important because it can delineate bowel wall thickening or mucosal abnormalities or signs of parastomal hernia [242].

7.13.5 Therapy

It is fortunate that the condition is extremely rare, and when it does occur the majority of babies have reached the age of viability. It would seem sane to suggest, then, that when intestinal obstruction intervenes in the course of normal intrauterine pregnancy, the abdomen be opened and the cause, if at all possible, be ascertained. If there are no causes of obstruction except bowel compression by the enlarged uterus, then Cesarean section should be performed.

If there is suspicion that intestinal obstruction is due to pregnancy, without strangulation, and is present near term, the delivery should be started, vaginally or by Cesarean section. This method

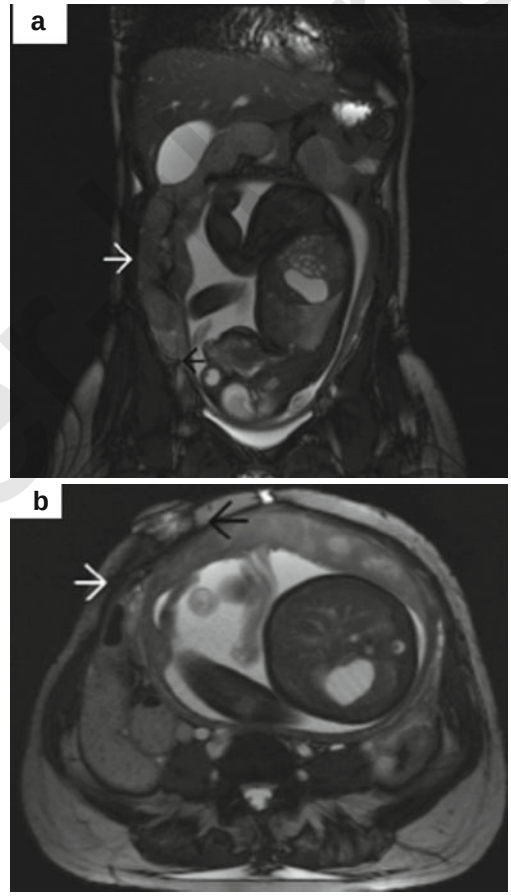

Fig. 7.38 (**a**) Coronal T2-weighted images identify dilated loops of the small bowel (indicated by the *white arrow*) from the left upper quadrant down to the level of the ileostomy in the right iliac fossa (indicated by the *black arrow*); (**b**) Axial image at the level of the stoma identifies a change in caliber, (indicated by the *white arrow*) from the dilated small bowel to the collapsed bowel adjacent to the uterus indicating the compressive effect of the uterus to be the cause of obstruction; (**c**) Dilated loops of the small bowel in the midline posterior to the uterus (indicated by the *white arrow*) [242]

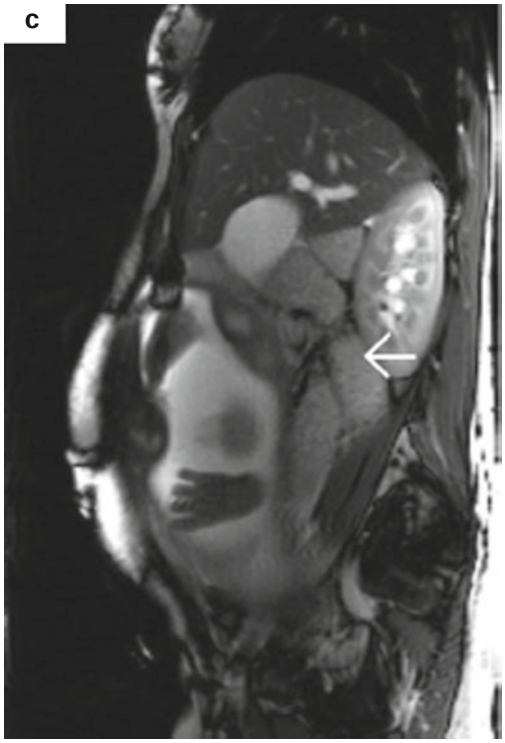

Fig. 7.38 (continued)

can be therapeutic [379] but should be performed with caution.

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Acute Inflammatory Bowel Disease 8

8.1 Acute Crohn's Disease

8.1.1 Introduction

Approximately 50 % of patients are less than 35 years of age at the time of diagnosis and 25 % conceive for the first time after their diagnosis of inflammatory bowel disease (IBD) [1–3]. This age range corresponds to female reproductive age and increases the likelihood of Crohn's disease (CD) during pregnancy.

8.1.2 Effect of Pregnancy on Crohn's Disease

Crohn et al. took the view that if the onset of the disease occurs during pregnancy, then its subsequent course is severe [4]. Currently, pregnant patients with CD can be classified in four categories [5]:

- Inactive at conception
- Active at conception
- Arising during gestation
- Arising during the puerperium

Approximately one-third of women with inactive IBD at conception will relapse during the pregnancy or puerperium. This risk of a flare is no greater than any other year of the patient's life [6, 7]. If conception occurs at a time when IBD is active, disease will settle only in about one-third of women with ulcerative colitis (UC) or CD [8, 9]. One-quarter of patients with active IBD during pregnancy will experience chronically active disease and in about half of these patients, disease will worsen (45 % UC, 33 % CD) [10]. Active disease has been associated with miscarriage, stillbirth, prematurity, and low birth weight [11]. Thus, conception is advised when IBD is in remission. Disease activity may even be slightly lower during pregnancy [12]. The rate of relapse may decrease in the 3 years following pregnancy [13]. This was further supported by a study from a 10-year follow-up of a European cohort of patients with 580 pregnancies [14]. Patients with CD who were pregnant during the course of their disease did not have higher rates of stenosis (37 % vs. 52 %) or resection (0.52 vs. 0.66). The rates of relapse decreased in the years following pregnancy in both UC (0.34 vs. 0.18 flares/year) and CD patients (0.76 vs. 0.12 flares/year). While the etiology for this is not understood, a possible factor inducing quiescent disease may be disparity in HLA class II antigens between mother and fetus, suggesting that the maternal immune response to paternal HLA antigens may result in immunosuppression that affects maternal immune-mediated disease. This has been demonstrated in rheumatoid arthritis [15] as well as in IBD [16].

Patients whose Crohn's disease is in remission at the time of conception usually remain symptom-free during pregnancy, with relapse rates similar to those documented in the *National Cooperative Crohn's Disease Study* [17], and their pregnancy outcomes are similar to those in the general population. Of women who have active Crohn's disease at the beginning of pregnancy, 60–70 % continue to have active disease

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during the pregnancy despite medical therapy [9, 18]. In this group there is a suggestion of a decreased rate of live births [9]. There is no evidence that patients developing symptoms for the first time during pregnancy experience unusually severe disease.

During the puerperium the risk of relapse seems no higher than usual. Severe exacerbations of Crohn's disease in pregnancy are rare. Even less common are acute manifestations that require surgery [4, 9, 19, 20], but in reported cases, maternal and fetal mortality rates have been high [20].

8.1.3 Clinical Presentation

8.1.3.1 Intestinal Perforation

Pathophysiology of Free Intestinal Perforation

Two possible mechanisms may account for free perforation of Crohn's disease during pregnancy. Either an abscess adjacent to the Crohn's segment ruptures by the mechanical stress of labor or there is failure of the intra-abdominal viscera to "wall-off inflamed segments." In the latter case, the large uterus may prevent the omentum and other abdominal contents from adequately localizing the inflammation [21].

Presentation

Free intestinal perforation presents as acute abdominal pain with signs of peritonism.

8.1.3.2 Intestinal Obstruction

Presentation

Abdominal distension, nausea, vomiting, and crampy abdominal pain in the early stages are the leading symptoms. Later in the course of the disease, pain is constant and there is no passage of stool or flatus.

8.1.4 Diagnosis

Standard radiological investigations for CD such as small and large bowel enemas and labeled white cell scans are contraindicated because of the radiation exposure to the fetus. Several reports have been published on the safety of colonoscopy and flexible and rigid sigmoidoscopy in pregnant patients. These results suggest that endoscopy does not induce labor or result in significant side effects to the mother or fetus and can be performed safely in medically stable pregnant patients [19, 22, 23]. Abdominal ultrasound may identify thickening of the wall of the terminal ileum or the presence of an intra-abdominal abscess. Abdominal MRI imaging is a safe non-invasive investigation in pregnancy and has been useful in establishing the diagnosis of CD [24]. In cases when patients present with acute abdominal pain, electronic fetal monitoring is an essential. It is also a diagnostic modality because changes in fetal signs can be indirect sign of acute abdominal condition. Fetal monitoring consists of periodic fetal heart rate auscultation by Doppler or by cardiotocography.

8.1.5 Differential Diagnosis

8.1.5.1 Intestinal Obstruction

As in general IBD population, the most common causes of intestinal obstruction are adhesions, bowel inflammation with or without strictures, or bowel ischemia. In pregnancy compression by enlarged uterus during pregnancy can also be the cause (see Chap. 7). There are two cases of successful decompression by Malecot catheters during pregnancy. One case was of recurrent sigmoid volvulus [25] and another of compression of pouch (IPAA) [26].

8.1.6 Treatment

8.1.6.1 Indications and Procedures

The rarity of acute surgical problems in pregnancy may lead to delays in management [27]. It is therefore advisable that an obstetrician, a surgeon, and a gastroenterologist are involved in the patient's management [28]. When a woman with a history of CD presents with peritonism, the possibility of an acute manifestation of the disease must be considered. In such circumstances surgery should not be long delayed. Five of the

six patients described in the series by Hill et al. had a free perforation of CD [29].

Intra-abdominal surgery performed during the first trimester is associated with an increased risk of miscarriage; for planned procedures in the second trimester, the risk is lower. In the third trimester laparotomy may be complicated by premature delivery and technical difficulties [30]. However, it is the surgical condition, not the operation, that determines maternal and fetal risk [31].

Indications for surgical therapy in both CD and UC during pregnancy are the same as in non-pregnant patients. When acute manifestations of CD are present, it is recommended to remove the source of sepsis and exteriorize the bowel ends [29]. Active intraperitoneal sepsis increases the risk of anastomotic leakage and miscarriage. Intestinal stomas seldom cause difficulty; if, after delivery, the residual bowel is healthy, reanastomosis can be performed.

A stomal therapist should mark the patient before surgery. In pregnant patients, the optimal location for the stoma on the abdominal wall is usually higher than normal because the stoma will drop to a lower position after delivery.

After colectomy a decision should be made regarding the rectal stump. Stump breakdown and leakage leading to intra-abdominal sepsis is a major concern. The stump can be handsewn in two layers and wrapped with the omentum or brought out as a mucus fistula. If a mucus fistula is to be placed, the remnant stump should be kept long. Because of the enlarged uterus, the stump will need to be brought out through an extraperitoneal plane deep to the broad ligament and dilated ovarian vessels. The rectum is irrigated with Betadine at the time of surgery to remove the excess bloody mucoid material and a rectal tube left in place to keep it decompressed in the postoperative period [32].

Small Bowel Disease

The indications for small bowel surgery in pregnant women with CD are not different from the general population and include intestinal obstruction or perforation, hemorrhage, or abscess. Multiple case reports of small bowel surgery for CD during pregnancy historically had revealed high mortality to both the mother and the fetus; however, more current reports reveal better outcome [33]. A case series of six surgeries from 11 to 30 weeks gestation for intraperitoneal sepsis from CD reported successful deliveries of healthy infants at or near term (one delivered at 31 weeks) in five cases and one patient had a miscarriage [29]. Temporary ileostomy is generally preferred to reduce the risk of postoperative complications that can be seen after primary anastomosis.

8.1.6.2 Perioperative Considerations

Thromboprophylaxis in General IBD Patients (ECCO Consensus)

Pregnancy increases the risk of venous thromboembolism (VTE) by four to sixfold [34] and is a leading cause of direct maternal death in developed countries [35]. The time of highest risk is in the first 6 weeks of the postnatal period [36]. IBD patients, particularly hospitalized with active disease, are at increased risk for VTE [37, 38]. Hospitalized pregnant IBD patients have an increased risk of VTE compared to their non-IBD pregnant controls, for CD an OR 6.12 and for UC an OR 8.44. Low-molecular-weight heparin in a prophylactic dose reduces the risk of VTE in medical and surgical patients by 60–70 % [39]. Low-molecular-weight heparin has been shown to be safe and efficacious in the pregnant population [40]. Therefore, consideration of the use of prophylactic low-molecular-weight heparin in pregnant IBD patients experiencing a relapse and/or admitted to hospital is strongly recommended. All women should undergo a documented assessment of risk factors for VTE in early pregnancy or before pregnancy. This assessment should be repeated if the woman is admitted to hospital for any reason and again after delivery [41].

8.1.6.3 Obstetric Considerations

Mode of Delivery in General

There is an increased rate of Cesarean sections in women with IBD [42]. Using the *2005 Nationwide Inpatient Sample*, Nguyen et al. examined 2,372 CD deliveries and 1,368 UC deliveries. In this population-based study, the adjusted odds of a Cesarean section were higher in women with CD (aOR 1.72) and UC (aOR 1.29) compared to non-IBD controls [38].

Elective Delivery with or Without Elective IBD Surgery

In general, the indications for elective Cesarean section are:

- Obstetric
- Active perianal disease
- Presence of an ileal pouch-anal anastomosis

Obstetric indications for Cesarean section are not in the scope of this textbook.

A perianal fistula or an abscess was considered to represent perianal CD; however, anal fissures or hemorrhoids were not [43]. Patients with inactive perianal disease or no history of perianal disease are not at increased risk for perianal disease after a vaginal delivery [43]. However, if they have active perianal disease they can risk aggravating their injury with a vaginal delivery. One report noted an increased incidence of perianal disease following episiotomy [44]. In another study, 69 % (27/39) of CD patients without a history of perianal disease had an episiotomy at delivery. Only one patient, who had a third-degree laceration and an episiotomy, developed perianal disease within 1 year postpartum. Moreover, of the ten patients with inactive perianal disease at the time of their episiotomy, none reported a recurrence of perineal disease over a 2-year follow-up period [43]. Other studies have also shown that vaginal delivery in patients with inactive perianal disease does not appear to lead to adverse outcomes [45, 46]. The results from Ilnyckyji et al. are interesting because episiotomy was performed in equal percentage on patients with active and inactive perianal disease. The group with inactive perianal disease had higher percentage of second- and third-degree lacerations. It is obvious that patients with histories of previous perianal disease may receive more vigilant attention to their perineum during delivery. There are several unknown facts from the data in this study. One is *Perianal Disease Activity Index* which is important for comparison of the results and also activity of the disease in general because subclinical infection can be present which is only confirmed by colonoscopy and/or biopsy. Also there are several types of episiotomies and the length is not mentioned and compared [43].

Patients who have an IPAA can have a normal vaginal delivery without fears of damaging the pouch [47]. In general, anal sphincter function (daytime and nighttime stool frequency or continence) may be altered during the third trimester and immediate postpartum period, but its function typically returns to baseline in most patients, usually within 3 months after delivery [47–50]. Although a few patients may have long-term disturbances in anal function, it appears unrelated to the method of delivery [48]. A small study of three patients with a history of IPAA did not demonstrate an increased risk of injury or fissuring of the anal sphincter despite vaginal delivery [50]. A survey of 232 pregnant females with a history of IPAA showed no increase in pouch complications or functional problems when comparing those who underwent vaginal delivery as compared to those who had a Cesarean section [47]. However, damage to the anal sphincter may be compounded by aging and the effects on the pouch will not be seen for several years. The patient, the obstetrician, and the surgeon should discuss the theoretical risk to long-term pouch function prior to making a decision on mode of delivery.

Emergent Delivery in the Course of Emergency IBD Surgery

In patients presenting with acute abdomen, the treatment depends on the trimester of pregnancy. During the first two trimesters, only surgical treatment of the cause of acute abdomen is carried out. After 28 weeks of pregnancy, Cesarean section is recommended (due to higher incidence of postoperative complications leading to spontaneous induction of labor) [32, 51].

After surgery without Cesarean section, fetal monitoring should begin in the postanesthesia recovery room, and the patient should be watched carefully for spontaneous labor.

8.1.6.4 Medications for Crohn's Disease in Pregnancy

The use of medications during the conception period and pregnancy is a cause of great concern for patients and the physicians caring for them. Overall, the majority of medications used for the treatment of IBD are not associated with significant adverse effects (Table 8.1), and maintaining the health of the mother remains a priority in the

Table 8.1 Medications used in the treatment of inflammatory bowel disease [52–54]

Drug	FDA	Pregnancy	Breastfeeding
Adalimumab	B	Limited human data: low risk	No human data; probably compatible
Alendronate	C	Limited human data; animal data suggest risk	No human data: probably compatible
Ampicillin/clavulanic acid	B	Low risk	
Azathioprine/6-mercaptopurine	D	Transplant literature suggest low risk	No human data: potential toxicity
Balsalazide	B	Low risk	No human data: potential diarrhea
Budesonide	C	Data with inhaled drug low risk. No human data for oral drug	No human data
Cephalosporins	B		
Ciprofloxacin	C	Potential toxicity to cartilage	No human data: probably compatible
Corticosteroids	C	Low risk: cleft palate, adrenal insufficiency, premature rupture of membranes	Compatible
Cyclosporine	C	Low risk	Limited human data: potential toxicity
Etanercept			Excreted in milk – probably too large molecule for oral absorption
Fish oil supplements	–	Safe, possibly beneficial	No human data
Infliximab	B	Low risk; limited human data	Limited human data: probably compatible
Loperamide	B	Low risk	
Mesalamine (oral and topical)	B	Low risk	Limited human data: potential diarrhea
Methotrexate	X	Teratogenic	Contraindicated
Metronidazole	B	Limited efficacy in IBD – avoid in 1st trimester	Limited human data: potential toxicity
Olsalazine	C	Low risk	Limited human data: potential diarrhea
Risedronate	C	Limited human data	Unknown
Rifaximin	C	No human data: animal teratogen	Unknown
Sulfasalazine	B	Low risk. Give folate 2 mg daily	Limited human data: potential diarrhea
Sulfonamide	C	Not recommended	
Tacrolimus	C	Low risk	Limited human data: potential toxicity
Tetracycline	C	Not recommended	Not recommended
Thalidomide	X	Teratogenic	Limited human data: potential toxicity

Low risk is defined as "the human pregnancy data does not suggest a significant risk of embryo or fetal harm"

management of these patients. If a flare does arise during pregnancy, most patients can be managed successfully with a 5-ASA drug or corticosteroids, carry their babies to term, and deliver successfully [55]. Mogadam et al. found that only 2.7 % patients with UC and CD required surgical intervention; the rest were controlled with medical therapy alone [18].

Folate supplements, recommended for all pregnancies to reduce the risk of neural tube defects, are especially important for those taking sulfasalazine, because the sulfapyridine moiety in sulfasalazine competitively inhibits the brush border enzyme folate conjugase [11] and therefore absorption of folate (Table 8.1). Other 5-ASA drugs do not contain sulfapyridine and do not carry the risk of folate malabsorption. In patients whose therapy with 5-ASA drugs fail, prednisone, azathioprine, cyclosporine, and infliximab can be considered, after weighing the risks and benefits, informing the patients, and having the patient participate in the decision about starting one of these drugs. The option of surgery, if the pregnancy is at a suitable stage, should be discussed as an alternative to immunotherapy.

Fish oil supplements are used by some patients with IBD as an adjunct to medical therapy. A randomized controlled trial of fish oil supplementation demonstrated prolongation of pregnancy without detrimental effects on growth of the fetus or course of labor [56]. Fish oil supplements are not rated by the FDA since they are not classified as a drug.

Most clinicians believe that the chimeric structure of the *infliximab* molecule containing a human IgG_1 constant region limits placental transfer during the first trimester [57]. However, the safety of infliximab beyond the first trimester is unknown because IgG subclasses are readily passed into the fetus during the second and third trimesters [58]. Until recently, the medical literature contained no evidence that engineered therapeutic antibodies could cross the placenta when administered to expectant mothers. One case report documents clinically significant fetal exposure to infliximab via placental transfer and a prolonged half-life of the medication in newborns [59]. The presumed mechanism of fetal exposure to infliximab is transplacental maternal IgG antibody transfer beginning in the second trimester and peaking at term. No fetal abnormalities were apparent in this case, but the long-term implications of infliximab exposure during early childhood development are unknown. These findings suggest that pregnant patients should avoid therapeutic antibody treatments after 30 weeks' gestation, and if necessary, the expectant mother can be bridged with steroids to control the disease activity until delivery [59, 60]. Two large studies reported that birth outcomes of women treated with infliximab were comparable with those of the general population or of pregnant women with CD who were not treated with infliximab [61, 62]. Mahadevan et al. reported that the benefits of achieving and maintaining clinical remission in patients receiving infliximab during pregnancy superseded the potential risk of exposing the unborn child to the medication [58].

A pregnant woman with treatment-refractory CD who failed treatment with infliximab was successfully treated with *adalimumab* (Humira; Abbott Laboratories, Chicago, IL), a recombinant human IgG_1 monoclonal anti-TNF antibody [63]. The pregnancy was uncomplicated, and at 6 months, the infant showed normal growth and development [64]. Another case reported the use of *etanercept* (Enbrel; Amgen, Thousand Oaks, CA), a soluble TNF receptor fusion protein that binds to and inactivates TNF, in an uneventful pregnancy of a patient with refractory rheumatoid arthritis [65]. Etanercept has been shown to be excreted in breast milk, but it is not known whether the drug can be absorbed orally because it is such a large protein [66].

Thalidomide (FDA class X) is used in treatment of refractory CD. It has extensive teratogenic sequel including limb defects, central nervous system effects, and abnormalities of the respiratory, cardiovascular, gastrointestinal, and genitourinary systems. Thalidomide is contraindicated during pregnancy and breastfeeding. Women of childbearing age taking thalidomide should use two methods of contraception 1 month prior to starting therapy, during therapy, and for 1 month after stopping therapy.

Breastfeeding

Although the *American Academy of Pediatrics* recommends breastfeeding for at least 6 months after birth [67], many women who require drug therapy initiate breastfeeding less frequently, discontinue breastfeeding earlier than women who are not receiving medication [68], or do not breast-feed at all [69]. To date, infliximab has not been detected in human breast milk of nursing mothers [58, 59, 70, 71]. Also, Kane et al. found that infliximab was present in the mothers' sera, but not in the infants' sera [71]. Physicians should be aware that the fetus may be exposed to therapeutic monoclonal antibodies when administered to pregnant patients and the long-term implications on the child's developing immune system are unknown at this time.

8.1.7 Prognosis

8.1.7.1 Inheritance of CD in General

Patients are naturally concerned about passing their disease on to their offspring. Unfortunately, family history is the strongest predictor for developing

IBD. If one parent is affected, the risks of the offspring developing IBD are 2–13 times higher than in the general population [72–74]. One study estimated that the risks of IBD in first-degree relatives of probands with UC and CD were 1.6 % and 5.2–7.5 %, respectively, values that were even higher in the Jewish population [74, 75]. If both parents have IBD, the risk of their offspring developing IBD over their lifetime was estimated to be 35 % [74, 76].

Several studies suggest that breastfeeding may be protective against the development of IBD in the infant. In a meta-analysis of 17 studies, the eight highest quality studies showed a pooled odds ratio of 0.45 (0.26–0.79) for CD and 0.56 (0.38–0.81) for UC [77]. However, these were not mothers who had IBD themselves.

8.1.7.2 Fertility and Sexual Heath in General

The effect of CD on fertility is controversial. Some studies, especially older, claim that fertility is subnormal [78, 79]. Relationships, sexual health, and fertility in IBD patients are interrelated. Chronic IBD decreases quality of life [80]. The symptoms of IBD, including diarrhea, problems with continence, and weight loss undoubtedly, have an effect on body image particularly in adolescents and young adults. The side effects of treatment such as weight gain due to steroids may also cause feelings of unattractiveness and loss of self-esteem. Children with IBD may experience delays in growth and puberty, and this also has a serious effect on confidence and body image. Young people with IBD may therefore experience difficulty in forming intimate relationships and worry that they may not be able to have a normal sex life. Fear of inheritance of IBD in the offspring and fear of fetal exposure to IBD therapies can lead to voluntary childlessness. Stoma surgery is a major life event, particularly in teenagers [81]. The development of IBD may put great strain on a previously good relationship, and women who are in a relationship experience more difficulties in their sexual life than nonaffected women of a similar age [82, 83].

Variables such as systemic effects of disease, for example, fatigue and anemia, as well as medication effects, such as corticosteroids, on libido can impact sexual activity. Postoperative dyspareunia can similarly affect sexual activity and impact the chance of conceiving [78].

Dyspareunia, involvement of the Fallopian tubes in the disease process, general ill health, and medical advice against pregnancy have all been implicated [3, 84]. Dyspareunia and vaginal candidiasis are more common than in healthy women, which may account for some of these difficulties [85]. Fertility appears to revert to normal after induction of remission in women with CD. Women who have their first pregnancy after the onset of IBD have fewer pregnancies than population controls, whereas women who became pregnant prior to onset of IBD have similar reproductive history [86]. In addition, women with CD have a delayed age of first pregnancy after being diagnosed [87] and have been shown to have fewer children than might be expected after diagnosis with a higher rate of failure to conceive [84]. These are probably some of the reasons for lower incidence of IBD in pregnancy. Community-based and population-based studies suggest infertility rates of CD patients in general (5–14 %) similar to the general population [86, 88]. Surgery for CD may decrease fertility compared with medical therapy alone. Development of postoperative pelvic adhesions contributes to higher infertility rate [88]. Khosla et al. found that the infertility rate of 112 married women with CD was similar to that in the general population [89]. The results of a case-control study of 275 women with CD from five European countries [84] are in sharp contrast to those of Khosla et al. [89]. Mayberry and Weterman determined whether the patients were using birth control, were having sexual relations, and were advised by their physicians not to become pregnant. Patients with CD had a notable reduction in the number of children born and a substantial increase in the incidence of prematurity. The rate of miscarriage and Cesarean section was unaffected by CD. The site of the disease did not affect these findings. Although 40 women with CD were told not to have children, the women used birth control less but still had fewer pregnancies.

8.1.7.3 Pregnancy Outcomes

Pregnancy Outcomes in General

Population-based studies in women with CD have shown an increased risk of preterm delivery, low birth weight, and small for gestational age infants [8, 42, 90, 91]. In 1972 authors stated that in case of an unplanned pregnancy occurring in a patient with active CD whose family is already complete, there are strong indications for suction termination in the first trimester [92].

Predictors of poor outcome (preterm birth, low birth weight, intrauterine growth retardation, small for gestational age infants, congenital anomalies, APGAR scores, and stillbirth, and complications of labor) in large study by Mahadevan et al. were having IBD, either UC or CD, and having had surgery for IBD [52]. Unlike other studies, disease activity and medication use were not predictors of adverse outcome. In prior studies, disease activity at conception was associated with a higher rate of fetal loss [93] and preterm birth [94]; disease activity during pregnancy was associated with low birth weight and preterm birth [95, 96]. Many theories have been put forth for this observation, but the etiology is unclear. One hypothesis is that an increase in circulating prostaglandin levels during a flare could initiate preterm labor with the induction of smooth muscle contraction [97, 98]. Another theory is that the role of increased gut permeability during increased inflammation could alter nutritional and immunological factors affecting labor [97].

Other potential predictors of an adverse outcome include ileal CD [99] and previous bowel resection [99, 100]. In the general population, smoking is a known risk factor for LBW infants and for disease activity in CD women [2]. Pregnant CD patients who smoke are at a substantially increase risk for LBW and preterm delivery [2, 101].

Subclinical infection is another problem. Although the women are free of symptoms at the beginning of the pregnancy, it is possible that inflammation may have been present on colonoscopy and/or biopsy and that this subclinical inflammation is responsible for the higher rate of small for gestational age births [99]. These women felt too well to present for investigation, and so such data are unavailable. Whether subclinical inflammation is the factor responsible must be examined in future prospective trials.

The patients with ileostomies have been shown to be capable of normal pregnancies [44, 79, 102]. In a study by Porter and Stirrat, patients with ileostomies were shown to have lower hemoglobin during pregnancy [103] but apparently without ill effect. Stomal problems of displacement and prolapse are not uncommon, but remit postpartum.

Perinatal Outcome

Once pregnancy has been achieved, healthy offspring can be expected. Abnormal birth weight, stillbirth, spontaneous abortion, and congenital abnormalities are no more common than in the population without inflammatory bowel disease [89]. Mahadevan and Li found that the disease activity was not predictive of an adverse outcome in any category [104]. Even when limited to the presence of moderate to severe disease activity, there was still no association with an adverse outcome. The majority of patients in this cohort with both UC and CD, however, did have inactive or mild disease throughout pregnancy. Similarly, a population-based study from Denmark also did not find an increased risk of adverse events associated with disease activity [105]. They reported that women with active disease had adjusted risks of LBW, LBW at term, preterm birth, and congenital anomalies of 0.2 (0.0–2.6), 0.4 (0.0–3.7), 2.4 (0.6–9.5), and 0.8 (0.2–3.8), respectively. However, the crude risk of preterm birth was increased, with an odds ratio (OR) of 3.4 (1.1–10.6) in those with moderate-high disease activity. Overall, these two population-based studies did not show a significant role of disease activity in predicting adverse outcomes above that expected with the diagnosis of IBD alone.

Pregnancy Outcomes After Emergency Surgery

Emergency surgery during pregnancy has been reported to be associated with a high risk of fetal loss (60 %). Five of the six patients described in the series by Hill et al. had a free perforation of CD and one fetus was lost [29].

Maternal Morbidity and Mortality

Vomiting has been reported to cause stomal prolapse requiring revision after delivery. Back in 1972 there was a concern about patients with abscess and fistula formation, because in the puerperium, the rapid involution of the uterus may tear apart adhesions which wall-off abscess cavities, thus leading to spreading peritonitis [92].

Five of the six patients described in the series by Hill et al. had a free perforation of CD. The maternal mortality was nil [29].

8.2 Acute Ulcerative Colitis

8.2.1 Introduction

An association between UC and pregnancy was noted by Gossage and Price over century ago at a symposium held at the *Royal Society of Medicine* in 1909 [106].

8.2.2 Effect of Pregnancy on Ulcerative Colitis

Pregnant patients with UC, as well as CD, can be classified in four categories [5]:

- Inactive at conception
- Active at conception
- Arising during gestation
- Arising during the puerperium

Willoughby and Truelove found that patients with UC who had inactive disease at conception tended to remain so during the pregnancy, whereas those with active disease had continued and even worse disease activity [107]. Others show that around 50 % of active cases had improvement and in all cases it was by the end of eighth week of pregnancy [102]. Nielsen et al. reported an exacerbation rate of 34 % per year during pregnancy and 32 % per year when not pregnant in women with UC [94]. In general, women with IBD are as likely to flare during pregnancy as they are when not pregnant. It has been reported that 30–50 % of female patients with UC will have an exacerbation while pregnant or in the early postpartum period [108].

The effects of multiple pregnancies on UC do not show definite pattern, and although the numbers are small, there is an agreement that there are no consistent effects in successive pregnancies [102].

Relapses of UC usually occur in the first trimester or the puerperium [107, 109–113]. It has been suggested that the high circulating levels of serum 17-hydroxycorticosteroids during the second and third trimesters induce remission at this time [114]; levels fall sharply following delivery [115]. Although cortisol comprises 90 % of total plasma 17-hydroxycorticosteroids in the third trimester of pregnancy, the increase is actually due to elevated levels of the glucocorticoid-binding protein, transcortin. Biologically active cortisol remains unchanged [111] and there is no increased steroid action in pregnancy. Severe colitis during pregnancy is rare [116].

8.2.3 Incidence

History taking is very important because the causes of acute abdomen between operated (due to UC) and never-operated patients are different. Although UC and pregnancy frequently coexist, therefore, it is rare for fulminating disease to ensue and require operation to save the mother's life before or after delivery. Up to 1987 there were only 35 cases in the literature [5, 102, 117–126]. It is even rarer to have patients operated for UC before pregnancy presenting as acute abdomen during pregnancy. The causes of small bowel obstruction in operated patients are small bowel adhesions, small bowel volvulus or external compression of gravid uterus on IPAA, or small bowel proximal to IPAA [26, 127].

8.2.4 Diagnosis

8.2.4.1 UC in General

Several reports have been published on the safety of colonoscopy and flexible and rigid sigmoidoscopy in pregnant patients. These authors concluded that endoscopy does not induce labor or result in significant side effects to the mother or fetus and can be performed safely in medically stable pregnant patients [19, 22, 23].

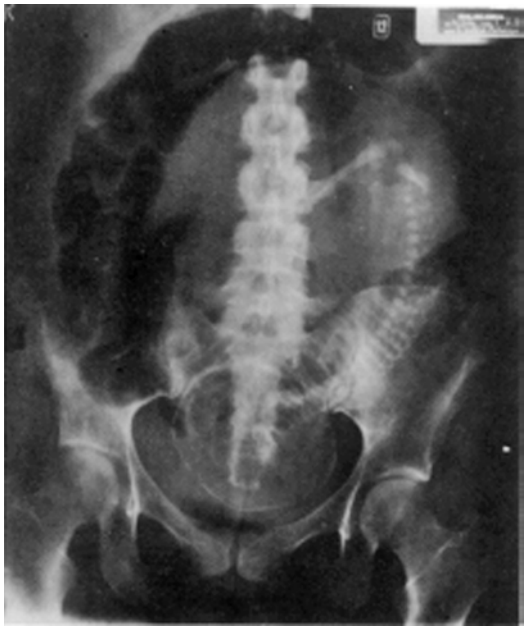

Fig. 8.1 Supine X-ray in 30 weeks pregnancy. Gravid uterus displacing gas-filled colon without dilatation [128]

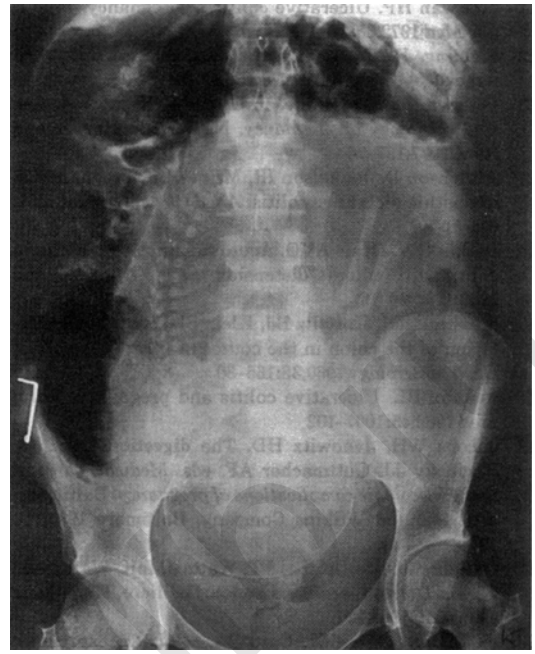

Fig. 8.2 Toxic dilatation of the colon in 33rd week of pregnancy [129]

Ultrasound is used extensively in obstetric practice and is the safest form of radiological imaging. It can be used to assess abscess formation, as well as bowel wall thickness (as evidence of active inflammation).

8.2.4.2 Emergency Settings

Clinical examination is especially difficult in the third trimester of pregnancy due to enlarged gravid uterus and displacement of intraperitoneal organs. Additional difficulty is that physicians are reluctant to perform initial and repeated plain X-rays of the abdomen which would otherwise be done in nonpregnant patients if indicated. Specific difficulty during the third trimester is dislocation of small and large bowel making radiologic diagnosis more difficult (Fig. 8.1).

It is difficult to measure colonic dilation in different colonic segments if toxic megacolon is suspected, again, especially in the third trimester (Fig. 8.2).

More recently, MRI has been used safely in pregnancy [130, 131], but its use in emergency settings is still limited.

8.2.5 Treatment

8.2.5.1 Indications for Emergent Operation

From the available data around the 1980s, between 2.3 and 3.9 % of patients with UC during pregnancy required surgical intervention [117, 132]. Indications for emergent operative intervention in patients with UC in general include intractable hemorrhage, perforation, toxic colitis, and fulminant disease refractory to medical therapy. The same indications and timing of the emergent operation are the same in pregnant patients (Fig. 8.3).

8.2.5.2 Surgical Procedures

Multiple procedures, ranging from diverting loop ileostomy to total proctocolectomy, have been described to treat fulminant and toxic UC in pregnant patients. Some have proved to be unsuitable. For example, ileostomy alone is inadequate because of the continued risk of perforation of the diverted colon. Proctocolectomy also is inappropriate in the acute situation because it is a

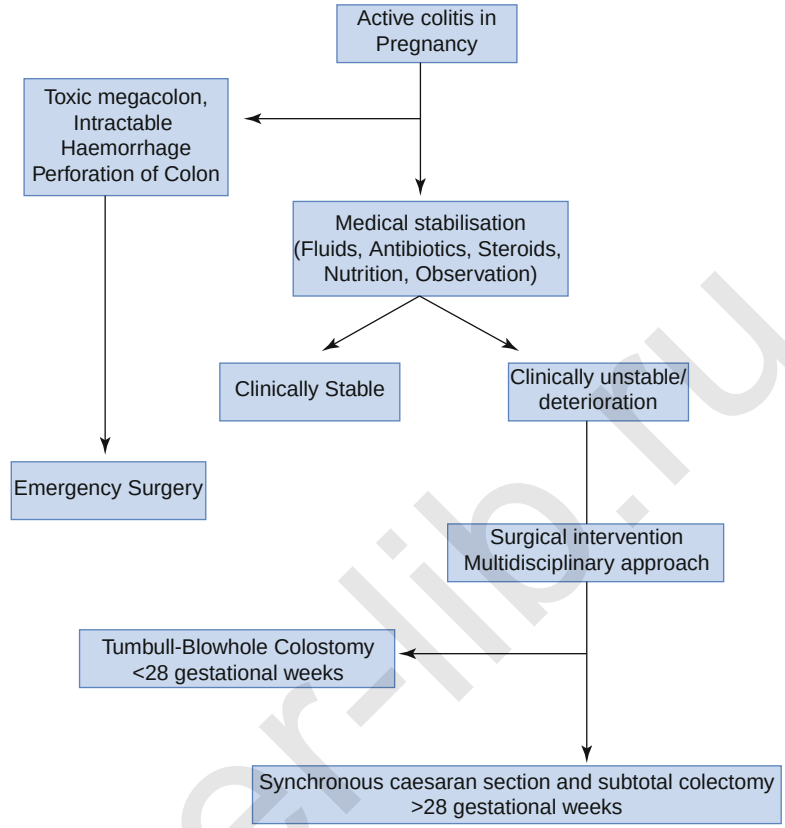

Fig. 8.3 Treatment algorithm for pregnant patients with ulcerative colitis [133]

long, complex operation and requires pelvic dissection, which may be difficult because of uterine enlargement and grossly dilated pelvic vessels. Moreover, increased manipulation of the gravid uterus increases the risk of spontaneous delivery and preterm labor.

Turnbull "Blowhole" Procedure

In 1971, Turnbull et al. advised colonic decompression and diversion by cutaneous blowhole colostomy and loop ileostomy for patients with toxic dilation of the colon to prevent perforation and sepsis in the severely ill patient [134]. Emergency colectomy in this situation is reported to have a high maternal and fetal mortality rate of 53 and 29 %, respectively [135]. Newer studies show no maternal and fetal mortality performing emergency colectomy [133]. Ooi et al. reported good success with Turnbull technique in two pregnant patients with toxic colitis (Figs. 8.4 and 8.5) [136]. This procedure has the advantage of a short anesthesia time and minimal surgical trauma, which may dramatically improve outcome in extremely ill patients. Moreover, some patients have colons so severely diseased

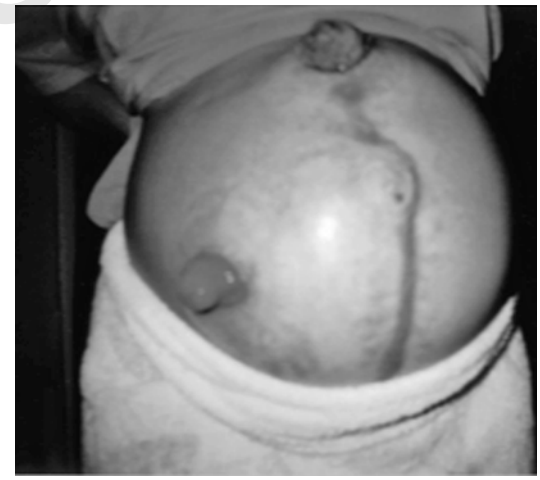

Fig. 8.4 The gravid patient with healed midline scar, loop ileostomy (to the right of midline), and skin-level transverse colostomy [136]

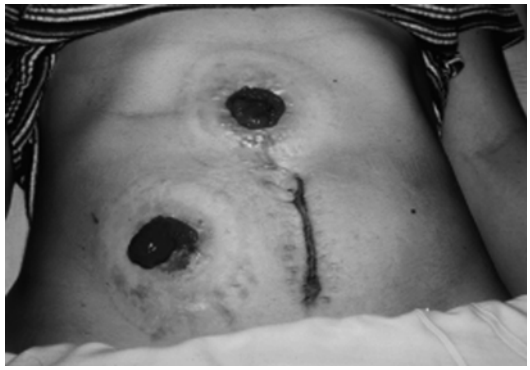

Fig. 8.5 The same patient after elective Cesarean section, showing a scaphoid abdomen with transverse colostomy and ileostomy and ready for definitive restorative proctocolectomy [136]

that mere mobilization puts them at risk for iatrogenic perforation and diffuse fecal contamination. The disadvantage of a blowhole colostomy is that the remaining colon may cause ongoing toxicity (severe hemorrhage, sepsis) requiring repeat operation leading to increase risk to mother and fetus. Therefore, the Turnbull "blowhole" procedure is far less practiced currently.

Total Abdominal Colectomy

In 1951, Crile and Thomas advised total abdominal colectomy and end ileostomy with preservation of the rectum for toxic megacolon [137]. Because simple ileostomy produced unsatisfactory results, the dilated colon could perforate despite diversion. Mortality rates of 50–70 % were commonly reported, a rate not much better than that achieved with medical therapy alone in general population [138]. Total abdominal colectomy, with preservation of the rectal stump and Brooke ileostomy, is the most commonly performed procedure for severely ill patients who require urgent or emergent colectomy for fulminant or toxic UC. This option is preferable because it eradicates most of the disease and requires no bowel anastomosis or deep pelvic dissection, while allowing the patient to be weaned from most medical agents. In addition, it does not preclude or compromise the results of subsequent IPAA [32, 139]. After colectomy a decision should be made regarding the rectal stump. Stump breakdown and leakage leading to intra-abdominal sepsis is a major concern. The stump can be handsewn in two layers and wrapped with the omentum and this is a safe procedure as long as the inflammatory process has not compromised the integrity of the bowel wall. Another option is to bring out the rectal stump as a mucus fistula. If a mucus fistula is to be placed, the remnant stump should be kept long. Because of the enlarged uterus, the stump will need to be brought out through an extraperitoneal plane deep to the broad ligament and dilated ovarian vessels. The rectum is irrigated with Betadine at the time of surgery to remove the excess bloody mucoid material and a rectal tube left in place to keep it decompressed in the postoperative period [32].

Rectal excision when indicated, for example, in intractable rectal hemorrhage, may be complicated by the need for hysterectomy. This is because of the risk of traumatizing the engorged pelvic veins leading to severe hemorrhage.

A stomal therapist should mark the patient before surgery. In pregnant patients, the optimal location for the stoma on the abdominal wall is usually higher than normal because the stoma will drop to a lower position after delivery.

Synchronous Cesarean Section and Subtotal Colectomy

According to previous reports, the majority of pregnant women requiring urgent surgery for colitis have undergone metachronous colonic surgery and Cesarean or vaginal delivery with a high maternal and or fetal morbidity and mortality. Only three cases have previously been reported where synchronous colectomy and delivery have taken place, two occurring at 32 weeks and one at 28 weeks gestation without maternal or neonatal morbidity or mortality [124, 133, 140].

8.2.5.3 Perioperative Considerations

Thromboprophylaxis in General IBD Patients (ECCO Consensus)

See Sect. 8.1.

8.2.5.4 Obstetric Considerations

In patients presenting with acute abdomen, the treatment depends on the trimester of pregnancy.

During the first two trimesters, only surgical treatment of the cause of acute abdomen is treated. In the third trimester, due to high incidence of postoperative (during first few days) spontaneous induction of labor, Cesarean section is recommended [32, 51].

After surgery without Cesarean section, fetal monitoring should begin in the postanesthesia recovery room, and the patient should be watched carefully for spontaneous labor.

IPAA alters the anatomy of the gastrointestinal tract, placing the ileal pouch at risk from compressive obstruction by the gravid uterus. Induction of labor in a near-term fetus is a reasonable initial method of management preventing possible external compression on the IPAA and small bowel obstruction [127].

8.2.6 Prognosis

8.2.6.1 Fertility and Sexual Health in General

Relationships, sexual health, and fertility in IBD patients are interrelated (contrary to CD, studies have shown that UC does not affect fertility [107, 117, 141]. Other studies that found reduced fertility were probably flawed owing to short follow-up periods, patient selection, and an inadequate medical control of the disease [114, 142] or inadequate numbers of patients observed [143]. Therefore, women with UC have fertility rates similar to the general population prior to surgery [86, 88, 107]. There is severalfold increase in infertility rate after an ileal pouch-anal anastomosis (IPAA) [144]. This finding was confirmed by Johnson et al. who showed a 38.6 % infertility rate in UC patients after IPAA versus 13.3 % in UC patients managed nonoperatively [145]. The reduction in fertility may be due to surgery in the pelvis and the consequent adhesions and damage to the reproductive organs. Patients who undergo a proctocolectomy with ileostomy also experience a reduction in fertility [146], as do patients with familial adenomatous polyposis who undergo IPAA [147].

The risk of infertility after IPAA should be discussed with the patient prior to surgery as one of the potential risks of the operation. It is unclear if techniques such as laparoscopic IPAA or a subtotal colectomy with rectal stump and ileostomy during the childbearing years and then creating an IPAA later in life are helpful in reducing infertility rates. The drawbacks of the latter procedure include rare ileostomy complications during pregnancy such as obstruction and stoma-related problems [148], technical difficulties in creating a functioning pouch several years after the initial surgery, and the patient's reluctance to have a long-term ostomy. The most recent studies show that total laparoscopic total colectomy with IPAA causes significantly less infertility rates compared to the same operation by open approach [149, 150]. "Easier" decision is when an acute abdomen is present with absolute indication for emergent operation. In such cases, it is a lifesaving operation, and fertility is then the third goal after mother and fetal outcome.

More significantly, in a study by Anderson et al., 50 % (2/4) of operated patients developed severe postoperative pelvic and subphrenic abscesses. Three patients had difficulty conceiving or secondary infertility since the surgery. The social morbidity as a result of this was high, with three of four patients divorced by their spouses [129].

8.2.6.2 Pregnancy Outcomes in General

UC occurring for the first time during pregnancy has previously been considered dangerous, with a maternal mortality rate in the range of 15 % [129]. In years past, the risk to the mother was considered so high that therapeutic abortion was advocated if severely active disease occurred during pregnancy [5]. Currently, prompt and aggressive medical therapy is the first line of treatment and has the best chance of halting disease progression. In contrast to CD, women with UC had similar rates to controls of preterm delivery, low birth weight, and small for gestational age infants but a significantly higher rate of congenital malformations (7.9 % vs. 1.7 %) [91]. The study did not account for medication use and the results have not been replicated in other studies. The *H*ungarian *C*ase *C*ontrol *S*urveillance of congenital anomalies was queried from 1980 to 1996,

with the odds ratio of congenital anomalies in UC patients versus controls of 1.3 (0.9–1.8), adjusted for parity, age, and medication use [151].

Predictors of poor outcome (preterm birth, low birth weight, intrauterine growth retardation, small for gestational age, congenital anomalies, APGAR scores, stillbirth, and complications of labor) in large study by Mahadevan and Li were significantly higher having IBD, either UC or CD, and having had surgery for IBD [104]. Unlike other studies, disease activity and medication use were not predictors of adverse outcome. In prior studies, disease activity at conception was associated with a higher rate of fetal loss [93] and preterm birth [94]; disease activity during pregnancy was associated with low birth weight and preterm birth [95, 96]. Many theories have been put forth for this observation, but the etiology is unclear. One hypothesis is that an increase in circulating prostaglandin levels during a flare could initiate preterm labor with the induction of smooth muscle contraction [97, 98]. Another theory is that the role of increased gut permeability during increased inflammation could alter nutritional and immunological factors affecting labor [97].

Conversely to CD, smoking in UC women does not increase their risk of preterm delivery [152]. However, given the known risk of smoking on the individual and the baby, smoking cessation should be encouraged in all scenarios.

8.2.6.3 Maternal and Fetal Outcome After Emergent Operation

Elective Surgery

Surgery is to be avoided as far as possible, because earlier reports claim that colectomy in pregnancy has been previously reported to carry a 60 % risk of inducing spontaneous abortion. In the period between 1951 and 2004, a total of 37 cases were found [5, 51, 102, 118, 119, 123, 124, 128, 129, 136, 140, 153–156]. Overall, the fetal and maternal mortality was 49 and 22 %, respectively. The majority of maternal and fetal mortality seen in this review was found in cases reported before 1987. From 1951 to 1987, the fetal and maternal mortality was 67 and 24 %, respectively. Similar outcomes up to 1987 were found by another study with 35 cases (fetal mortality 53 %, maternal mortality 29 %) [129]. While maternal death is becoming less frequent, the high stillbirth rate probably reflects the severity of the disease rather than the effects of operation. After 1987, the fetal and maternal mortality was zero and the postoperative morbidity was negligible. Recently, a small case series from Manchester recently reported six women who had surgery for intraperitoneal sepsis in CD during pregnancy. Five healthy babies resulted from these pregnancies although one miscarriage occurred in a patient with a surgical complication [29].

Emergency Surgery

Higher fetal mortality is found during and after emergency surgery during pregnancy. A review in 1972 by Becker of the surgical treatment of toxic colonic dilation in pregnancy revealed maternal mortality of 36 % (4/11) and fetal mortality of 100 % [157]. Anderson et al. reported three pregnant patients who had subtotal colectomy and ileostomy for toxic dilation during the third trimester or within 5 days of delivery, and the fourth underwent proctocolectomy postpartum for intractable colitis [129]. There were no maternal deaths but fetal mortality was 50 % (2/4), with one surviving child weighing only 1.4 kg at the 33rd week of gestation.

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Spleen

9

9.1 Splenic Rupture

9.1.1 Definition and History

Splenic rupture can occur with any degree of trauma to a normal spleen or minimal trauma to a diseased spleen. Eastman and Hellman made three important statements with respect to rupture of the spleen in pregnancy [1]:

- Rarity of the condition
- Danger of confusing it with obstetric complications
- Importance of preexisting disease of the spleen

The first case of splenic rupture in pregnancy was reported by Sylvester Saxtorph (Fig. 9.1) in 1803 [2].

Fig. 9.1 Sylvester Saxtorph, Danish obstetrician (1772–1840), first described splenic rupture during pregnancy in 1803

In 1866 Simpson referred to three cases of fatal rupture of the spleen which had occurred respectively in the pregnant, parturient, and puerperal state. He pointed out the circumstance that, during pregnancy, there is often, if not generally, an increase of the white particles in the blood – in other words, a kind of normal or physiological leukocythemia. A certain amount of softening very frequently accompanies the hypertrophy of the spleen and predisposes to the laceration of the organ under strong exertion and muscular effort, blows, etc. [3]. One of the earliest cases was by Hubbard in 1879, but the authenticity of this report is open to question as the findings are not recorded too clearly or soundly [4]. Kotschnew and Manankow gave the first overview of splenic rupture in 1930. The first nine cases were confirmed through autopsies. In 1958, Sparkman provided an overview of 44 recorded cases of splenic ruptures in pregnancy, with detailed analysis of their etiology [5]. In 1967, Buchsbaum added an additional 27 cases to the list [6]. Literature up to 2003 indicates 18 more cases, bringing the total up to 89 [7]. Classification is made according to the cause:

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Incidence according to the cause is presented in Table 9.1.

- Traumatic
- Following antecedent disease
- Associated with toxemia of pregnancy
- Spontaneous

9.1.2 Classification

9.1.2.1 Traumatic Splenic Rupture

Etiopathogenesis

In its position behind the rib cage, cushioned under the left hemidiaphragm, the spleen is protected from most forms of direct trauma. The pathogenesis of rupture has been explained by Schamaun as a countercoup mechanism in which the spleen, because of its relative mobility, is driven against the vertebral column and ruptures [9]. Another mechanism explains the rupture on the basis of the ligamentous suspension of the spleen, which allows a limited degree of motion and then sudden fixation and laceration. Schonwerth described the deep inspiration at the instant of trauma (the fright mechanism) displacing the superior pole downward, while the lower pole is relatively fixed by the phrenocolic ligament causing flexion of the spleen. Trauma over the rib cage then results in capsular laceration on the stretched convex surface [10]. Sometimes underlying pathology and minor (repeating) trauma are unknown or unrecognized. In cases of previously changed spleen or additional pathology, even a minor or minimal but repetitive trauma is sufficient for splenic rupture. In one case, the prominent exostosis arising from the tenth rib had roughened and thickened a circumscribed area of the splenic capsule (Fig. 9.2) over the years as a result of the respiratory excursions and movement of daily life. Laceration of the unthickened lower pole finally occurred during pregnancy, at a time when splenic size, vascularization, and position may be altered [11]. In two cases, initially spontaneous splenic rupture was diagnosed but cavernous hemangioma of the spleen as the source of hemorrhage was confirmed. It may be that minor trauma was the precipitating factor [12, 13].

Specific etiology is complicated delivery where the spleen can be traumatized [14]. It is also mentioned in the section *Postpartum Splenic Rupture*.

Table 9.1 Pregnancy-related causes of splenic rupture [8]

Etiology	Incidence (%)
Normal pregnancy	58
Splenic ectopic pregnancy	24
Post-vaginal delivery	5
Post-Cesarean section	5
Preeclampsia	2.5
Ruptured ectopic pregnancy	2.5
HELLP syndrome	2.5

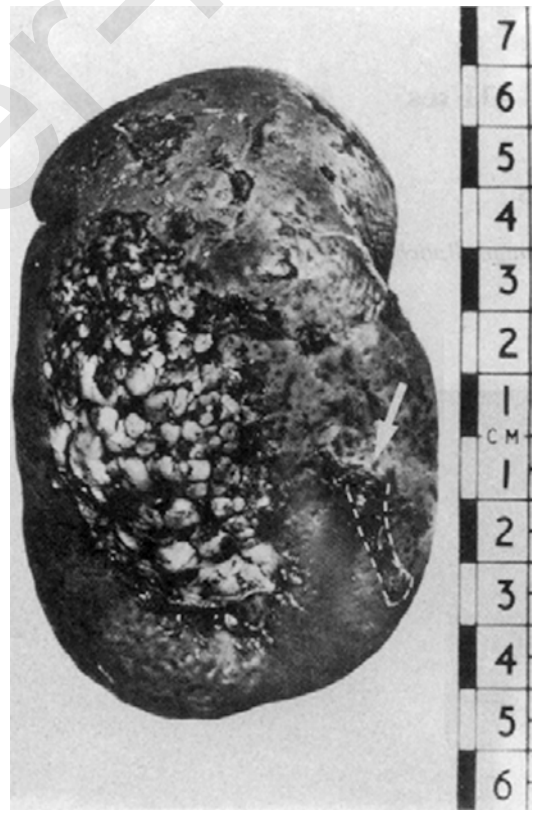


Fig. 9.2 The convex surface of the spleen to show the roughened capsule. The exostosis (*dotted outline*) has been replaced in the laceration (*arrow*) [11]

9.1.2.2 Splenic Rupture Associated with Toxemia of Pregnancy

This classification was introduced by Sparkman in 1958 because a number of cases were associated with toxemia of pregnancy [5]. The authors suggest that toxemia may be associated with specific changes, such as hypertension, thrombosis, and diffuse angiitis, which may predispose toward vascular or visceral rupture [15–19].

9.1.2.3 Spontaneous Rupture of Normal Spleen

Definition

Opinion is divided as to whether the normal spleen ever ruptures spontaneously. Some authors deny the possibility [20], while others accept it as a rare occurrence [21]. No creditable experimental work could be found to describe changes in the spleen during pregnancy. Nelson and Hall reported a markedly diminished and almost total absence of germinal centers in lymph nodes of pregnant women at term [22]. Denehy et al. reviewed 89 cases of splenic rupture in pregnancy; only 2.2 % (2/89) were documented to be spontaneous in the puerperium [16]. In 1958, Orloff and Peskin established the following four criteria for the diagnosis of spontaneous rupture of a normal spleen [23]:

- No history of trauma
- No systemic disease that can affect the spleen
- No evidence of perisplenic adhesions to suggest previous trauma
- Splenic parenchyma, vasculature, and capsule normal macroscopically and histologically

A similar definition is by Sparkman [5]. More frequent examination of the surgical specimen will reveal pathologically changed spleens. The high incidence of secondary rupture indicates that as more adequate histories are obtained and reported, more cases of minor trauma forgotten by the patient during the long latent period will be revealed [6]. It is likely that the so-called spontaneous rupture in fact occurs as a result of capsular injury by the lower ribs from trivial blunt trauma (for instance, coughing and straining) either unnoticed by the patient at the time, or forgotten since, in the light of subsequent events [23]. These factors will markedly lower the number of cases designated as spontaneous rupture of the normal spleen in pregnancy. Sheehan and Falkiner in 1948 analyzed 163 routine obstetric necropsies and found that in the three following clinical conditions, the spleen was commonly enlarged (>200 g) in the second half of pregnancy [24]:

- Severe anemia of pregnancy
- Accidental hemorrhage of the abruptio type
- Puerperal thrombophlebitis or gross septic endometritis

This enlargement is an important risk factor for the splenic rupture.

Incidence

Zuckerman and Jacobi reviewed the world literature up to 1937 and collected 28 such cases, regarding 21 of these as genuine spontaneous rupture of the normal spleen and 7 as doubtful [25]. Another 21 cases of spontaneous rupture of a normal spleen during pregnancy or labor have been reported in the English language literature since 1958 [26]. However, spontaneous rupture in pregnancy without antecedent trauma is rare and occurs most commonly in the third trimester or puerperium [15, 26].

Pathophysiology

Hershey and Lubitz in discussing spontaneous rupture of the malarial spleen cite the pathogenesis and mechanisms of rupture of the normal spleen, suggesting a threefold mechanism [27]: firstly, local lesions as points of weakness; secondly, increase of tension due to hyperplasia and engorgement; and thirdly, compression by the abdominal musculature. The influence of increased intra-abdominal pressure and the physiological engorgement of the spleen during pregnancy seems significant. However, the authors are unable to postulate any one theory as to the etiology of spontaneous rupture of the normal spleen. Therefore, it is obvious that minimal trauma, such

as straining for a bowel movement, coughing, vomiting, sneezing, or jumping, may be causally related to splenic rupture by increasing intra-abdominal pressure, which is then transmitted to a number of intra-abdominal organs. In addition, the hemodynamic changes that accompany pregnancy may predispose to spontaneous splenic rupture via two possible mechanisms. First, the combined effects of the increased circulating blood volume and reduced volume of the peritoneal cavity due to expansion of the gravid uterus may make the spleen more fragile and therefore more vulnerable to rupture [28]. In keeping with this hypothesis, it is interesting that almost all cases have occurred in multiple pregnancies or in the third trimester of pregnancy. Secondly, circulating hormones such as estrogen and progesterone cause structural changes to the spleen that may increase the risk of splenic rupture during pregnancy even after minor trauma [29]. In earlier works pregnancy was thought to predispose the spleen to rupture. Therefore, pregnancy was listed as an etiological factor in splenic rupture. This view completely disregarded Barcroft's work, in which he demonstrated on a small number of dogs that the exteriorized spleen shrinks markedly during pregnancy [30]. Furthermore, examination of the spleen at autopsy in eight pregnant female dogs with normal spleens failed to reveal any correlation between splenic weight and duration of pregnancy.

9.1.2.4 Postpartum Splenic Rupture

Incidence

To date, only eight cases of spontaneous postpartum splenic rupture are reported in the literature [15–19, 31]. There are also several cases during labor [2, 32].

Etiopathogenesis

The etiology of spontaneous postpartum splenic rupture remains speculative at best.

Splenic Enlargement (*Per Se*)

It has been suggested that splenic enlargement and increased blood volume normally seen in pregnancy in addition to the trauma of parturition could be implicated in the pathogenesis of some cases of splenic rupture (Fig. 9.3), but this is controversial.

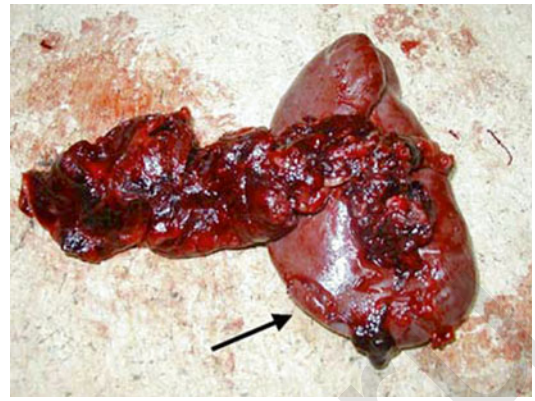


Fig. 9.3 Rupture of splenic capsule (*arrow*) on the lower pole [7]

Blunt (Internal) Trauma

Suggested etiological factors in cases of true spontaneous rupture include blunt internal trauma, as proposed by Barnett (i.e., occasioned by coughing, vomiting, coitus in the latter stages of pregnancy, and the bearing-down efforts of the second stage of labor) [14, 33]. Several authors have suggested a short splenic pedicle or deeply recessed location of the spleen as congenital factors that might contribute to rupture by compressing the diaphragm during coughing, sneezing, or vomiting [23]. Whether the episode of tonic-clonic seizure that occurred in one case could be considered traumatic enough to induce injury to the spleen will remain unanswered [34].

Intrasplenic Aneurysm

Another widely held theory is that rupture of a small intrasplenic aneurysm may occur, with all trace of the aneurysm being destroyed by the hemorrhage, thus preventing its discovery by the pathologist. Certainly larger aneurysms of the splenic artery are more prone to rupture during pregnancy, and even spontaneous rupture of the splenic vein has been reported.

Manipulation During Cesarean Section

During operation, traction with undue force with sharp- or blunt-edged instruments during Cesarean delivery and insertion of packs could

theoretically cause abrasive injuries to an already congested organ such as the spleen. Excessive force in exploring the upper abdomen and manual expression of the fetus by forceful pushing on the upper abdomen at the time of Cesarean delivery or even while removing clots from the paracolic gutters might lead to splenic injury, especially in those with high blood pressure [31].

Rapid Plasma Expansion

It might also be possible that rapid plasma expansion with blood products and other volume expanders could result in a rapid volume increase within the spleen, predisposing it to rupture [34].

9.1.3 Clinical Presentation

9.1.3.1 History Taking

When the patient has been involved in some obvious and serious accident and when there is associated bony and soft tissue injury (the most common is fracture of ribs, which occurs in 35 % of cases of traumatic rupture of the spleen in the general population), it is frequently obvious that intraperitoneal bleeding has taken place. In some instances the date of accident may be remote from the time of admission and may, under some circumstances, be forgotten altogether. In approximately 40–50 % of cases of rupture of the spleen, no history of trauma is obtained.

9.1.3.2 Clinical Examination

Rupture may become manifest:

- *Immediately* following the trauma
- *Delayed* and only recognized following a latent period

The immediate rupture usually presents no problem in diagnosis. The significance of the delayed form of rupture of the spleen was first emphasized in the general population by McIndoe in 1932 [35]. He reported that the acute onset of symptoms of rupture must occur 48 h or longer following the original injury if it is to be called *delayed* rupture. In many cases the latent period exceeds 1 week.

The classical triad of epigastric pain, tenderness, and Kehr's sign is said to be characteristic of ruptured spleen. Pain and tenderness are commonly reported. Epigastric pain is perhaps the symptom most commonly and most consistently reported. In some cases there is an associated episode of vomiting. By and large the pain is made worse on coughing, deep breathing, and moving. At rest the pain may be almost completely relieved. Progressive severity of pain is common. In most cases reported, pain that was well tolerated at rest becomes more severe and analgesic medication is requested. In a few cases dyspnea is reported due to the expanding intraperitoneal mass, to declining circulating blood volume, or to loss of hemoglobin.

Kehr's sign presents diaphragmatic irritation referred to the left shoulder tip region, and some authors say it is almost pathognomonic when present. Blood from any cause in the left subphrenic space causes positive Kehr's sign and the most common are splenic rupture and ectopic pregnancy. Kehr's sign is present in a small minority of these patients.

Dullness on percussion over the left upper quadrant is an important sign. The enlarging uterus makes percussion and palpation of upper abdominal masses more difficult. Barnett states that in pregnancy, the enlarged gravid uterus does not give rise to *Ballance's sign* [33]. It is dullness to percussion in the left flank/left upper abdominal quadrant and shifting dullness to percussion in the right flank. The dullness in the left flank is due to coagulated blood, the shifting dullness on the right on altering position due to fluid blood.

In later stages the pain can become generalized, with distention and rigidity. Muscle spasm may not be present even in the presence of intraperitoneal blood. Eventually more than half of the patients will suffer hemorrhagic shock if the condition is left untreated [16].

Some authors have noted the confusing coexistence of hypertonicity of uterine muscle. Whether this is due to local peritoneal irritation is not known.

Postpartum Splenic Rupture

Rupture of the spleen in the postpartum period poses a significant difficulty for early diagnosis,

because more common entities present with similar clinical findings especially early in the course of the rupture.

9.1.4 Differential Diagnosis

9.1.4.1 During Pregnancy

The differential diagnosis of spontaneous splenic rupture in the general, nonpregnant population includes local splenic disorders, such as splenic cysts and diffuse angiomatosis; hematologic diseases, such as hemophilia, congenital afibrinogenemia, and hemolytic anemia; metabolic disorders, such as amyloidosis, Wilson's disease, Gaucher's disease, and Niemann-Pick disease; drug induced, such as intravenous heparin, warfarin, and streptokinase; iatrogenic causes, such as extracorporeal shock wave lithotripsy and clamping of the portal triad; and miscellaneous, such as vomiting, uremia, systemic lupus erythematosus, and other connective tissue diseases. Most notable in the differential diagnosis are the infectious causes, such as infectious mononucleosis, which is considered the most common cause of spontaneous splenic rupture, as well as malaria [36].

In the first trimester it is usually confused with ruptured ectopic pregnancy. In the last trimester placental abruption and rupture of the uterus are the two most likely differential diagnoses. However, in the case of rupture of the spleen, the uterus is not tender or hard, and fetal heart sounds can usually be heard. The presence of referred pain in the left shoulder area should always alert the examiner to the possibility of splenic pathology (see previous section *Clinical Presentation*).

9.1.4.2 Postpartum Splenic Rupture

Differential diagnoses include exaggerated postpartum pains, uterine rupture, intra-abdominal bleeding in general, and injury of a viscus. Signs and symptoms of severe shock states might be mimicked by septic shock, amniotic fluid embolus, pulmonary embolus, cardiogenic shock, and disseminated intravascular coagulopathy.

9.1.5 Diagnosis

The true rate of preoperative diagnosis is unknown. One of the reasons for the complicated diagnosis is the unclear etiology of rupture itself. The frequency of correct diagnosis during the 1950s varied in the literature between 14 and 25 % [5, 37]. Perhaps the most confusing in the later months of pregnancy is the finding of uterine tetany, suggesting the strong possibility of placental abruption. The presence of hemoperitoneum and peritoneal irritation may make adequate uterine palpation difficult and auscultation of fetal heart sounds uncertain. Albuminuria may be present and add further to the difficulty of distinguishing between intraperitoneal bleeding due to splenic rupture and that due to placental abruption.

Diagnosis is frequently difficult because the presence of the pregnancy leads the obstetrician to concentrate on the possibility of uterine or adnexal injury. The clinical symptoms and signs normally associated with intraperitoneal bleeding may be poorly defined. When blood is lost swiftly and in large amounts, all of the characteristic features of physical shock are recognized without difficulty; however, when blood loss is slower and smaller in quantity, the appropriate abdominal findings may be obscured.

The diagnosis of spontaneous postpartum splenic rupture was not considered in either case preoperatively, even though there was no doubt as to the need for immediate surgical intervention and transfusion.

9.1.5.1 Paracentesis

Before the era of the ultrasound and CT, paracentesis was used to diagnose intraperitoneal bleeding. The necessity of performing paracenteses in the four abdominal quadrants with a No. 18 needle has been strongly emphasized by Wright and Prigot; in 87 % of patients with splenic rupture in the general population in whom paracentesis was performed, blood was obtained [38]. Dependence on the paracentesis has been criticized by Maughon et al., who state that false taps lead to dangerous delay [39]. In one case reported by these authors, the patient died when the correct

diagnosis was not made because of a negative intraperitoneal tap. A repeat paracentesis is mandatory if doubt exists as to the cause of the patient's symptoms. Maughon et al. believe that abdominal incision in the doubtful case is worth any number of paracenteses [39].

9.1.5.2 Plain Abdominal X-Ray

By and large the radiographic examination is not of much value in diagnosing rupture of the spleen. Careful observation may indicate:

- Elevation of the left hemidiaphragm
- Displacement of the gastric shadow to the right
- Subphrenic opacity in the left upper quadrant
- Descent of the left part of the transverse colon

These signs are less useful in the third trimester because of physiological displacement of intraperitoneal organs by the enlarged uterus.

9.1.5.3 Abdominal Ultrasound

Currently, abdominal ultrasound is an inexpensive and practical way to obtain a quick diagnosis of intraperitoneal fluid accumulation or hematoma, which can be performed at the patient's bedside or in the emergency unit [40]. This can aid in the initial workup of a patient with hemodynamic instability and abdominal distention, especially if exploration is contemplated or if CT is not feasible. Free fluid in the upper abdomen or left upper quadrant should raise suspicion of splenic rupture [41, 42].

9.1.5.4 Angiography

In most cases it is not known preoperatively whether splenic rupture or rupture of the splenic artery aneurysm (SAA) occurred. In a suspected unruptured SAA, the gold standard for the diagnosis is arteriography [43], although ultrasonography and pulsed Doppler are preferable in pregnancy [44].

9.1.5.5 Abdominal CT Scan

Native abdominal MSCT scan especially with i.v. contrast can define SAA with or without rupture preoperatively but is almost never used in pregnant patients, as well as angiography. Abdominal CT scan is used when MRI is not available in emergency settings (Fig. 9.4).

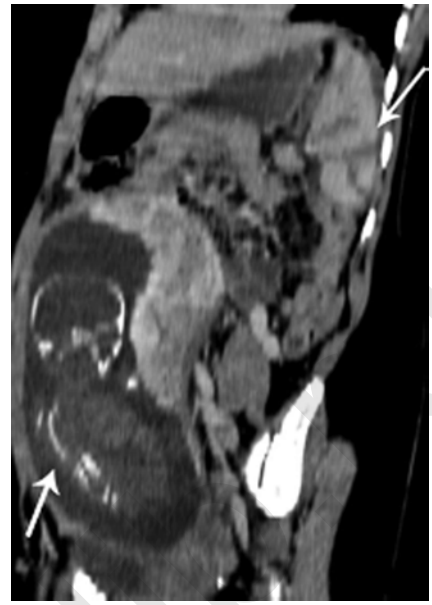


Fig. 9.4 An oblique sagittal reformatted CT scan image showing traumatic splenic laceration (*right arrow*) and the 26-week fetus (*left arrow*) [45]

9.1.5.6 Diagnostic Laparoscopy/ Laparotomy

Sometimes the cause of the hemorrhage is not known preoperatively especially when the patient presents with hemodynamic instability. In such cases laparotomy is the preferred method.

9.1.6 Treatment

Splenectomy for ruptured spleen in pregnancy was first performed by Savor in 1898 [46]. The patient survived and delivered a full-term infant 3 and a half months later.

9.1.6.1 Conservative Approach

Conservative approach with close hemodynamic monitoring has been advocated in well-selected cases, most of which are traumatic in origin. There are no criteria for pregnant patients, but to

be eligible for nonoperative management, patients should meet several criteria based on data on general population [47]:

- Hemodynamic stability
- Absence of peritoneal signs
- Absence of other abdominal injuries requiring surgery

Factors that predict failure of conservative measures in the general population include [47]:

- Preexisting splenic disease
- Age older than 55 years
- High-grade injury
- Significant hemoperitoneum
- Contrast blush in the spleen (suggesting false aneurysms) on CT

9.1.6.2 Surgical Treatment

Postpartum Splenic Rupture

The standard of care for patients with spontaneous postpartum splenic rupture remains emergency splenectomy. Of the 66 pregnant patients with splenic rupture who underwent splenectomy, 63 survived (survival rate 95.4 %), compared with a 100 % mortality rate in the 20 patients who did not undergo splenectomy [16]. Therefore, the survival of patients with spontaneous postpartum splenic rupture rests on several factors, including aggressive transfusion management, early diagnosis, and splenectomy.

Operative Principles

Consideration should be given to performing a midline or paramedian (if the diagnosis is known preoperatively) vertical incision to facilitate access and visualization. The problem is that the patient is often seen first by the obstetrician, with diagnosis of pelvic pathology, and the most common incision is a lower midline. In the 71 cases of spontaneous rupture of the normal spleen reviewed by Orloff and Peskin, 75 % of the cases that resulted in splenectomy were opened through an inadequate incision [23]. Some patients needed extensions, some a new incision, and in the balance, the surgery was made extremely difficult by the original incision. The diagnosis of spontaneous postpartum splenic rupture was not considered in either case preoperatively, even though there was no doubt as to the need for immediate surgical intervention and transfusion. Therefore, compulsory evaluation of the entire abdomen in posthysterectomy hemoperitoneum is advisable.

Cesarean section in patients with intraperitoneal bleeding due to splenic rupture may serve one of two purposes. In some patients, adequate surgery for the ruptured spleen cannot be undertaken until the uterus is evacuated because a term-sized uterus prevented adequate exposure of the splenic fossa. In others, Cesarean section is necessary to prevent intrauterine death due to maternal hypoxia and/or hypotension.

Laparoscopic Splenectomy

Currently there are two case reports of successful laparoscopic operation after blunt trauma causing splenic rupture in 18- and 27-week pregnant women (one with diaphragmatic rupture and intrathoracic ruptured spleen). In both operations, the mother and the fetus survived [48, 49]. Laparoscopic procedures are indicated in early presentations, because in delayed presentation, blood clots obscure the operative field and there is a difficulty in visualization. Also in hemodynamic unstable patients, definitive treatment must be swift; therefore, laparotomy is recommended.

9.1.6.3 Radiologic Interventions

Splenic Artery Embolization

Splenic artery angiography followed by embolization in the general population has been described, with a reported success rate of 85 % [50]. First, its role in the assessment and management of patients with hemoperitoneum is still unclear, and second, if the pregnancy continues, there is a risk of ionizing radiation.

9.1.7 Prognosis

Due to the rarity of the condition, maternal and fetal outcome for every etiology is difficult to estimate. Therefore, outcome is mostly presented for the whole group of splenic ruptures.

9.1.7.1 Maternal Outcome

Maternal death is commonly due to massive hemorrhage and accompanying hemorrhagic

shock and consumptive coagulopathy. In 1952 Barnett stressed the severity of the condition with the maternal mortality of 54 % (15/28) [33]. Of the 15 deaths, eight were recorded before 1880. Excluding these, seven deaths occurred in 20 patients, which is a more accurate reflection of the results in the 1950s (maternal mortality of 35 %). The importance of correct diagnosis and early operation is apparent when it is noted that of the 16 patients who were taken to the operating room for splenectomy, only three died (19 %) [33]. The same percentage of overall maternal mortality was found in other studies from the same decade [5]. Also, in the 1950s the mortality from the spontaneous form of splenic rupture was 10 % [23]. Up to 1967 reported overall maternal mortality was lowered to 8 % in a series of 25 patients [6].

9.1.7.2 Neonatal Outcome

Maternal hemodynamic decompensation leads to an acute decrease in uteroplacental perfusion, resulting in "fetal distress" and, ultimately, fetal demise [51]. Specific information on infant survival is lacking. However, in an analysis of 32 infants up to 1958, a fetal mortality was 59 % [5]. Others claim fetal mortality of 70 % for all types of ruptured spleen [6, 33]. With 20 reported cases in the English literature since 1958, the maternal and fetal mortality rate in spontaneous splenic rupture in pregnancy is 14.3 % and 42.9 %, respectively [26].

9.2 Ruptured Splenic Pregnancy

9.2.1 Definition and Classification

In about 20/1,000 cases in pregnancy, the site of implantation is different from the uterine cavity (ectopic pregnancies): the most common site of ectopic implantation is the Fallopian tube (95.5 %). Although rare (1.3 % of ectopic pregnancies), an ovum could implant within the peritoneal cavity (abdominal pregnancies) either directly (primary abdominal pregnancies – extremely rare) or because of tubal rupture (secondary abdominal pregnancies). The criteria for primary abdominal pregnancy have been described by Studdiford in 1942 [52]:

- Normal Fallopian tubes and ovaries.
- No evidence of uteroplacental fistula.
- Pregnancy is related exclusively to the peritoneal surface and early enough to eliminate the possibility of secondary implantation after primary nidation of the Fallopian tubes.

9.2.2 Incidence

There are 13 case reports in the literature of primary splenic pregnancies. The patients have a mean age of 29.7 years (range 24–41 years) [53].

9.2.3 Pathophysiology

The liver and the spleen are more favorable for implantation because they are flat organs, rich in blood flow, and easily reached by the fertilized ovum (Figs. 9.5 and 9.8) [54]. However, both cannot allow placental attachment, thus leading to rupture with massive hemoperitoneum, if the pregnancy is left untreated [55].

9.2.4 Risk Factors

Risk factors related to abdominal pregnancies are similar to those of other ectopic pregnancies:

- Prior history of pelvic inflammatory disease
- Prior ectopic gestation
- Endometriosis
- Reproductive assistance
- Uterotubal malformation
- Previous tubal surgery

9.2.5 Clinical Presentation

Mostly patients have prolonged amenorrhea but also in a period when the menstruation should

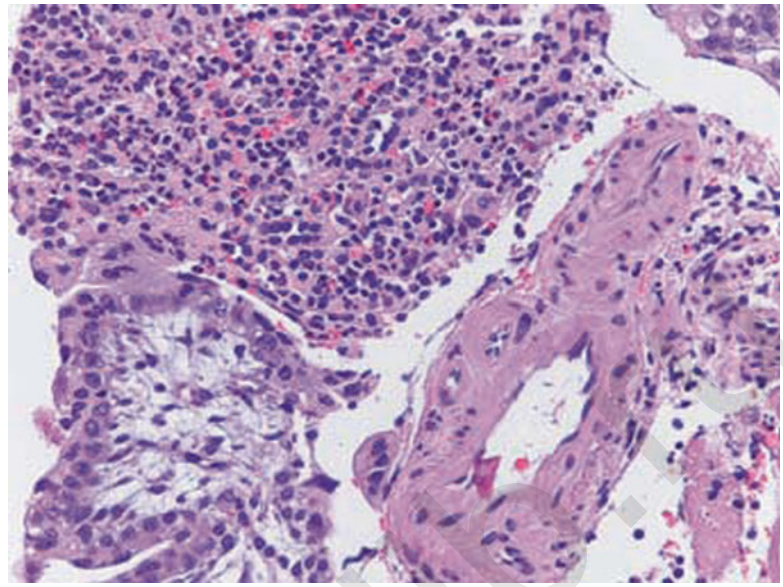


Fig. 9.5 Histopathological examination (20×): chorionic villi within the splenic tissue [53]

occur. They present most commonly with sudden or short-lasting abdominal pain, radiating to the left shoulder (*Kehr's sign*). Depending on the severity of intraperitoneal bleeding, the pain can be localized or diffuse. If the bleeding is massive, the patient can present with hemodynamic shock with pallor and cold sweat.

9.2.6 Diagnosis

In cases when pregnancy can be expected, βHCG should be checked. If elevated, transvaginal ultrasonography should be performed to define the uterine status and fetal status with gestational sac. If normal-size uterus with a thickened endometrium without individual gestational sac is found, ectopic pregnancy should be suspected. If Fallopian tube ectopic pregnancy is excluded, which is the most common, transabdominal ultrasound should be performed. Most of the gestations were subcapsular in location and assumed the appearance of an irregular mass that exceeds the contour of the spleen (Fig. 9.6) [53]. Agreeing with Yagil et al., the appearance of an irregular mass outside the contour of abdominal viscus should raise the suspicion of ectopic abdominal pregnancy [56]. Nearly all patients with ruptured splenic pregnancy had preoperative diagnosis of ruptured ectopic pregnancy. In unequivocal cases without hemodynamic instability, abdominal CT is indicated (Fig. 9.7).

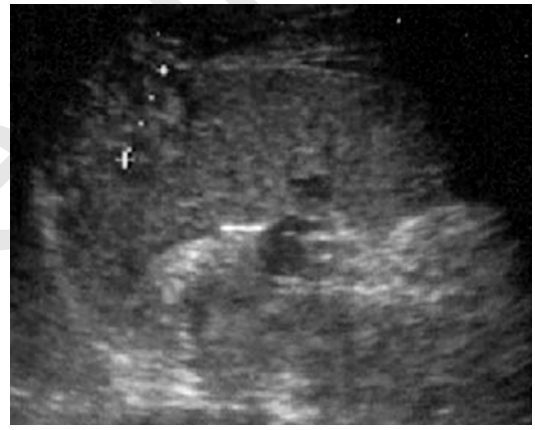


Fig. 9.6 Abdominal ultrasound (*US*), mass at the superior splenic pole [53]

9.2.7 Therapy

Sometimes it is difficult to make preoperative diagnosis, and therefore, laparoscopy should be performed for diagnosis and possible treatment (Fig. 9.8).

The entire abdominal cavity must be evaluated, and removal of ectopic pregnancy could be attempted, especially in case of timely diagnosis. Successful emergency laparoscopic treatment of abdominal pregnancy associated with extensive hemoperitoneum has been reported in two cases [53, 56]. This shows that hemoperitoneum in abdominal pregnancy may be treated with laparoscopy and that conversion to laparotomy may not be necessary, at least in the case of splenic pregnancy, especially if the diagnosis is made early in the course of hemorrhage. Otherwise, median laparotomy should be made for visualization of all four abdominal quadrants and easier performance of the operation according to underlying pathology.

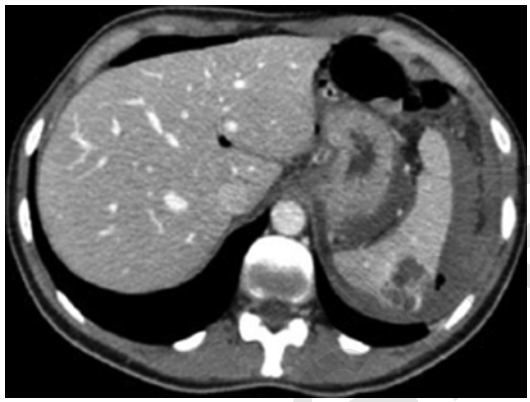


Fig. 9.7 Computerized tomography scan, heterogeneous hypervascular mass at the superior splenic pole [53]

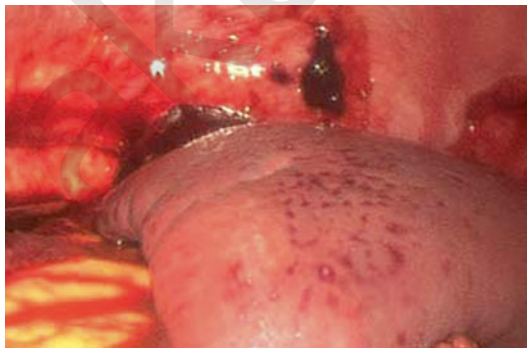


Fig. 9.8 Laparoscopic view, hemorrhagic lesion at the superior splenic pole [53]

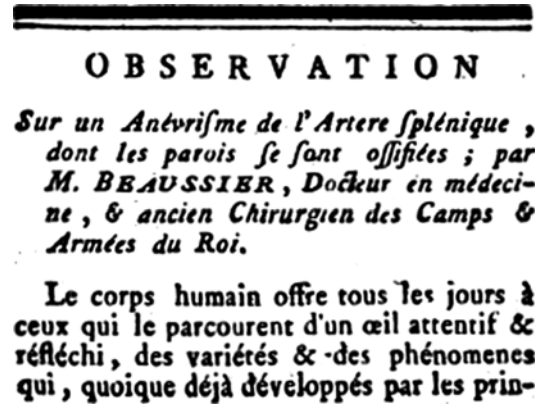
9.3 Spontaneous Rupture of the Splenic Artery (Aneurysm)

9.3.1 History

The first case of splenic artery aneurysm (SAA) was published in 1770 by Beaussier during the anatomic dissection of a 60-year-old female cadaver which he performed 10 years before publishing it (Fig. 9.9) [57].

This and the second case reported by Parker in 1844 [58, 59] were for many years omitted from the literature and priority mistakenly given to Crisp from 1847 by all subsequent authors, possibly because he himself had also erroneously credited Parker with the description of the first case [60]. Winkler, in 1903, was the first to identify SAA in a living person (a nurse) during laparotomy in a patient with abdominal pain of an 8-year duration [61].

There is a strong association with pregnancy since Corson's first description of the sudden and unexpected death of a 29-year-old multigravida at 8 months' gestation in whom the diagnosis of rupture of a splenic artery aneurysm was only made following postmortem examination in 1869 [62]. Sheehan and Falkiner in 1948 noted that 56 % (23/41) females who suffered a rupture of a



OBSERVATION

Sur un Anévrisme de l'Artere ſplénique, dont les parois ſe ſont oſſifiées ; par M. BEAUSSIER, Docteur en médecine, & ancien Chirurgien des Camps & Armées du Roi.

Le corps humain offre tous les jours à ceux qui le parcourent d'un œil attentif & réfléchi, des variétés & des phénomenes qui, quoique déjà développés par les prin-

Fig. 9.9 Original part of the text on the first case of SAA in nonpregnant female by Beaussier. The text was published in 1770 in *Journal de Medecine, Chirurgie, Pharmacie*

splenic artery aneurysm were pregnant and in their last trimester [24].

9.3.2 Incidence

9.3.2.1 General Population

Splenic artery aneurysm is the most common (60 %) of all visceral artery aneurysms. More than 50 % of aneurysmatic ruptures in women under the age of 40 years are correlated to pregnancy, and the arteries most often involved are, in declining order, the aorta, cerebral arteries, splenic artery, renal artery, coronaries, and ovarian artery [63]. The incidence of SAA is unknown because a vast majority of SAAs, being smaller than 2 cm, remain asymptomatic and is generally encountered as autopsy findings [44]. Berger et al. in 1953 found 152 cases of ruptured and unruptured SAA [64], while Owens and Coffey in the same year found 198 cases recorded up to 1952 and added six of their own [65]. The incidence of SAA in reports of autopsy series ranges from 0.01 to 10.4 % [66, 67], although in one series of 28,512 consecutive autopsies performed at the Mayo Clinic from 1911 to 1957, the incidence was 0.16 % [68]. It is likely that the figures quoted in most autopsy series represent underestimates as the aneurysms can be difficult to identify unless their presence is specifically sought. Increasingly, they are being detected incidentally in the course of sophisticated imaging for unrelated conditions.

9.3.2.2 Splenic Artery Aneurysm Rupture

The principal complication of an SAA is rupture, and the reported risk varies from 3 to 9.6 % [69, 70]. Nevertheless, to date, more than 400 cases of ruptured SAAs in the general population have been reported in the literature, with approximately 20–50 % of these during pregnancy [44, 69–72]. A summary of 58 recorded cases was made by Anderson and Gray in 1929, adding their own case [73], and Machemer and Fuge in 1939 collected a further 24 cases and added one of their own [74]. Sherlock and Learmonth in 1942 [75] stated that splenic aneurysm sometimes declares itself during pregnancy and this may partly account for the larger number of females in the general population. This incidence is particularly interesting as aneurysms at all other common sites are undoubtedly more frequent in males [76, 77]. Splenic artery aneurysms are the most frequent in the general population with incidence around 60 %. Among visceral aneurysms, the splenic artery aneurysm is the most common (95 %) in young pregnant women, and a greater number of diagnoses are made during pregnancy, often due to aneurysmal rupture. Of all splenic artery aneurysms, 65 % present in pregnant women and 50 % rupture during pregnancy [78]. In Owens and Coffey's series, 24 % of the women were pregnant. When only the group in the childbearing age is considered, the incidence of splenic artery aneurysms rises to 53 % [65].

9.3.2.3 Distribution During Pregnancy

A significant percentage of women are pregnant when the diagnosis is made probably due to augmented use of ultrasonography and use of high-resolution cross-sectional imaging techniques [79]. Sheehan and Falkiner in 1948 noted that 56 % of females who suffered a rupture of a splenic artery aneurysm were pregnant and in their last trimester [24]. The incidence of rupture of the SAA during pregnancy is as follows [70, 80–87]:

First to second trimesters	12 %
Third trimester	69 %
Childbirth	13 %
Puerperium	6 %

9.3.2.4 Splenic Artery Pseudoaneurysm

In contrast to splenic artery aneurysm, splenic artery pseudoaneurysm is even rarer. In a large series from the Mayo Clinic, ten splenic artery pseudoaneurysms were compiled over 18 years [88]. To date, fewer than 200 cases in the general population have been reported in the English language literature.

9.3.3 Risk Factors

There are two distinct types of splenic artery rupture. One is spontaneous splenic rupture where no underlying pathology of the splenic artery could be found and another is spontaneous rupture of the SAA. True aneurysms of the splenic artery have been thought to be associated with a number of conditions – pregnancy and portal hypertension being the most common [67, 89, 90]; other conditions include essential hypertension.

Early reports of SAA suggested the risk of rupture of 10 % [91]; however, more recent data suggest rupture rates closer to 2–3 % [87, 92]. The size of the SAA is usually more than 2.5 cm in most patients at the time of rupture [69]; however, rupture of smaller aneurysms has also been reported [69, 84, 87].

9.3.3.1 Spontaneous Splenic Artery or Vein Rupture

Cases of spontaneous rupture of normal splenic artery (or vein) had risk factors of long-standing cirrhosis of the liver with portal hypertension [93]. Prolonged hypertension may be a contributory factor [94, 95].

9.3.3.2 Spontaneous Splenic Artery Aneurysm Rupture

Almost all cases of ruptured SAAs in pregnancy have occurred during the third trimester [72]. Therefore, it is evident that the physical history of pregnancy gradually increases the risk of rupture of SAA. Apart from the late stage of pregnancy, other risk factors include portal hypertension [41, 96, 97], atherosclerosis, congenital abnormalities of the vessels, inherited vascular and connective tissue disorders (medial fibrodysplasia), vascular trauma, inflammatory processes, and degenerative arterial disease [28, 67, 70]. Although the average parity of women at rupture is 4.5 [72, 79, 87, 89, 92], there are cases with nulliparous women [96, 98, 99]. High blood pressure as in preeclampsia-eclampsia especially during labor is a precipitating factor for SAA rupture [100].

9.3.4 Pathophysiology

The mechanisms which are involved in the formation of this vascular defect still remain unclear. Various theories have been proposed for the explanation of this phenomenon, mainly considering hemodynamic and hormonal alterations in the late stages of pregnancy [101]. Although the risk of rupture mainly exists in the third trimester of pregnancy [101], to date, only two cases of SAA rupture during the first trimester of pregnancy have been reported in the literature [102, 103].

One of the mechanisms promoting the vascular defect in splenic arteries during the late stages of pregnancy seems to be the escalating increase of the circulating estrogens and progesterone during pregnancy [89]. The elevation of the levels of these hormones has been associated with promotion of various structural alterations in the arteries, such as the disruption of the internal elastic lamina, fragmentation of elastic fibers, degeneration of smooth muscle fibers, and failure of elastin formation [104]. Additionally, it appears that the elevated levels of relaxin throughout the third trimester of pregnancy may affect the elasticity of the splenic artery wall [105] and could probably weaken the arterial wall [79, 83, 106]. Especially in case of multiparity, the repeated exposure to these hormonal shifting could explain the increased incidence of rupture of SAA in this group of pregnant women.

It is also assumed that hemodynamic changes which occur during the late stages of pregnancy are implicated in the etiology of SAA ruptures during this period. More specifically, due to the fact that the increased size of the uterus tends to compress the aorta and the iliac arteries, resulting in higher flow in the splenic artery, the development of the SAA is enhanced; moreover, the increases of blood volume and cardiac output, along with the relative portal congestion, can definitely contribute to the formation of SAAs [101]. Studies during the last decade highlight that the vessel wall is in a continual state of self-maintenance and self-regulation including remodeling that occurs in response to

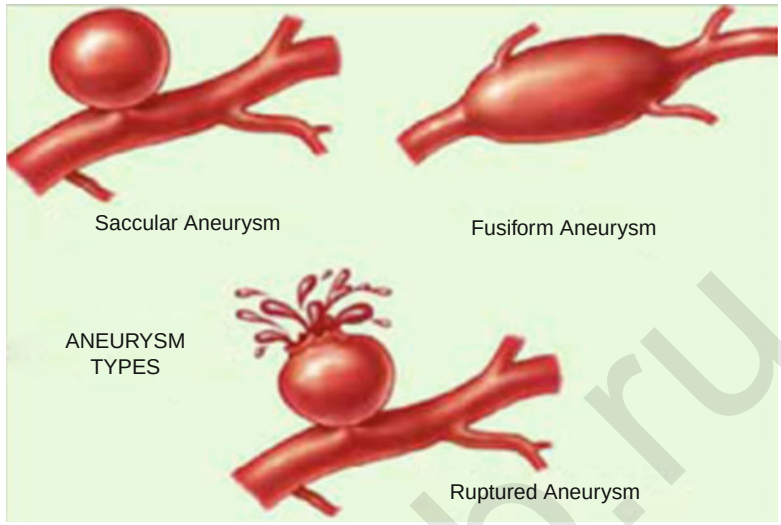


Fig. 9.10 Types of splenic artery aneurysm [86]

hemodynamic stress. It is suggested that remodeling of the vessel wall causes similar histological lesions, regardless of the pathogenic factors [107]. There are two principal types of splenic aneurysms: saccular and fusiform (Fig. 9.10).

9.3.5 Clinical Presentation

Apart from asymptomatic SAA found incidentally during pregnancy, there are two types of presentations depending if the SAA is only symptomatic or there is true rupture.

9.3.5.1 Ruptured Splenic Artery Aneurysm

This rupture can be either sudden rupture or a two-stage rupture, which is present in 20–25 % of cases [84, 85, 87]. In terms of clinical manifestations, the rupture of SAA is undoubtedly presented as an acute abdomen. In the early stages of rupture, diffuse tenderness in the upper abdomen, in the left hypochondrium, or over the uterine fundus may be elicited, accompanied by vomiting and in severe cases derangement of the vital signs, compatible with developing hemodynamic shock. The physical course either can consist of one stage, leading to dramatic collapse as a result of inability of self-containment of bleeding, or can present in a two-stage sequence, when initial tamponade of hemorrhage in the lesser sack was made by clots blocking the foramen of Winslow [105]. In these patients, initial hemorrhage into the lesser sac may cause pain and transient hypotension; the gradual increase of pressure in the lesser sac would be suddenly followed by a rupture into the greater sac and lead to massive intraperitoneal bleeding and shock, causing the patient to collapse. The initial phase where hemorrhage remains confined to the lesser sac provides vital time for diagnosis and preparation for intervention [79, 83, 84, 106]. The "sentinel" period between the initial and subsequent hemorrhages may take anywhere between 6 and 96 h. This phenomenon of "double rupture" is found in 25 % of reported cases [66, 98]. When ruptured, it usually causes acute left-sided abdominal pain that may radiate to the back, flank, and subscapular region and may cause shock, abdominal distension, and death.

In the series reported by Owens and Coffey, ruptures in the general population were distributed as follows: 38 % into the peritoneal cavity, 10 % into the stomach, 7 % into the colon, 4 % into the pancreas, and 2 % into the splenic vein [65].

9.3.5.2 Symptomatic (Unruptured) Splenic Artery Aneurysm

The symptoms of an unruptured aneurysm are variable and may be completely lacking.

According to Pasternack and Shaw [108], pain of a colicky nature in the left epigastrium or hypochondrium may occur and is characteristically increased by exertion or by changes of posture. There may also be symptoms referable to the stomach, gallbladder, or colon. A periumbilical pulsating mass may be felt or a systolic bruit heard. There are no physical signs that reliably indicate the presence of an SAA [79].

9.3.6 Diagnosis

Key to effective management of a ruptured SAA is increased clinical suspicion, combined with accurate implementation of the diagnostic means available, particularly abdominal sonography and angiography, if permitted by the hemodynamic condition of the patient. SAA should be considered when we encounter hemorrhagic shock in a pregnant woman without obstetric hemorrhage [96, 109]. Högler, in 1920, made the first preoperative diagnosis on the basis of bruit and a pulsatile mass on fluoroscopy [110]. Another case of one of the first preoperative diagnoses in the general population based on roentgen examination alone was made by Lindboe in 1932 [111]. In 1950, Evans obtained the first translumbar aortogram demonstrating a splenic artery aneurysm which was operated successfully. Baum in 1965 used selective angiography in making preoperative diagnosis.

Screening of the splenic artery by abdominal ultrasound and Doppler should be considered selectively in pregnant patients with predisposing factors like hypertension, multiparity, and liver and pancreatic diseases (Fig. 9.11). However, its utility is limited by operator dependency, obese patients, bowel gas shadow, and arteriosclerosis [112, 113]. The likelihood of missing smaller lesions is also quite high because of limited spatial resolution [114, 115].

Although it is not the first-line investigative tool for SAA, plain abdominal X-ray carried out for some other abdominal pathology may reveal calcified SAA as characteristic calcified ring with a central lucent area to the left of the first lumbar vertebral body [101].

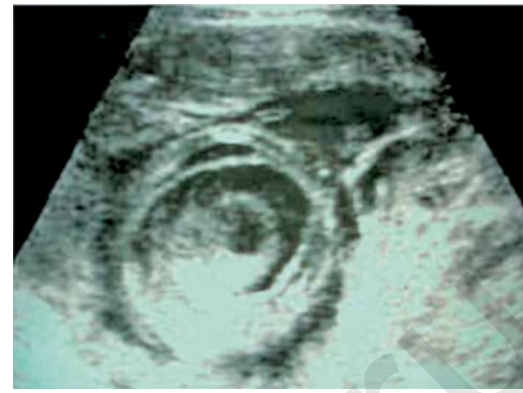


Fig. 9.11 Abdominal sonography of ruptured splenic artery aneurysm showing clots around [86]

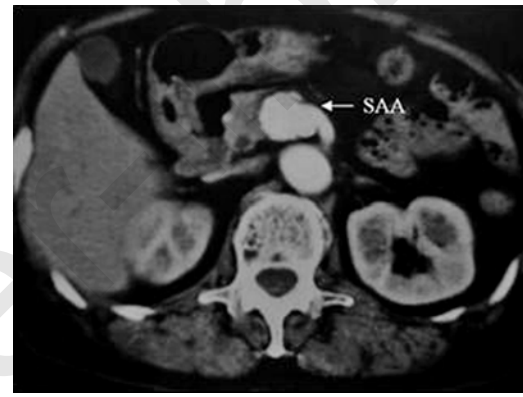


Fig. 9.12 Contrast-enhanced abdominal CT showing unruptured splenic artery saccular aneurysm (4.3 × 3.9 × 3.8 cm) [116]. *SAA* splenic artery saccular aneurysm

Contrast-enhanced (i.v.) abdominal CT can reveal abdominal aorta with its branches. Splenic artery with saccular aneurysm formation with an 8 cm neck and greater diameters of 4.3 × 3.9 × 3.8 cm can be delineated (Fig. 9.12).

Magnetic resonance angiography of the abdominal aorta and branches revealed patent abdominal aorta with normal diameter. There is presence of saccular aneurysmal dilatation in the splenic aorta, originating from the emergence of the superior mesenteric artery, measuring 3.6 × 3.0 cm. Considering that common hepatic, splenic, and gastric arteries branch off the celiac trunk, imaging confirmed a splenic artery with anomalous anatomy branching off the superior mesenteric artery (Fig. 9.13).

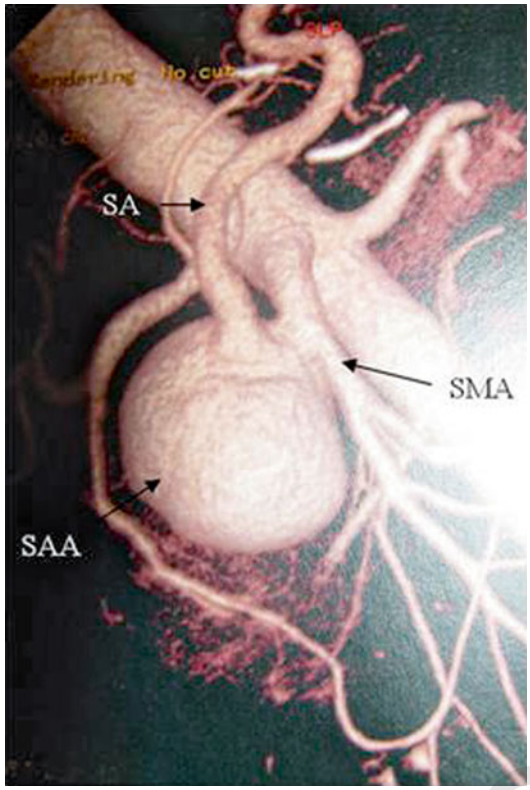


Fig. 9.13 Abdominal MR angiography: splenic artery saccular aneurysm with dimensions of 3.6×3.0 cm emerging from superior mesenteric artery [116]. *SA* splenic artery, *SAA* splenic artery aneurysm, *SMA* superior mesenteric artery

9.3.7 Differential Diagnosis

There are only four cases presented during the first trimester of pregnancy making ectopic pregnancy a strong differential diagnosis [102, 103, 117, 118]. Approximately 70 % of cases are diagnosed initially as a uterine rupture [63].

Differential diagnosis of pancreatic cysts or pseudocysts should be made, by location, this condition being more frequent in patients with past history of pancreatitis. Serous cystadenoma should also be considered as a hypothesis, but it occurs mainly in the seventh decade of life [119, 120].

9.3.8 Treatment

9.3.8.1 Ruptured SAA

Concerning intervention options, apart from the need of initial aggressive resuscitation, embolization of the aneurysm or emergency surgical operation with ligation of the ruptured aneurysm, followed or not by splenectomy, stands for the most realistic treatment options [101, 105]. The first successfully treated case in pregnancy was described in 1940.

The management of ruptured SAA requires awareness and aggressive surgical approach. Aneurysmectomy with splenectomy or distal pancreatectomy with splenectomy with ligation of the proximal and distal splenic artery or aneurysmectomy alone with splenic conservation are the procedures described [63, 83]. Splenic conservation is desirable but is difficult in the emergency setting with ruptured SAA [42, 83]. Angiography and embolization have been described for pseudoaneurysms and for unruptured true aneurysms [83]. In the high-risk patients, arterial embolization using coils can be an effective early treatment [63, 79, 106].

9.3.8.2 Symptomatic/Unruptured SAA

The management of the unruptured aneurysm is more controversial, although elective resection of those found in pregnant women and women of childbearing age is recommended if the SAAs are larger than 2 cm [67, 72, 87].

Surgical treatment options include resection of the aneurysm, with or without splenectomy, via laparotomy or laparoscopy. Aneurysms located in the proximal or middle third of the splenic artery may be treated with simple excision, with proximal and distal ligation of the artery and splenic preservation (through the short gastric vessels). For aneurysms located in the distal third, resection with splenectomy is most often performed, which is unfortunately the case in 70 % of the patients with portal hypertension [92, 121].

Endovascular radiological techniques that have also been employed in the general population include transcatheter embolization and percutaneous angiographic embolization [122–124] and could be used in the postpartum period. Postembolization syndrome and infarcts are common events (30 %) but generally resolve without sequel. The gestational age is an important parameter for the indication of this technique in pregnancy.

9.3.9 Prognosis

In the cases reported by Cosgrave et al. in 1947, the rupture was fatal in 93.3 % (14/15) pregnant women [125]. Poidevin found that in 30 cases of rupture during pregnancy, only two patients have survived, making the same maternal mortality of 93.3 % [126]. Early consideration and diagnosis of ruptured SAA significantly increases the chances of survival for both the mother and the fetus. In Australia, in 30 years (1967–1999), there have been only four maternal deaths due to rupture of an SAA [127]. By way of comparison, in the UK for the period 1988–2002, there were seven definite (and one possible) cases of a ruptured SAA [67]. But in a 10-year review of maternal mortality in Singapore, not a single case of SAA was identified [128]. Other reviews from North America confirm the rare mortality of the entity [129]. In the general population, there are some 400 individual reports in the literature with an overall mortality rate of 25 % [67]. Approximately 25 % involve pregnant women, and in this group, the mortality is disproportionately higher at 75 % for mothers and a fetal mortality rate approaching 95 % [41, 67, 98, 130]. The literature now contains more than 100 cases of ruptured SAAs in pregnancy but only 16 cases of both maternal and fetal survival [67, 131, 132], underlining the necessity of immediate intervention. The literature suggests that pregnant women tend to be younger and have fewer adhesions from previous surgery than the general population; therefore, rupture occurs almost exclusively into the free peritoneal cavity [67, 89, 133].

In early pregnancy where clinicians do not expect rupture of splenic artery (aneurysm), three cases [118] were described with two maternal deaths due to cardiac arrest during the early postoperative period [102, 103].

9.4 Spontaneous Splenic Vein (Aneurysm) Rupture

9.4.1 History and Incidence

Portal system aneurysms can be divided into two types: extrahepatic and intrahepatic. SVA is a true aneurysm and belongs to the extrahepatic category. Since 1953 when Lowenthal and Jacob [134] described the first case of SVA, fewer than 50 cases of portal system aneurysm [135–137] and only eight cases of SVA rupture in nonpregnant women have been reported in the English literature. The eight patients with SVA included five women and three men with mean age of 50 years [138–144]. There are five pregnant women with splenic vein rupture described [95, 145–148]. Up to 1961 there were only two references of the *spontaneous* rupture of the splenic vein in the general population [93, 149] and also two spontaneous cases in pregnancy [94, 95]. Splenic vein rupture in a pregnant woman was first described in 1959 by Rahn and Steffen [147].

Splenic vein rupture usually occurs during the third trimester, whereas splenic artery rupture has been described at any time from the first trimester through to the puerperium. There is only one case of SVA rupture occurring immediately postpartum published [145]. Despite the difference in incidence, SAA and SVA share a number of etiological factors, presenting symptoms, clinical course, complications, and management.

9.4.2 Etiology

The origins of the ruptures due to vascular pathologies at pregnancy may be hormonal, genetic, thrombotic, or mechanical. The etiology of splenic aneurysms is speculative and may include congenital causes such as local failure of connective and elastic tissue [150, 151]. Aneurysms may also be acquired due to trauma, inflammation, or portal hypertension [152, 153] or cirrhosis [93, 149, 154].

Splenic aneurysms are more common in multiparous women; it is therefore possible that pregnancy may influence their development because of changes in hemodynamic and increased levels of progesterone [92]. The physiological increase in blood volume and cardiac output during pregnancy could lead to portal congestion and splenic arteriovenous shunting and, together with progesterone-induced vasodilatation and vessel wall weakness, could favor aneurysm formation. Tolgonay et al. [140] described a case of splenic size increase and

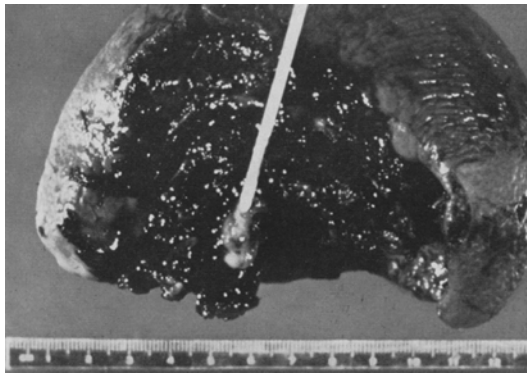


Fig. 9.14 Hilar surface of the spleen showing hemorrhage about splenic vessels. Probe inserted into spontaneous perforation of splenic vein [95]

splenic vein aneurysm due to a systemic infection in a patient with leukemia. After appropriate therapy, they observed a reduction in spleen size followed by a decrease in splenic vein blood flow and a regression of the aneurysm. Recent studies have shown an alteration of elastic fibers in the internal elastic lamina and fibrodysplasia of the media lamina as the consequence of hormonal changes. These factors may become cumulative, explaining the increase of rupture of the splenic vessels as parity rises [63]. The etiology of SVA in nonpregnant women includes portal hypertension and liver cirrhosis [139], chronic pancreatic inflammation [143], and vessel wall weakness [138]. Splenic vein rupture during pregnancy is associated with acute pancreatic necrosis eroding the splenic vein, acute vessel wall inflammation [95], and splenic artery aneurysm rupture into the splenic vein [155, 156]. In other cases the etiology remains unknown and splenic vein rupture is labeled "spontaneous" to account for the lack of apparent trauma or disease.

9.4.3 Risk Factors

There are only two cases of pregnant patients with spontaneous rupture of normal splenic vein. In one case the patient recovered. Gross and microscopic examination of the spleen revealed splenomegaly with the spleen measuring 11.5 × 8.5 × 7 cm and weighing 252 g (Fig. 9.14). No specific pathologic lesion was seen grossly or microscopically in the spleen. There was a perforation of one of the branches of the splenic vein at the hilum of the spleen without underlying pathology. Prolonged hypertension may be a contributory factor [94, 95]. Mechanical factors such as torsion of the spleen can cause splenic vein rupture [157].

9.4.4 Pathophysiology

9.4.4.1 Cirrhosis in Nonpregnant Patients

The SVA was associated with portal hypertension and liver cirrhosis in four of the eight nonpregnant patients. The pathogenetic mechanism of splenic vein rupture could be supported by three clinical observations:

1. Splenomegaly in cirrhosis is not only caused by portal congestion, but it is mainly due to tissue hyperplasia and fibrosis. The increase in spleen size is followed by an increase in splenic blood flow, which participates in portal hypertension actively congesting the portal system [158].
2. Increased resistance to portal blood flow is the primary factor in the pathophysiology of portal hypertension and is mainly determined by the morphological changes occurring in chronic liver diseases. The transmission of the increased blood flow and pressure to the splenic vein may lead to progressive dilation and weakness of the vein wall.
3. Portal hypertension in advanced cirrhosis is characterized by an increase in vasoactive mediators such as prostaglandins, nitric oxide, serotonin, and hormonal derangements, which may cause structural and functional changes in the splenoportal venous system [159, 160].

Furthermore, Tolgonay et al. reported that the reduction in the size of the aneurysm was related to a decrease in splenic vein blood flow [140]. These observations suggest that the persistent stagnation of blood flow in the portal system may have played a major role in the development of the SVA.

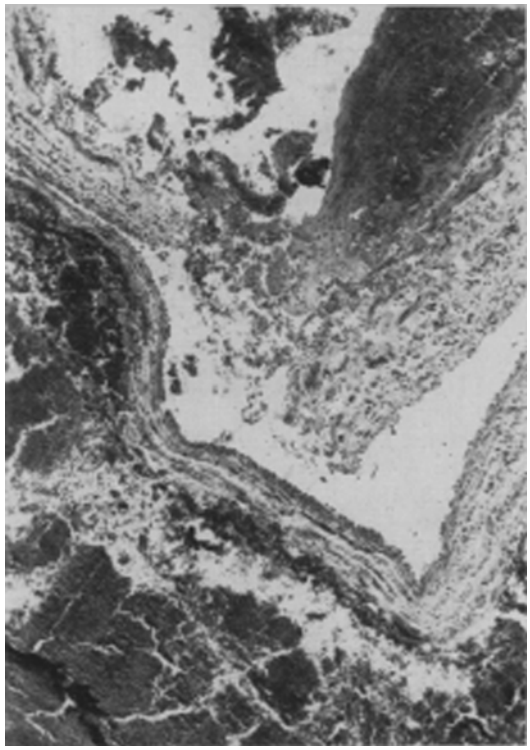


Fig. 9.15 Photomicrograph of splenic vein showing an acute inflammatory reaction and fibrinoid alteration in the vein wall with perforation and surrounding hemorrhage [95]

9.4.4.2 Hemodynamic and Hormonal Changes in Pregnancy

An increase in cardiac output and blood volume, usually found in the later months of pregnancy, is an important factor in the precipitation of vascular accidents [63]. Estrogens are believed to make capillary fragile, and progesterone is responsible for the enlargement of the venous system [161]. The increase of blood volume, the hypertrophy, or the dilation of the veins and changes in venous pressure related to pregnancy seem to be involved in the pathogenetic mechanism [150, 162]. Hemodynamic and hormonal changes may be the cause of vascular alterations, which can lead to weakening of the vein wall (Fig. 9.15).

9.4.4.3 Mechanical Factors

Splenic torsion in the general population leading to splenic vein rupture is rarer still and is associated with high mortality [157, 163].

9.4.5 Clinical Presentation

Abdominal venous aneurysms including SVA are usually incidental findings. However, 75 % (6/8) nonpregnant patients had clinical complaints: 50 % had abdominal pain and all had abdominal fullness and hepatic dysfunction. One patient presented in a state of shock with intra-abdominal bleeding. The similarity between spontaneous perforation of the splenic vein and perforation of SAA is striking in many aspects: symptoms, signs, the lucid interval of amelioration of symptoms, occurrence in late pregnancy, and the therapeutic indications in both conditions [93, 95, 164–166].

Depending on the mechanism, extent, and location of the splenic vein rupture, the severity of the bleeding can be variable. If significantly severe, upper abdominal pain and nausea are followed by collapse. The patient recovers after several minutes but abdominal pain continues. The pain can be present on the top of the left (*Kehr's sign*) or both shoulders [95]. If the hemorrhage is slower or the patient is referred to the hospital early, there is no collapse in the course of the disease [157].

9.4.6 Diagnosis

Angiography is the study of choice for diagnosing the presence of visceral aneurysm and rupture if the patient is hemodynamically stable. Also abdominal CT scan with i.v. contrast (arterial and venous phase) can reveal the correct diagnosis in a hemodynamically stable patient [167, 168]. In certain cases the diagnosis is made intraoperatively or unfortunately during autopsy (Fig. 9.16) [148].

9.4.7 Therapy

The natural course of non-ruptured SVA is uncertain; therefore, when patients in the general population are asymptomatic, treatment is controversial. In order to avoid the risk of rupture, it has been suggested that for 1–2 cm

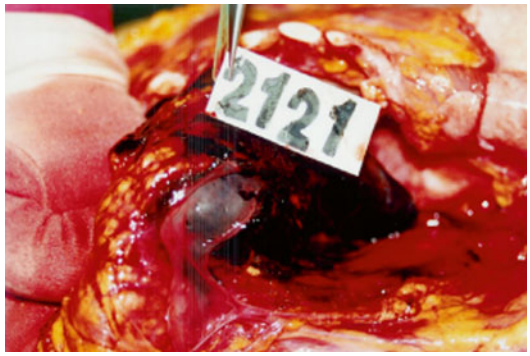


Fig. 9.16 Hematoma and spontaneous rupture at the lienal vein 3 cm far from the hilum of the spleen on autopsy of a 28-year-old woman in the fifth month of pregnancy [148]

lesions, patients should be followed up on a regular basis with abdominal CT, abdominal MRI, or abdominal color Doppler ultrasound scanning. If inflammation is present as in accompanying chronic pancreatitis, every SVA should be treated surgically because rupture is possible despite aneurysm diameter [143]. However, we would recommend that in pregnancy, even the smallest SVA should be treated surgically [145].

Because of the already damage on the vein wall, repair of the vein should be avoided. Control of the bleeding, ligation of the vein, meticulous hemostasis, and splenectomy are the appropriate treatments. Splenectomy has long been advocated to correct the pancytopenias which result from the hypersplenism, associated with portal hypertension in cirrhotic patients. However, even though this intervention may correct the hematological picture, it should be noted that it rarely changes the course of the underlying disease. The standard management of SVA rupture remains emergency surgery which allows SVA resection, distal pancreatectomy, splenectomy, and splenorenal shunt [138].

9.4.8 Prognosis

It is difficult to discuss the prognosis due to several patients with splenic vein rupture during pregnancy. Probably due to slower bleeding then with rupture of splenic artery (aneurysm), the prognosis could be better. The patient described by Shepard in 1961 recovered but intrauterine fetal death occurred [95].

9.5 Splenic Torsion

9.5.1 History and Incidence

Splenic torsion is an exceedingly rare complication in pregnancy. The first case of successful splenectomy due to the splenic torsion in pregnancy was made by Meek in 1907 [169].

9.5.2 Etiopathogenesis

It is a complication of the wandering spleen [157], a rare condition characterized by increased splenic mobility due to the absence or laxity of its suspensory ligaments that may present as acute abdomen when it is twisted on its pedicle [170]. It has been reported in conditions such as abdominal trauma, splenomegaly, nonspecific abdominal muscle laxity, and laxity resulting from the hormonal effects of pregnancy [171]. It has been suggested that the softening effect of pregnancy hormones on ligaments, the abdominal musculature, diminished peritoneal cavity volume as a result of the gravid uterus, and a maximal third trimester increase in whole-blood volume might be the predisposing factors in pregnancy [172, 173].

9.5.3 Clinical Presentation

Symptoms of splenic torsion vary depending on the degree of torsion. Mild torsion might manifest with chronic abdominal pain resulting from congestion; moderate torsion might manifest with severe intermittent abdominal pain related to intermittent rotation and derotation [172]. Severe and acute torsion present with symptoms suggestive of an intra-abdominal catastrophe [157, 171, 173, 174]. It should be stressed that the patients sometimes had similar symptoms

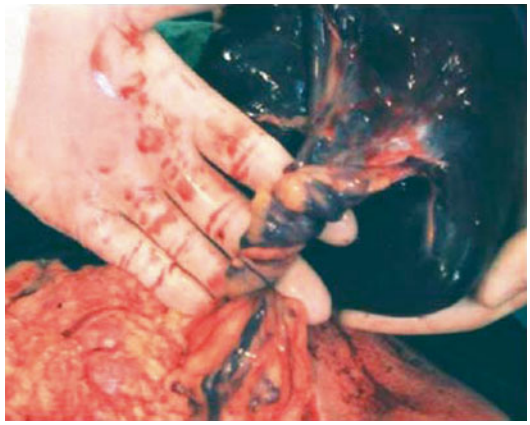


Fig. 9.17 Torted vascular pedicle of wandering spleen with infracted, hypermobile spleen [173]

previously with one to several attacks that were attributed to other diseases [169].

9.5.4 Diagnosis

Splenic torsion during pregnancy creates a diagnostic dilemma because intrinsic pregnancy complications might mask its symptoms. It is a rare cause of acute or recurrent abdominal pain during pregnancy or the puerperium [16, 175].

9.5.5 Therapy

Treatment is always surgical. Initial exploration by laparoscopy or laparotomy depends on surgeon's preference. Further surgical procedure depends on the status of the spleen. If longstanding detorsion is present with infarction and gangrene of the spleen, splenectomy is indicated (Fig. 9.17) [173, 176]. If exploration is done early with vital spleen, detorsion is indicated (Fig. 9.18) [176].

9.5.6 Prognosis

Prognosis depends on the severity of torsion (presentation). If operated early in the course of the diseases, prognosis is excellent. If the patient presents with hemorrhagic shock, fetal mortality is likely [176].

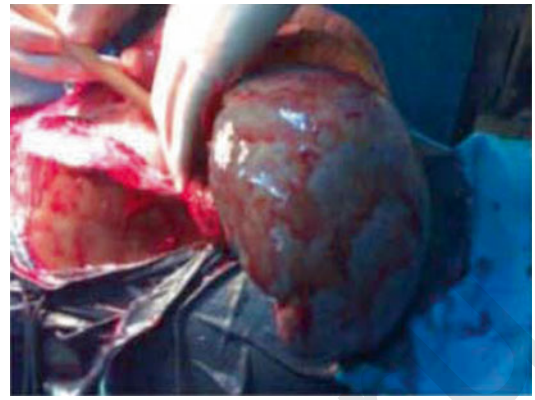


Fig. 9.18 Enlarged spleen on its twisted pedicle [176]

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Abdominal Trauma

10

10.1 General Considerations

10.1.1 Incidence

Changed attitudes to pregnancy have resulted in women involving themselves increasingly in social, commercial, and professional activities virtually throughout their pregnancies, thus exposing themselves to a risk of accidental injury similar to that in the nonpregnant population. Pelvic ligamentous laxity and the protuberant abdomen of pregnancy contribute to instability of gait, predisposing the pregnant woman to falls especially with progression of pregnancy. The prominent abdomen, especially toward term, becomes vulnerable to any form of trauma, and it has been suggested that minor accidental injury is more common during pregnancy than at any other time in adult life. A study from 2008 estimated that injuries resulting in an emergency department visit occurred in 3.7 % of pregnancies [1]. A reported 0.3 % of pregnant women require hospital admission because of trauma [2, 3] or less than 1 % of all trauma admissions in Australia [4]. Unintentional injuries are the leading cause of death among 18–34-year-old women in the United States and account for more than 8.6 million emergency department visits each year among adult women [5].

In the past, most causes of maternal death were obstetric and due to a lack of prenatal care and inadequate assistance during delivery. Because of improved medical services, hospital deliveries, and reduced parity, a significant reduction in maternal mortality is noted. On the other hand, although there have been dramatic improvements in the management and treatment of medical and obstetric conditions, fetal mortality has not been reduced because of a rise in non-obstetric causes (mostly MVAs).

Motor vehicle accidents (MVAs) are becoming an increasingly common cause of trauma in pregnancy and in such cases fetal death may be due to maternal shock or damage to the uterus or placenta. However, when a pregnant woman is involved in an accident, her injuries rarely involve the uterus. The pregnant trauma victim may present the casualty officer with problems seldom seen in other trauma cases, such as placental abruption, premature labor, and a ruptured uterus. If casualty department staff is aware of these complications, it is unlikely that their attention will be diverted from the pregnancy to the other more familiar injuries. Griswold and Collier have shown that MVAs are responsible for about 50 % of non-penetrating abdominal wounds and that the trauma is often severe and associated with other injuries [6].

Although trauma in pregnancy is uncommon, it is the leading non-obstetric cause of maternal mortality. Approximately 6–7 % of all pregnant women experience some sort of physical trauma in the United States and it accounts for 20 % of maternal mortality [2, 7–11]. Significant trauma occurs to approximately 8 % of pregnant women.

The etiology of maternal trauma is most often MVAs (55 %), followed by falls (22 %), assaults (22 %), and burns (1 %) [10, 12]. Younger gravid

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patients are at a higher risk for trauma than older ones [13]. Penetrating injuries constitute a greater proportion of injuries at inner-city centers [14, 15]. Fetal deaths have a different etiology: MVAs (82 %), gunshot wounds (6 %), and falls (3 %), with maternal death accounting for 11 % of the fetal deaths [16]. Reports show that 10–30 % of women are exposed to significant physical abuse during pregnancy, with an associated 5 % rate of fetal death [17–24].

The pattern of serious injuries in pregnant women is different from that of nonpregnant trauma patients: injuries to the abdomen are more common than injuries to the head and chest. The possibility of domestic violence should be considered, especially where the injuries are inconsistent with their alleged cause. The risk to the pregnancy in "minor" or noncatastrophic trauma is still significant, with preterm labor occurring in 8 %, placental abruption in 1 %, and fetal death in 1 %. For those with major trauma, maternal mortality is about 9 % [2], and the fetal death rate is 20 % or greater. About 5 % of fetal injuries occur without injury to the mother. When compared to nonpregnant trauma patients, pregnant women are younger, less severely injured, and more likely to be African-American or Hispanic. Twenty percent of pregnant trauma patients tested positive for drugs or alcohol in one study. In one series, 19–24 % of trauma patients delivered when they required hospitalization for an injury. Unfortunately, significant numbers of pregnant women who are injured have elevated blood levels of alcohol or illegal drugs. These substances contribute to automobile accidents as well as low birth weights.

10.1.2 Risk Factors

According to the literature, major risk factors for maternal trauma include [22, 25–30]:

- Young age (<25 years)
- African-American or Hispanic race
- Illicit drugs, alcohol, or smoking
- Domestic violence
- Noncompliance with proper seat belt use
- Epilepsy or other seizures
- Overweight and obesity
- Work outside the home
- Low socioeconomic status

The impact of mind-altering substances is significant. Ikossi et al. presented data from the American College of Surgeons National Trauma Data Bank, which revealed that 19.6 and 12.9 % of pregnancy-related traumas were associated with the use of illicit drugs or alcohol, respectively [22]. One institutional study showed intoxicants use in up to 45 % of the pregnant population involved in MVAs [28]. Intoxication, as anticipated, also contributes to a significantly lower use of restraints while driving when compared with sober patients (22 % vs. 46 %, respectively) [28].

Mothers who reported an injury during pregnancy were more likely to be aged <18 years versus 18–29 years and less likely to be aged ≥30 years. They were more likely to use alcohol during pregnancy, to smoke during pregnancy, to have epilepsy, and to be employed than mothers who did not report an injury [31]. The distribution by trimesters is more or less equal (Fig. 10.1).

However, knowledge of characteristics specifically associated with injury among pregnant women can be used to help identify women who may be at higher risk for experiencing an injury during pregnancy and can potentially inform the development of prevention programs for women to reduce the risk of injury during pregnancy. Many of these characteristics have been associated with adverse pregnancy outcomes, such as alcohol with fetal alcohol syndrome, smoking with orofacial defects [19] and preterm delivery [32], and obesity with neural tube defects [33] and Cesarean delivery [34]. Therefore, efforts to modify these exposures may have multiple positive impacts. For example, prevention of alcohol use during pregnancy could both reduce the fetus' direct risk from the alcohol exposure and

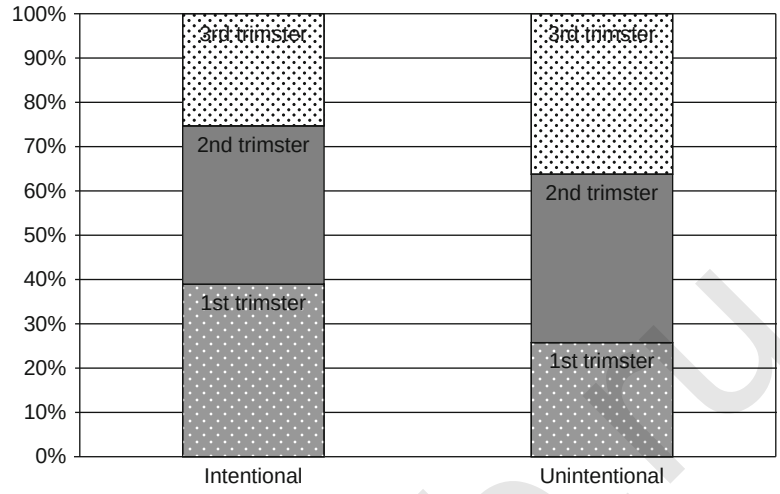

Fig. 10.1 Timing of injuries during pregnancy reported by mothers of control infants, by intention. National Birth Defects Prevention Study, 1997–2005 [30]

reduce the risks of maternal injuries, which can also adversely affect pregnancy outcome. It is recommended that all pregnant women be screened for alcohol use at their first prenatal visit [35] and screening questionnaires developed specifically for women are available [36]. Physician guidance has been demonstrated as an effective tool for reducing alcohol use [36].

10.1.3 Prevention

Despite advances in trauma management, the fetal and maternal mortality rates after traumatic injury have not declined. Because current management has little effect on mortality, prevention is a key to increasing maternal and fetal survival. MVAs and domestic violence are common preventable causes of trauma in pregnancy. Although, MVAs are responsible for most severe maternal injuries and fetal losses from trauma [9, 37–40]. Pregnant women have low rates of seat belt use [2, 26, 38, 41]. Proper seat belt use is the most significant modifiable factor in decreasing maternal and fetal injury and mortality after MVAs [11, 42, 43]. Seat belt-restrained women who are in MVAs have the same fetal mortality rate as women who are not in MVAs, but unrestrained women who are in crashes are 2.8 times more likely to lose their fetuses [17]. More on the subject can be found in section 10.2. Prenatal care must include three-point seat belt instruction [22, 44–46]. The lap belt should be placed under the gravid abdomen, snugly over the thighs, with the shoulder harness off to the side of the uterus, between the breasts and over the midline of the clavicle [43]. Seat belts placed directly over the uterus can cause fetal injury [47]. Airbags should not be disabled during pregnancy [43, 47]. Because many women are unaware of the potential for placental abruption without evidence of maternal injury, pregnant patients should be instructed to seek care immediately after any blunt trauma. Screening of younger patients is particularly important, because they have higher rates of MVAs and domestic violence [17, 48]. Resource materials in waiting rooms and restrooms allow patients to gather information without confrontation [26].

10.1.4 Anatomic and Physiological Changes in Pregnancy Relevant to Trauma

The possibility of pregnancy should be considered in all female trauma patients of reproductive age. Pregnancy causes anatomic and physiological changes involving nearly every organ system in the body, making the treatment of a pregnant trauma patient complex [49–51]. Some of the anatomic and physiological changes in pregnancy that are relevant to trauma are presented in Table 10.1 [52].

Table 10.1 Anatomic and physiological changes in pregnancy relevant to trauma

Organ system	Changes relevant to trauma
Uterus	*First trimester*: intrapelvic organ protected by the bony pelvis *Second trimester*: becomes an abdominal organ; the fetus is cushioned by a relatively large amount of amniotic uid *Third trimester*: the uterus is large and thin walled
Blood	Increase in plasma volume greater than in RBC results in a decreased HCT
Cardiovascular system	Increase in plasma volume and decrease in vascular resistance of the uterus and placenta cause an increase in cardiac output Increase in the cardiac rate *Second trimester*: decrease in both systolic and diastolic blood pressure
Respiratory system	Increased tidal volume and minute ventilation Hypocapnia in late pregnancy Decreased residual volume
GI system	Gastric emptying time is prolonged *Third trimester*: the bowel is pushed upward and lies mostly in the upper abdomen
Other systems	Dilatation of the renal calyces, pelvis, and ureters The pituitary gland increases in size The symphysis pubis and the sacroiliac joints widen

RBC red blood cell, *HCT* hematocrit, *GI* gastrointestinal

These changes, by altering the signs and symptoms of injury, may in uence the interpretation of the physical examination as well as laboratory results of traumatized pregnant women. This may affect the approach and the response to resuscitation [50, 51, 53]. During the first trimester of pregnancy, the uterus is confined and protected by the bony pelvis. It remains an intrapelvic organ until around the 12th week of gestation, when it rises and becomes an abdominal one. In the second trimester the small fetus remains cushioned by a relatively large amount of amniotic uid. By the third trimester the uterus is large and thin walled [54]. The uterus and its contents have increased susceptibility to injury (penetration, rupture, placental abruption, and premature rupture of membranes). Some of the characteristics causing this increased susceptibility include the difference in elasticity between the uterus and placenta, which causes the uteroplacental interface to be subject to sheer forces, and may lead to placental abruption [55]. Plasma volume increases throughout pregnancy and plateaus (peaks at the 34th week) at about 34 weeks of gestation. A smaller increase in the number of red blood cells results in a decreased hematocrit [51, 54]. The placental vasculature is maximally dilated, yet it is very sensitive to catecholamine stimulation [51, 54–56]. An acute decrease in the intravascular volume may result in a significant increase in the uterine vascular resistance. This could cause a reduction in fetal oxygenation, even though the maternal vital signs can stay within normal range [9, 51, 53, 55–57].

There are hemodynamic changes that are noted during pregnancy and that are relevant when dealing with injured pregnant patients. An increase in cardiac output is noted after 10 weeks of gestation that is due to the increase in plasma volume and the decrease in vascular resistance of the uterus and placenta. During the third trimester the uterus and placenta receive 20 % of cardiac output. A gradual increase in the cardiac rate, maximizing in the third trimester, must be considered when evaluating the tachycardic response to hypovolemia. In the second trimester there is a decrease in both systolic and diastolic blood pressure. Turning the patient to the left lateral decubitus position may, in some women, prevent hypotension [51, 54, 58]. Increased levels of progesterone in pregnancy are thought to increase tidal volume and minute ventilation. Hypocapnia is common in late pregnancy. The diaphragm elevates causing decreased residual volume. Maintaining adequate arterial oxygenation is important in the resuscitation of injured pregnant patients because of increased oxygen consumption during pregnancy [51]. The cardiovascular changes during pregnancy may complicate the evaluation of intravascular volume, the assessment of blood loss, and the diagnosis of hypovolemic shock [59]. Maternal hemodynamic measurements may not accurately re ect the status of the uteroplacental circulation. Animal

studies have demonstrated that maternal heart rate and blood pressure may remain within normal ranges during a 20 % acute blood loss or during a more gradual loss of 30–35 % of estimated total blood volume [60, 61]. Also Hoff et al. had documented the unreliability of maternal blood pressure and pulse rate in predicting fetal loss [62]. Physicians providing care to pregnant trauma victims should remember that pregnancy maximally dilates the uterine vasculature, so that autoregulation is absent, and uterine blood ow is entirely dependent on maternal mean arterial blood pressure (MAP). Pregnancy represents a state of accelerated but compensated intravascular coagulation, which has both advantages and disadvantages for the pregnant trauma victim [59]. Increased levels of coagulation factors may improve hemostasis following trauma; however, at the same time parturients remain at increased risk for thromboembolic complications during periods of immobilization. Because buffering capacity during pregnancy is diminished, pregnant trauma victims rapidly develop metabolic acidosis during periods or hypoperfusion and hypoxia.

Gastric emptying time is prolonged in pregnancy; therefore, in the emergency setting, early gastric tube decompression is important in order to avoid aspirations. In the third trimester, as the uterus enlarges, the bowel is pushed upward and lies mostly in the upper abdomen [54]. Therefore, in blunt trauma the bowel is relatively protected while the uterus and its contents (fetus, placenta) are more vulnerable. However, penetrating trauma to the upper abdomen can cause complex intestinal injury [51].

Other changes in pregnancy involving nearly every organ system in the body are important when treating a patient suffering a trauma. Physiological dilatation of the renal calyces, pelvis, and ureters is noted and should be taken into account when dealing with cases of pelvic and abdominal trauma. During pregnancy the pituitary gland increases in size. Shock can cause necrosis of the anterior pituitary gland, resulting in pituitary insufficiency. The symphysis pubis and the sacroiliac joints widen and should be considered when interpreting pelvic X-rays. In the vertex presentation, the fetal head is usually located in the pelvis and the rest of the body, above the pelvic brim. Pelvic fractures in late gestation may result in fetal head injury (skull fractures, intracranial injuries) [54, 63–65]. Differentiating between head trauma with convulsions and eclampsia (hypertension, proteinuria, and peripheral edema) as a cause for seizures is important [54].

Table 10.2 "Normal" laboratory values during pregnancy

Hematocrit	32–42 %
White blood cell count	5,000–12,000/μl
Toxicology screen	Negative
Arterial pH	7.40–7.45
Bicarbonate	17–22 mEq/l
pCO_2	25–30 mmHg
Fibrinogen	264–615 mg/dl

There is an increase in the level of maternal plasma fibrinogen, as well as factors II, VII, VIII, IX, and X, and a decrease in plasminogen activator levels. This is important to remember in any trauma situation where hypercoagulability and the risk of deep venous thrombosis are already increased.

The clinician should be aware of "normal" laboratory values during pregnancy (Table 10.2). Note that it is normal to have an elevated white blood cell count, slightly elevated arterial pH, decreased serum bicarbonate level and arterial pCO_2, and increased fibrinogen level. The finding of a normal nonpregnant value for pCO_2 or fibrinogen in the pregnant patient is especially concerning.

10.1.5 The Impact of Pregnancy on Trauma Mortality

Literature regarding hormonal in uences on outcomes after trauma is abundant, yet findings have been contradictory. In experimental models, relatively high estrogen (and progesterone) levels have been beneficial with respect to immunomodulatory and vasodilatory effects and ultimate outcome (survival) after traumatic injuries [66–69].

Findings in clinical publications vary widely, with some studies showing survival advantage in premenopausal women [70–72]. If a hormone-dependent survival benefit does exist, then pregnant women who have higher estrogen and progesterone levels might be expected to exhibit lower mortality compared with similarly injured nonpregnant women. Using the matching process, Preeti et al. found that pregnant trauma patients are approximately 40 % less likely to die than their nonpregnant counterparts [73]. On subgroup analysis, this survival benefit was evident in younger women, suggesting a possible additive beneficial effect of youth and pregnancy. Of interest, there was no survival benefit in pregnant women when severely injured patient subgroups were compared (ISS >15, severe head injury, severe abdominal injury, or patients in hypotensive shock), suggesting that whatever advantage that pregnancy may confer may be limited. Also of note is the trend toward increased likelihood of death in pregnant patients with severe abdominal injury, a finding which may be related to placental abruption contributing to internal hemorrhage in this subgroup [73].

A study with data from the *National Trauma Data Bank* for the period 1994–2001 analyzed outcomes in 1,195 pregnant trauma patients [22]. The crude mortality rate for pregnant patients who were injured in their study was 1.4 %, compared to 3.8 % for nonpregnant patients ($p < 0.001$). Another study using a smaller dataset found that "pregnancy does not increase maternal mortality from trauma" and that the most frequent cause of death in injured pregnant patients was head injury [37]. However, there is no proof that estrogen and progesterone are responsible for the survival advantage of pregnant patients. Probably hemodynamic changes are responsible as well as more close observation of pregnant than nonpregnant patients.

10.1.6 Major Obstetric Hemorrhage and Transfusion Protocol

10.1.6.1 Cardiopulmonary Resuscitation (CPR)

Hypovolemia will manifest as thready pulses, tachycardia, attened neck veins, pallor, and prolonged capillary refill. If a radial pulse is palpable, the systolic blood pressure is approximately 80 mmHg. The absence of carotid and peripheral pulses indicates pulseless electrical activity and *Advanced Cardiovascular Life Support* (ACLS) protocols should be initiated. If there is a need to defibrillate the patient, standard ACLS voltage should be used (Fig. 10.2). There is no evidence that the fetus is harmed by the current from defibrillation [74]. External fetal monitors should be removed before delivering shocks [74]. Chest compressions should be carried out with the understanding that the maternal heart is displaced upward in the chest by the gravid uterus at advanced gestations, and this should guide hand placement [74].

Protocols for defibrillation and doses of medications are not changed in pregnancy.

The CPR should not be interrupted for the sake of giving medications because they get circulated with compressions [75]. Giving medications in pregnancy through lower extremity lines should be avoided because they may not adequately reach the maternal heart because of compression by the gravid uterus [76]. Palpable femoral pulses have not been shown to be reliable indicators of blood ow during CPR because retrograde ow in the femoral vein could mimic femoral artery pulsations [77]. The presence of a carotid pulse during CPR is also not an indicator of adequate cerebral or coronary blood ow [77]. An end-tidal CO_2 monitor can be used as an indicator of adequate CPR efforts and return of spontaneous circulation [77].

10.1.6.2 Major Hemorrhage

Major obstetric hemorrhage is defined as a blood loss of ≥2,500 ml, transfusion of five units of red blood cells, or treatment of a coagulopathy [78, 79]. Transfusion of blood and blood products in trauma and major hemorrhage is changing as a result of experience in military medicine. Resuscitation in obstetric hemorrhage is similar to that in trauma as both aim to stop bleeding, maintain efficient oxygen delivery, and prevent development of the "lethal triad" of acidosis,

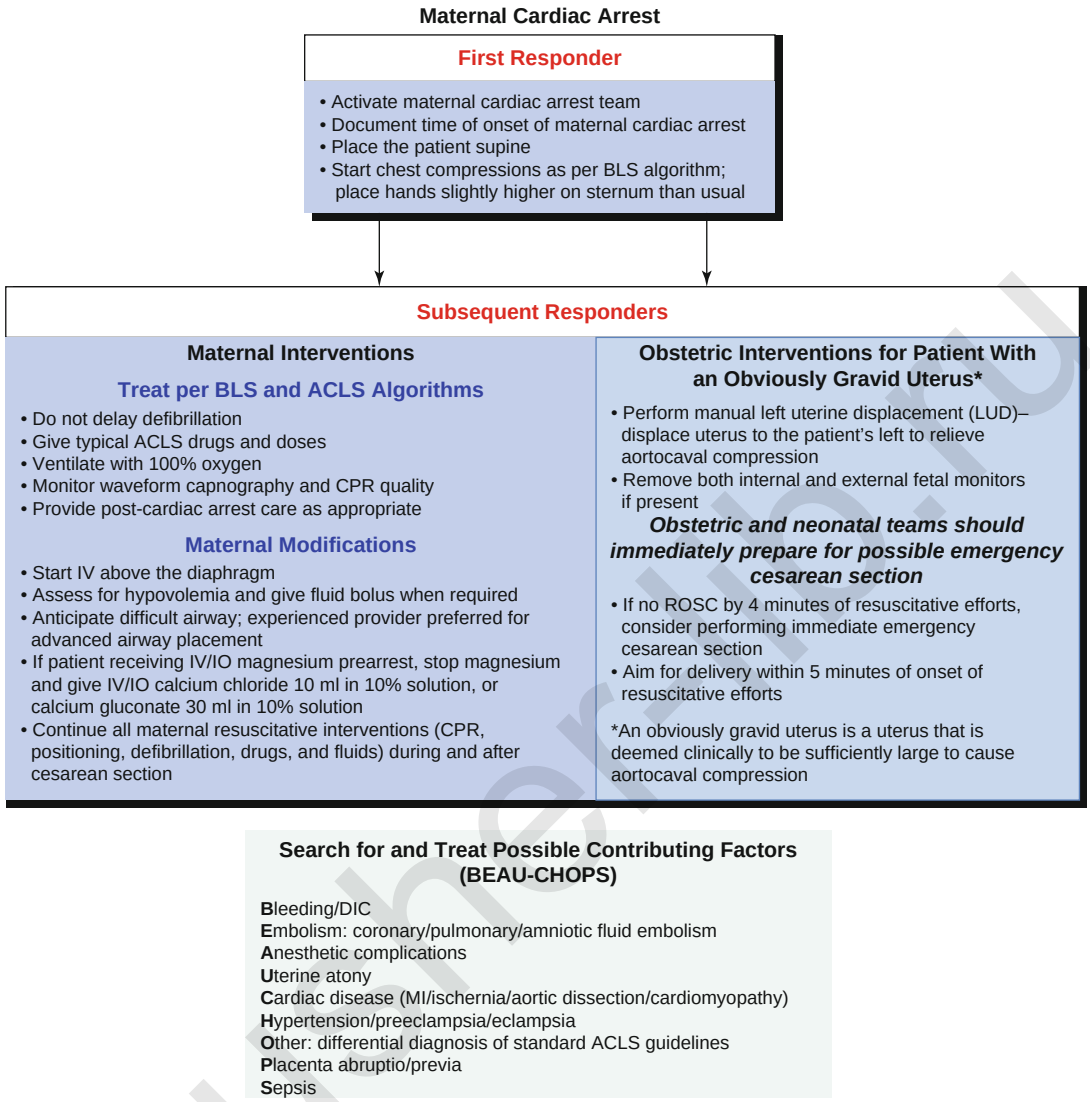

Fig. 10.2 Maternal cardiac arrest algorithm [74]

coagulopathy, and hypothermia [80–83]. Obstetric resuscitation often starts with administration of clear intravenous uids and packed red blood cells (pRBC), following which the use of clotting products and platelets is considered, often guided by coagulation studies that delay treatment [80]. The UK National Patient Safety Agency recommends monitoring laboratory blood tests during massive transfusion, but also that administration of blood and blood products should not be delayed while awaiting results [78, 80, 81].

Resuscitation of bleeding patients with crystalloid, colloid, and plasma-poor pRBC at the same time when clotting factors are being consumed results in the concentration of plasma coagulation factors falling to <40 % and typically occurs before 10 units of pRBC has been given [84]. Disseminated intravascular coagulopathy in obstetric hemorrhage can also occur early, especially if hemorrhage is not treated rapidly. Early treatment of massive hemorrhage after trauma using fresh frozen plasma (FFP) and pRBC in a 1:1 ratio, current practice in US and British military, is thought to improve survival [84–89]. Military guidelines for hemorrhagic shock also recommend administration of platelets in a 1:1 ratio with pRBC [85–87, 89].

Prevention of coagulopathy should be better than its treatment and requires anticipation [84]. Some authors advise that replacement of clotting factors should be made on clinical grounds, rather than based on laboratory results [85, 89, 90]. The Association of Anesthetists of Great Britain and Ireland guideline recommends early infusion of FFP (15 ml/kg) to prevent hemostatic failure and may need to be started if a senior clinician anticipates massive hemorrhage [91]. This guideline emphasizes the importance of preventing hemostatic failure because, once established, standard regimens of FFP infusion are likely to be inadequate and larger volumes will be required with greater risk to the patient and cost implications for the hospital [91].

For massive obstetric hemorrhage, a ratio of 6:4:1 for pRBC/FFP/platelets has been suggested. If bleeding continues after initial treatment, consideration should be given to increasing the amount of FFP to give a ratio of 4:4:1 [81]. Point-of-care tests can measure hemoglobin concentration and the coagulation profile and may guide blood product replacement following initial resuscitation.

Fibrinogen concentrations are also greater in pregnancy; the optimal posttransfusion fibrinogen concentration has been suggested as 1.0–2.0 g/l [80].

The high ratios of pRBC to coagulation products that are recommended for other types of trauma may therefore not be required in the obstetric patient, whereas greater replacement of fibrinogen may be necessary. There is evidence to support 1:1:1 ratios of pRBC/FFP/platelets in trauma but less so in obstetrics [80, 85–89, 92–96].

Maintenance of a platelet count of $50–100 \times 10^9$/l has been suggested although should only be used as a guide in conjunction with the patient's clinical condition [80]. pRBC/platelet ratios of 5:2 and 5:1 have been described with good results [80, 88].

Consensus guidelines in the literature suggest that recombinant factor VIIa (rFVIIa) should be considered before hysterectomy if hemostatic failure and hemorrhage continue despite optimal blood product replacement and obstetric management [80, 82, 97, 98]. Arterial thrombosis is a potential complication of rFVIIa use but has not been reported in a case series of 15 patients [97]. Its safety in the obstetric population is unproven, and it carries a significant cost implication. Using thromboelastography and thromboelastometry to guide optimum ratios of blood product replacement during obstetric hemorrhage may be limited by time during the initial resuscitation phase, and there is limited familiarity with their use in obstetrics [78, 80, 81, 96].

10.1.7 Prehospital Issues

The initial key to survival of both mother and fetus is prehospital management. Pregnancy is considered a triage criterion for transport to a trauma center by the *American College of Surgeons Committee on Trauma*. Despite this recommendation, literature on the appropriate level of care in injured pregnant patients is very limited. Goodwin and Breen [99] proved in a landmark contribution in 1990 that in addition to the accepted *Advanced Trauma Life Support* (ATLS) guidelines (first five on the list) for *transfer of patients to level I trauma centers*, there are four additional:

- Glasgow Coma Score <14
- Respiratory rate <10 or >29
- Systolic blood pressure <90 mmHg
- Revised Trauma Score <11
- Anatomy or mechanism of injury
- Pulse >110
- Chest pain
- Loss of consciousness
- Third trimester gestation

These criteria are particularly useful in mass casualty triage of patients in adjunction to prehospital trauma scoring systems in order to identify those patients who would benefit most from rapid transfer to trauma centers. In general, guidelines for adult prehospital trauma care also apply to pregnant trauma victims. Upon initial

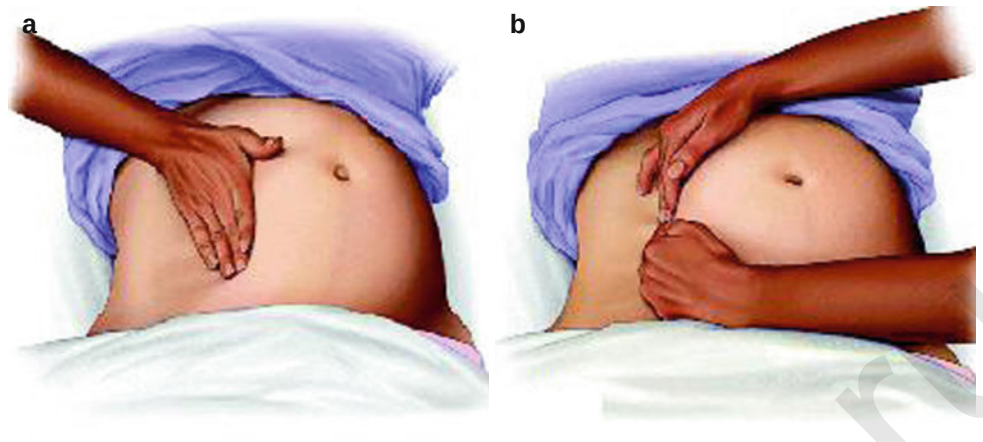

Fig. 10.3 Left lateral uterine displacement using (**a**) 1-handed technique and (**b**) 2-handed technique [74]

assessment, *emergency medical services* (EMS) should follow standard protocols like extrication with spinal immobilization and resuscitation as outlined in the ATLS guidelines. The decision to intubate the patient in the field is largely unaffected by pregnancy. Unique to the gravid patient in airway management are, however, as follows:

- Increased risk of aspiration due to delayed gastric emptying and decreased lower esophageal sphincter tone in combination with intra-abdominal hypertension.
- Despite safety of rapid-sequence intubation in pregnancy, because of lower serum pseudocholinesterase levels in pregnancy, using a lower dose of succinylcholine during induction is recommended [100].
- Both depolarizing and non-depolarizing muscle relaxants cross placenta. Effects of these drugs onto CTG pattern and fetal activity might lead to a falsely non-reassuring tracing and non-indicated intervention.

In the event of delivery, the neonatologist might be faced with a accid, apneic infant. Hence, it is pertinent to relate any prehospital use of medication by EMS to the receiving institution and trauma team. In general, the potential catastrophic consequences of the patient losing her airway in the field or during transport usually justify acceptance of the minor risks associated with using paralytic and induction agents. Early establishment of a definite airway is usually the safest option.

Avoidance of the supine hypotension syndrome (uterocaval compression) should be paramount part of all initial resuscitative measures in pregnant trauma patients. Placing the patient on a backboard with a 15° angle to the left is a pregnancy-specific intervention that should be employed in all patients beyond 20 weeks of gestation. Abundant clinical data have proven that the significantly decreased cardiac output of up to 60 % due to uterocaval compression leads to prolonged resuscitation with increased acidosis and vasopressor requirements [101, 102]. Below 24 weeks *manual left lateral displacement* might be sufficient. There is 1-handed (Fig. 10.3a) and 2-handed (Fig. 10.3b) technique according to the *American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care* from 2010 [74].

In gestations of >24 weeks, a 30° lateral tilt is recommended (Fig. 10.4) [74]. Although this reduces the efficacy of CPR compared to the supine position, in pregnant patient, the slightly reduced efficacy of chest compressions is outweighed by improved cardiac preload and overall cardiac output [101]. Therefore, current *Eastern Association for Surgery and Trauma* (EAST) guidelines now recommend a left lateral tilt of at least 15° during the initial phase of resuscitation.

Fig. 10.4 Patient in a 30° left lateral tilt using a firm wedge to support the pelvis and thorax in gestations of >24 weeks [74]

Placement of a hard backboard in the supine position might not be tolerable for third trimester gravida. The increased work of breathing due to increased diaphragmatic splinting might lead to respiratory failure. In this circumstance, transport in a 30° reversed Trendelenburg position seems acceptable [12]. As far as i.v. access routes in pregnant trauma patients are concerned, femoral access procedures should be avoided. Because of the risk of uterocaval compression, distribution of medication or uids might be significantly altered when using the femoral route in pregnant patients.

Whenever possible, pregnant females should be transported rapidly to a designated trauma center that has the facilities for adequately managing both mother and fetus. The transfer should occur rapidly even in cases of minor trauma because of the high incidence of fetal demise even under these circumstances. Paramedics should seek information regarding pregnancy from female patients of childbearing age. A distended abdomen may be due to a gravid uterus or intra-abdominal bleeding. Pregnancy should prompt positioning of the patient in the left lateral decubitus position to avoid compression of the vena cava by the uterus and resultant hypotension. Should the emergency medical technician suspect a spinal fracture, a left lateral tilt position can be utilized. Oxygen supplementation by nasal cannula or face mask should be routine. In the event that prehospital transfusion is required, O-negative blood should be used whenever possible. Emergency medical services that still use the military antishock trousers (MAST) should be aware that it is contraindicated to in ate the abdominal portion of this device for pregnant women. Not only can this maneuver cause reduced uterine perfusion, but it also can increase the cardiac workload.

Appropriate personnel must be present or readily available at the emergency room when the emergency vehicle arrives. A team should be assembled that includes a neonatologist, anesthesiologist, trauma surgeon, sonographer, and staff radiologist. If a pelvic fracture or bleeding is suspected, a senior interventional angiographer should be notified immediately to be on standby.

10.1.8 Anesthetic Perioperative Care

The recent literature documenting obstetric, anesthetic, and surgical management of pregnant trauma victims is limited [42, 103–108]. The pregnant trauma victim presents a unique spectrum of challenges to the trauma health-care team. The surgical diagnosis may be unknown at the time of incision, as may be the nature and extent of the procedure being undertaken. The fact that pregnancy may not always be known to be present to the health-care team (at the scene of transportation accidents, in the emergency room, or in the operating room) additionally complicates the situation. Pregnancy must always be suspected (until proven otherwise) in any female trauma patient of childbearing age [103].

Vasopressors, which are very rarely indicated in trauma patients, should be avoided unless absolutely necessary because of the risk of decreasing uterine blood ow. If it is required, ephedrine should be the first choice as it preserves the uterine blood ow, but there should be no hesitation in using other vasopressors when necessary.

10.1.8.1 Head and Neck Injury

If there is an uncertainty about the integrity of the cervical spine, direct laryngoscopy should be avoided, and fiberoptic (awake fiberoptic) intubation of the trachea, if feasible (time constraints and/or equipment availability), should be considered [104]. If direct laryngoscopy is deemed necessary, an "in-line stabilization" of the head and neck by an assistant to prevent extension and rotation of the cervical spine is indicated. If awake fiberoptic intubation of the trachea is selected, it is essential to titrate analgesic and sedative drugs carefully to maintain continual meaningful verbal communication between the anesthesiologist and the patient. Respiratory depression and aspiration of stomach contents during the application of a local anesthetic agent is much less likely to occur if the patient remains awake and alert. In addition, a rational alert mother minimizes the risk of neonatal depression. Midazolam is the benzodiazepine recommended for these purposes; however, it is highly unionized and very lipophilic, and its fetal/maternal ratio is 0.76 at 15–20 min after maternal administration. However, unlike other benzodiazepines, the ratio falls rapidly. No adverse fetal effects have been reported [109].

It has been empirically established that trauma victims with a GCS $\leq$8 usually require intubation and mechanical ventilation for both the airway control and control of the intracranial pressure. However, trauma victims with "good" GCS can "talk and deteriorate/die" following traumatic head injury, particularly an injury associated with loss of consciousness, and delayed deterioration has been observed up to 48 h after the initial insult.

The succinylcholine-induced ICP increase has been a concern in the past, nevertheless; recent analysis of the problem has shown that the magnitude and clinical importance of this increase has been grossly exaggerated. It is currently believed that when there is an urgent need to secure an airway in the head-injured pregnant trauma victim, succinylcholine is an appropriate and safe drug, and it should be used. All of the intravenous anesthetic agents (except ketamine) cause some degree of vasoconstriction and therefore decrease in cerebral blood ow. All of the inhaled agents have some cerebral vasodilatory effect; however, their administration is usually consistent with acceptable ICP levels [110, 111].

10.1.8.2 Intra-abdominal Injuries

In abdominal trauma, liver and splenic tears increase with increasing uterine enlargement as these organs are compressed by the uterus against the rib cage [112]. The uterus itself is relatively resilient [113]. In a study from the Denver General Hospital [114], the incidence of injuries encountered at laparotomy after blunt trauma in the general population was spleen 46 % and liver 33 %, followed by the mesentery (18 %), urinary tract (9 %), pancreas (9 %), small bowel (8 %), colon (7 %), and duodenum (5 %). Seat belts and compression against vertebrae are other causative factors in injuries to bowel, pancreas, kidney, etc. Bowel injuries occur at the sites of fixation such as the duodenum, cecum, splenic exure, and rectosigmoid. The duodenum is especially susceptible to injury. The third segment of the duodenum, because of its fixed position directly over the lumbar spine, is the most commonly injured segment of the intestinal tract [115, 116]. After the 12th week of pregnancy, trauma to the pelvic region is a serious problem because the urinary bladder has been displaced anteriorly and superiorly out of the protective bony pelvis [117].

10.1.8.3 Fetal Physiology and Assessment

Fetal Physiology

During the first week, the conceptus has not yet implanted in the uterus, making it relatively resistant to injury. Soon thereafter, the embryo attaches to the uterus via the anchoring villi. The placenta is not as elastic as the myometrium, potentially leading to shear stresses and disruption of the villi when force is applied to the uterus. The well-being of the fetus is dependent on the adequacy of the maternal blood ow to the placenta, which is mainly derived from the uterine arteries. The uterine vascular bed is a low resistance system, not capable of further dilation and devoid of autoregulation. Therefore, placental blood ow varies directly with the net perfusion pressure (uterine

Table 10.3 Factors predicting fetal death in trauma

Ejection from vehicle
Pedestrian injury
Lack of restraints
Maternal tachycardia
Maternal hypotension
Maternal hypoxia
Maternal contractions
Abnormal fetal heart rate
Injury severity score >9

artery pressure-uterine venous pressure) across the intervillous space and inversely with uterine vascular resistance. When faced with maternal hypotension, in order to preserve uteroplacental perfusion in a "pressure-passive" system, a more aggressive approach to management (rapid uid loading, vasopressor therapy, and Trendelenburg and left lateral positioning) is required compared to strategies for the nonpregnant patients. The ability of the fetus to withstand changes in uterine blood ow or oxygenation is variable. The fetus can redistribute blood ow to the most vulnerable organs, the brain and heart, but the protection afforded by this response ("the diving re ex") is limited. Decreased placental blood ow quickly leads to fetal distress.

Fetal Assessment

The aim of fetal assessment is to detect fetal distress and reduce the risk of fetal loss. Some authors have in the past been unable to identify any significant risk factors relating to injury or patient physiology that would predict poor outcome [118, 119]. More recently, a number of risk factors for fetal loss have been identified, including penetrating uterine injuries, severe maternal head injuries, and maternal pelvic fractures, but each series identifies slightly different factors (Table 10.3) [9, 38, 53, 62, 120].

Obstetric sonogram should be performed to assess fetal viability, fetal age, and fetal well-being [12]. Evaluation of fetal trunk and extremity movement, fetal breathing activity, amniotic uid volume, and fetal heart rate changes with fetal movement will establish fetal well-being. Any viable fetus of 24 weeks or more requires cardiotocographic (CTG) monitoring after maternal trauma. This includes patients with no obvious signs of abdominal injury. Pearlman et al. have recommended a minimum of 4 h of CTG observation to detect intrauterine pathology [118]; others recommend 6 h. This should be extended to 24 h if at any time during the first 6 h there is more than one uterine contraction every 15 min, uterine tenderness, non-reassuring fetal CTG monitoring, vaginal bleeding, rupture of the membranes, or any serious maternal injury. Rogers et al. studied 372 traumatic fetal deaths from several institutions. Sixty-one percent were in patients undergoing continuous fetal monitoring, but seven fetuses with CTG abnormalities were saved by Cesarean section [9]. Formal ultrasound of the fetus may provide important information [39], such as the presence of liver injury [121] or intracranial hemorrhage [122].

Most hospitals have limited experience in managing pregnant patients who are involved in trauma. Between 1989 and 1998, Liverpool Hospital has had six fetal deaths, of which five arrived in the resuscitation room with fetal heart sounds, or CTG evidence of viability [123]. Facilities for rapid Cesarean section must be available if fetal deaths are to be avoided. Fetal compromise is present in over 60 % of placental abruptions with a live fetus, and an immediate Cesarean section is indicated. The overall fetal mortality with placental abruption is 54 % [9]. Adequate resuscitation of the mother is absolutely vital. If maternal shock occurs, fetal mortality approaches 80 %. Fetal monitoring should be continued for 24 h for all patients with a risk factor listed in Table 10.3. Patients who enter preterm labor and those at risk of developing contractions (i.e., gestational age >35 weeks, victims of assault, and pedestrians hit by motor vehicles) should also be monitored for 24 h [38]. The recommended length of fetal monitoring can be reduced to 6 h or less in low-risk patients [38, 124]. Maternal plasma bicarbonate levels may be a predictor of outcome. Scorpio et al. found that injured mothers with fetuses who survived had a mean plasma bicarbonate level of 20.3 ± 2.2 mEq/l compared with 16.4 ± 3.0 mEq/l in those with fetal loss [40].

Restoration of both maternal and fetal circulation is the goal of adequate resuscitation. However, there are unusual situations in which exclusive attention to the mother may preclude delivery of a viable baby. Maternal revival after delivery of the fetus has been reported in perimortem circumstances, presumably due to relief of vena cava compression, or more effective cardiopulmonary resuscitation after pressure below the diaphragm is relieved, but this is rare. It is therefore suggested that there is no place for postmortem Cesarean section – only perimortem Cesarean section. If there is no response to advanced resuscitation within a few minutes, maternal cardiopulmonary resuscitation should be continued, and a Cesarean section should be performed.

In a review of 250 years of literature to 1961, Ritter found 120 successful perimortem Cesarean sections reported [125]. Strong et al. in 1989 reported that about half of the perimortem Cesarean sections in the literature had produced live infants, but the incidence of neurological squeal increases with increasing delays to delivery. The long-term survival rate of healthy infants was 15 % [126]. Perimortem Cesarean section is discussed in further sections in this chapter. Cesarean section should only be performed in the emergency department when:

- The uterine size exceeds the umbilicus.
- Evidence of fetal heart activity (Doppler or M-mode ultrasound).
- CPR for not more than 10 min.

It is important to consider the possibility of other complications of trauma in pregnancy such as amniotic uid embolism and fetomaternal hemorrhage (which affects about 30 % of pregnant women suffering recent abdominal and/or multiple trauma) [44].

Amniotic uid embolism is rare, but it is an important cause of disseminated intravascular coagulation and shock [127]. It was first described by Meyer in 1926 and established as a clinical entity by Steiner in 1941 [128]. Amniotic uid embolism is almost always fatal and should be suspected in every instance of the traumatized pregnant patient who develops signs of respiratory distress with or without right heart strain and disseminated intravascular coagulation. Wider application of right-heart blood smear and searching for monoclonal antibodies against fetal mucin may provide a better indication of the prevalence of the problem.

Fetomaternal hemorrhage is the transplacental passage of fetal cells into the maternal circulation and is a unique complication of pregnancy. The reported instance is 8–30 % in traumatized pregnant women, compared with 2–8 % for nontraumatized mothers [99, 118]. Anterior placental location and uterine tenderness have been associated with an increased risk of fetomaternal hemorrhage. Complications include Rh sensitization in the mother, fetal anemia, fetal tachycardia, and fetal death. The volume of fetal blood lost after trauma can vary between 5 and 40 ml – this can represent up to 34 % of fetal blood volume. As little as 1 ml of Rh+ blood can sensitize 70 % of Rh- women [44, 129]. Therefore, all Rh- mothers who present with a history of abdominal trauma should receive a prophylactic dose of Rh immune globulin. The Kleihauer-Betke test has been used to determine the presence of fetal-maternal hemorrhage. It is semiquantitative and may alert the obstetrician to a serious hazard for the fetus even in Rh+ women.

Complete diagnostic algorithm for the injured gravida is presented on Fig. 10.5.

10.2 Blunt Trauma

10.2.1 Incidence

MVAs, domestic violence, and falls are the most common causes of blunt trauma in pregnancy [2, 10, 11, 19, 26, 37–39, 53, 57, 118, 131]. In Australia, blunt trauma accounts for nearly all trauma during pregnancy (MVA, injuries to occupants 65–75 %; falls 10–20 %; motor vehicle collision, injuries to pedestrians 5–15 %; assault 1–10 %) [123, 132], whereas in the United States, penetrating injuries account for up to 10 % [2].

Different mechanisms of maternal injury occur in pregnant women with blunt abdominal trauma compared with their nonpregnant counterparts. Because the gravid uterus changes the

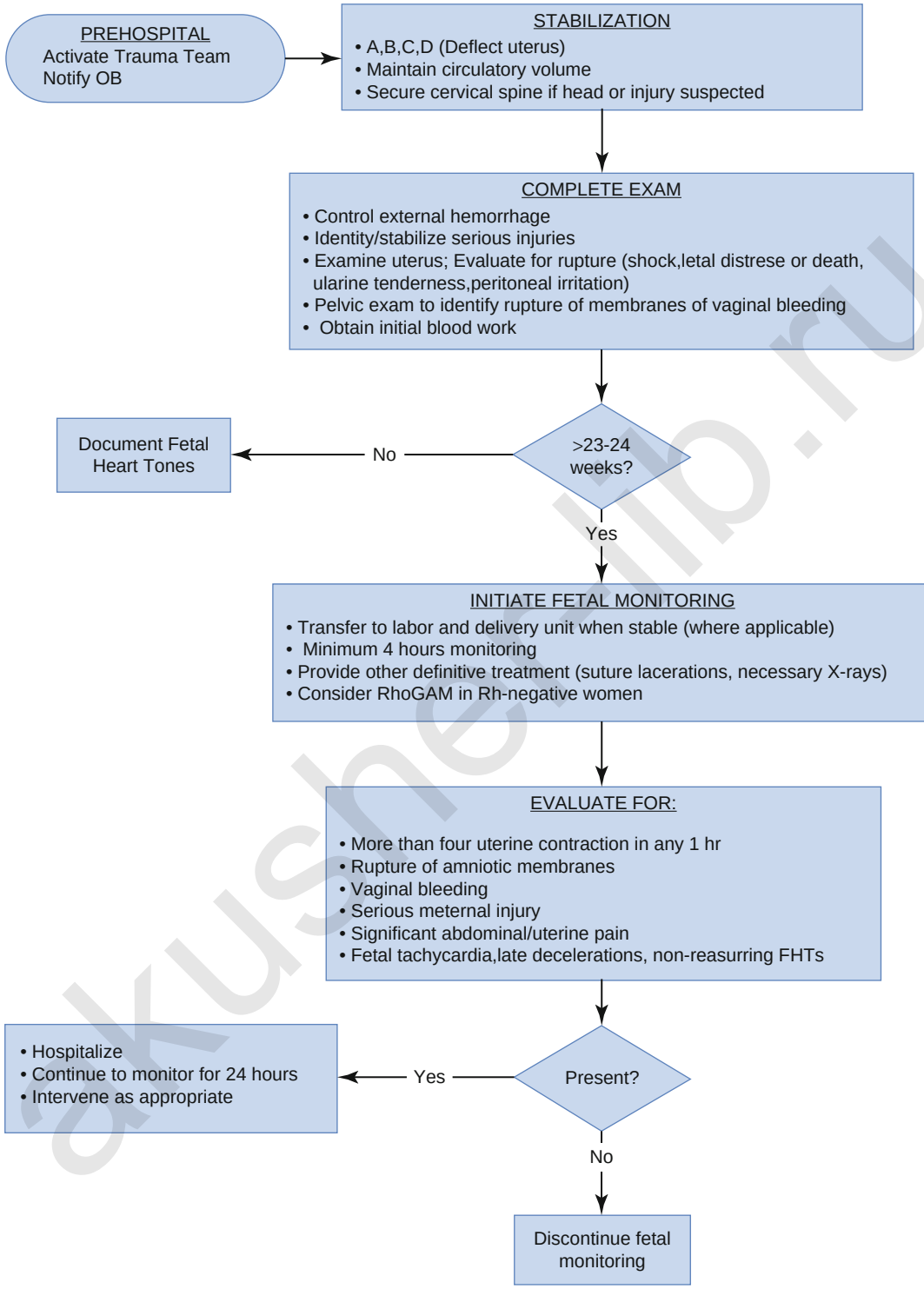

Fig. 10.5 Algorithm used at the University of Michigan, guiding care of the injured gravida [130]

relative location of abdominal contents, transmission of force may be altered in the pregnant abdomen [9, 55, 58, 63–65, 133]. Before 13 weeks of gestation, the uterus is protected by the bony pelvis. Fetal loss in the first trimester is not secondary to any direct uterine trauma but usually is due to maternal hypotension, with hypoperfusion of the uterus and its contents or the mother's death. Direct fetal injury is extremely rare following blunt trauma, complicating <1 % of all significant maternal trauma. Uterine rupture following blunt trauma is also rare, occurring in 0.6 % of cases of blunt trauma during pregnancy. Pelvic fractures are specific challenges because hemorrhage from the many dilated venous tributaries can cause significant retroperitoneal blood loss.

10.2.2 Motor Vehicle Accidents

10.2.2.1 Introduction

Automobile crashes are the largest single cause of death for pregnant females and the leading cause of traumatic fetal injury mortality in the United States [107, 134]. Each year, 160 pregnant women are killed in MVAs and additional 800–3,200 fetuses are killed when the mother survives in the United States [135, 136]. According to research by the *National Highway Traffic Safety Administration* (NHTSA), in the United States, passengers who use seat belts in the back seat of vehicles have 44 % more chance to survive a traffic accident than those travelers who are not tied. According to the same source, in 2006, there were 81 % of passengers in cars tied with safety belt in the United States, which according to NHTSA data saved 15,383 lives. However, research also shows that 37 % of passengers died in traffic accidents, despite the fact that they were fastened by a safety belt. The reason for this is the inappropriate handling of safety belt, which can result in fatal consequences. This was in particular expressed by the least-protected groups in transport, namely, children under 12 years of age and pregnant women. For these reasons, by legal requirements, the use of additional passive safety factors was prescribed for children less than 12 years, i.e., car seat. Because of that, in the final law on road traffic, safety requires that all children under 12 years must use a child safety seat adapted to their age, unless they are transported to a place where there is a zone in the two-point binding. There is no legal framework for a pregnant woman that obliges them to undertake special measures when driving.

The crash risk for reported pregnant occupants in these data was about one half that of all women in the same age range. However, one should use caution before presuming from these data that pregnant women are at lower crash risk. Identifying pregnancy status from crash and medical records is not always easy for crash investigators because early pregnancy cases may not be known or reported. Further, many women are not interviewed directly, resulting in reliance on written records that may or may not exist, especially for events that often do not result in hospital visits. Also, the methods for determining pregnancy and the completeness and accuracy of pregnancy status in National Automotive Sampling System/Crashworthiness Data System (NASS/CDS) have not been externally validated (e.g., by matching cases forward in time to birth certificates). Furthermore, NASS/CDS coding rules state that when pregnancy status is unknown, cases are to be assigned to the "female not-reported pregnant" category [137, 138]. There is evidence from a statewide injury inpatient study that the hospitalized crash injury rate of pregnancy-associated cases is not lower compared to that of all women of reproductive age (even after length of stay adjustment) [13].

The data also lack patient follow-up with the result that little is known or tracked about nonfatal fetal crash outcomes. MVAs are probably a larger threat to fetuses than to infants due to increased crash involvement, increased vulnerability due to dependence on placental circulation for survival, vulnerability to sensitive developmental periods of risk, and perhaps comparatively less protection from the in utero environment than infants receive from safety seats. With more women driving and driving more miles today than two decades ago [139], it has been estimated that about 2 % of all live

births in the United States, or 79,000 children (a rate of 26/1,000 person-years), are exposed in utero to a police-reported crash [107]. For comparison, the NHTSA reports that there are only about 23,188 infants reported in crashes each year (a rate of 6/1,000 person-years) [107].

Given the potential numbers of exposed fetuses, longitudinal research on nonfatal fetal outcomes is needed. Fetal trauma exposure has received very little attention among reproductive and environmental scientists and funding agencies. This is mainly due to the following: (1) major deficiencies in the way fetal trauma-related deaths are coded in vital statistics, (2) the lack or poor quality of pregnancy status variables and follow-up in most injury surveillance systems, (3) unfamiliarity by many reproductive health researchers with injury science and the large societal burden of injury, and (4) the difficulty of attributing adverse birth outcomes and developmental problems many months or years after trauma. However, the recent convergence of several research lines suggests reasons why this problem should receive urgent attention.

10.2.2.2 Mechanism of Maternal and Fetal Trauma

The first experimental research was on the Savannah Baboon (*Papio cynocephalus*), chosen because the uterine and placental anatomy is similar to that of the human. The baboon breeds well in captivity and pregnancy can be accurately diagnosed and dated. The gestational period averages 167 days and the neonate weighs 750–1,000 g at birth [140]. Physical characteristics of many automobile accidents closely agree with those used in that study [141]. The injuries observed are similar to those reported in automobile accidents involving pregnant women [142, 143]. No attempt was made to compare fetal survival between restraint systems because the number of available animals was small and because the surgical procedures resulted in fetal death in the absence of deceleration. There is a remarkable increase in uterine pressure during impact. The maximum pressure observed was approximately 10 times that observed during labor [144]. Simultaneous recordings of abdominal pressure during impact show that the uterus was not protected from rupture by an equal but opposing pressure within the surrounding abdominal cavity [145]. Nor was there a decrease in uterine pressure during impact when forward exion was prevented by shoulder restraint or rearward-facing impact. The findings also indicate that the gravid uterus is capable of withstanding extraordinary pressures of short duration and that such pressures are produced by deceleration with or without subsequent body exion. Maternal response to impact consisted of transient depression and bradycardia. The former resembled mild cerebral concussion. Postimpact bradycardia occurred only with violent motion of the body. Stapp and Taylor reported this phenomenon in deceleration experiments on human volunteers and attributed it to increased vagal tone secondary to acute hypertension in the carotid sinus. This effect can be abolished by atropine and occurs only when there is rapid forward motion of the head and neck [146].

In experimental crashes (Figs. 10.6 and 10.7), pregnant baboons were placed in two-point restraint in a Hyge sled accelerometer which simulates an automobile crash under conditions of rapid deceleration. At 40 km/h, a biphasic increase in intrauterine pressure is experienced. The first increase results from sudden deceleration of the pelvis, stopped by the lap belt. At the same time, the uterus continues to move forward striking the anterior abdominal wall. This results in an increase in intrauterine pressure approaching 500 mmHg. Later during this crash sequence, the upper torso of the animal is thrown forward essentially collapsing around the pregnant uterus creating a second increase in intrauterine pressure, approaching 550 mmHg. From this and other experiments with animals held by three-point restraints (*lap belt* and *shoulder belt*), it is clear that the second increase in intrauterine pressure can be eliminated by preventing the torso from collapsing around the pregnant uterus. This results in a decrease in fetal mortality from 100 to 40 % [147].

The first important research line comes from reports by the NHTSA and others, which have shown that in the period 1975–1990, primarily

because women are driving more miles, the number of fatal crashes involving female drivers has increased dramatically by 62 % [139]. This large increase in exposure may have resulted in a poorly documented trauma-induced epidemic of fetal loss, fetal injury, and adverse reproductive outcomes. While there is indirect corroborating evidence from national vital statistics data of similar increases in neonatal deaths due to maternal trauma during this time span [148], there is currently no way of confirming this because of the documentation problems mentioned above.

Fig. 10.6 The experimental research on the Savannah Baboon delivered the first knowledge on maternal and fetal physiology during and after motor vehicle accidents with belt restraint [140]

The second research line emerges from looking at the relationship between stress reactions and preterm labor. Although much of this work has focused on the stress of poverty, abuse, and social disparities, trauma itself is a widespread but often overlooked trigger of high levels of stress. It has recently been estimated that 9 % of survivors of serious crashes develop significant post-traumatic stress symptoms and that many other survivors have post-traumatic stress disorder-like reactions [148, 149]. In fact, MVAs may be the leading cause of post-traumatic stress disorder, providing fertile opportunities for stress/reproductive research. One thread suggests that stress either very early in pregnancy or in the 24–28th weeks of pregnancy leads to a twofold increase in the risk of autism [150]. Since autism is usually not apparent until a child is 1–3 years of age, it may be difficult to trace back to the original events. Recently, a study suggested that experiencing a stressful event during the periconceptional period was associated with increased congenital anomalies including heart and neural tube defects and cleft lips and palates [151].

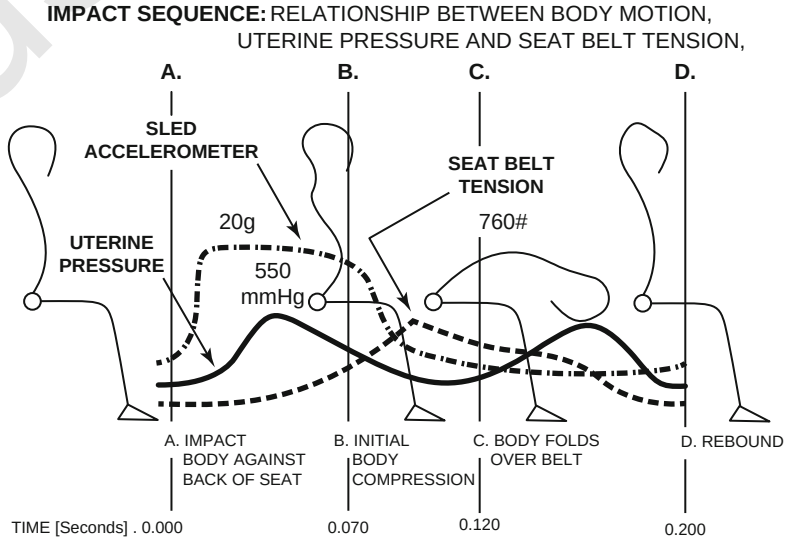

Fig. 10.7 Impact sequence (see test for details) [140]

The third research line comes from cohort studies of hospitalized injured pregnant women that linked to birth records. Wolf et al. reported in a 1980–1988 retrospective cohort study of seat belt use and pregnancy outcome after MVAs that unrestrained pregnant women were more likely to give birth to a low birth weight baby and more likely to give birth within 48 h after the MVA than restrained pregnant drivers [45]. One retrospective cohort study showed pregnancy outcomes from hospitalized injury of all types in Washington State in the period 1989–1997 [148]. It reported increased risks for placental abruption, low birth weight, prematurity, and fetal death.

The fourth line of research focused on the risk of fetal mortality versus infant mortality from MVAs. Drawing conclusions from a 15-state study of fetal death certificates, Weiss et al. provided evidence that fetal motor vehicle injury mortality rates were much greater than that of infants [16].

The fifth research line is not as strong because the evidence of harm does not come from population-based studies, but from several case series. An example is the report of Baethmann et al. on the effects of maternal trauma on surviving fetuses [152]. Seven mothers had MVAs; two had blunt abdominal trauma. Later clinical symptoms in the nine children included movement disorders and cerebral palsy among other findings. The causative role of maternal accidents was extremely likely in one patient and probable but "unproved" in the remaining cases. Another more cogent example is from Strigini et al. [153]. In five consecutive cases of fetal intracranial hemorrhage, the similarity of histories involving minor maternal physical trauma (three motor vehicle related and two falls), together with the absence of any known factor predisposing to fetal intracranial hemorrhage, suggested that minor trauma was at least a contributing factor to the observed pathology. Other similar but smaller case series or reports have been reported [154] raising the issue of trauma as a true teratogen (defined by the US Environmental Protection Agency as "The introduction of nonhereditary birth defects in a developing fetus by exogenous factors such as physical or chemical agents acting in the womb to interfere with normal embryonic development"). The most comprehensive study on the subject delivered the data found in Tables 10.4 and 10.5 [107].

Table 10.4 Rate calculations between women ages 15–39 in crashes by pregnancy status, *National Automotive Sampling System Crashworthiness Data System*, 1995–1999 [107]

	Reported pregnancy status	
Rate calculations	Pregnant	Not pregnant
Annualized age specific rate per 1,000 live births (using 1997 live births as denominator)		
15–19 (n = 7,478, SE = 3,265)	15	NA
20–24 (n = 8,230, SE = 2,187)	9	NA
25–29 (n = 8,850, SE = 10,048)	8	NA
30–34 (n = 6,164, SE = 1,737)	7	NA
35–39 (n = 2,088, SE = 558)	5	NA
All ages (n = 32,810, SE = 12,585)	9	NA
Annualized age specific rate per 1,000 person years (assuming pregnancy is detectable over 8 months)		
15–19	23	44
20–24	13	35
25–29	12	22
30–34	10	18
35–39	8	18
All ages	13	26

Numbers and rates derived from weighted estimates unless otherwise stated

Severe fetal injury can result from blunt trauma to the abdomen even in the absence of uterine injury, especially in advanced pregnancy. In early pregnancy the uterus is protected by the bony pelvis and by the amniotic fluid which acts as an hydraulic shock absorber, decreasing the force of the blow by transmitting it equally in all directions: later in pregnancy the fetal head is fixed in the pelvis and the buffering effect of the amniotic fluid is decreased, making the head prone to injury. Skull fractures with intracranial hemorrhage appear to be the most common injuries resulting from blunt trauma.

The importance of MVAs as a cause of pregnancy loss has been largely ignored as a public health problem. Published estimates of the number of fetal losses caused by MVAs each

Table 10.5 Selected comparisons between women ages 15–39 in crashes by pregnancy status, *National Automotive Sampling System Crashworthiness Data System*, 1995–1999 [107]

	Reported pregnancy status			
	Pregnant		Not pregnant	
Selected comparisons	No (%)	SE	No (%)	SE
Number of cases, 1995 9 (unweighted)	427		11,972	
Annualized number of cases (weighted)	32,810	12,585	1,251,269	127,522
Number (% within age group) that were drivers				
15–19	5,370 (72)	2,731	217,584 (55)	38,104
20–24	5,482 (67)	1,671	222,105 (76)	39,222
25–29	5,654 (64)	9,746	164,136 (81)	10,816
30–34	4,438 (72)	1,284	137,751 (75)	18,767
35–39	1,872 (90)	542	147,268 (83)	13,939
All ages	22,816 (70)	11,662	888,843 (71)	106,928
Treatment level (% within group)				
No treatment	7,908 (24)	2,868	635,197 (51)	76,723
Transport and release/treated at scene	19,217 (59)	10,546	422,593 (34)	60,488
Hospitalized or fatal	4,413 (14)	1,345	57,857 (50	13,092
Other or unknown	1,254 (4)	750	135,622 (11)	11,387
Total	32,810 (100)	12,585	1,251,270 (100)	127,522
Police reported belt use				
None used	4,395 (14)	1,696	158,021 (13)	42,023
Lap and shoulder	19,805 (59)	10,546	704,799 (59)	79,038
Lap or shoulder	824 (3)	391	29,280 (2)	5,916
Belt used, type not specified	5,716 (18)	3,162	240,731 (20)	155,053
Other response	68 (0)	59	1,321 (0)	284
No police indication	1,970 (6)	328	57,585 (5)	18,588

Numbers and rates derived from weighted estimates unless otherwise stated

year in the United States range from 1,500 to >5,000 [55]. Although some estimates suggest that these estimates may be somewhat high, it seems clear that the number is significantly greater than the number of infant deaths caused by MVAs and that it probably exceeds the total number of children aged 4 years and younger died in MVAs [155].

Although many clinical protocols have been published for managing trauma during pregnancy [99, 118, 124], few studies have evaluated how to prevent fetal loss by improving safety restraint systems or vehicle design. In order to determine the pregnant occupant crash exposure, the NASS/CDS searched all crashes involving pregnant occupants between 1993 and 2003 [156]. Distribution of impact direction according to the sitting position is presented on Fig. 10.8. One major barrier to

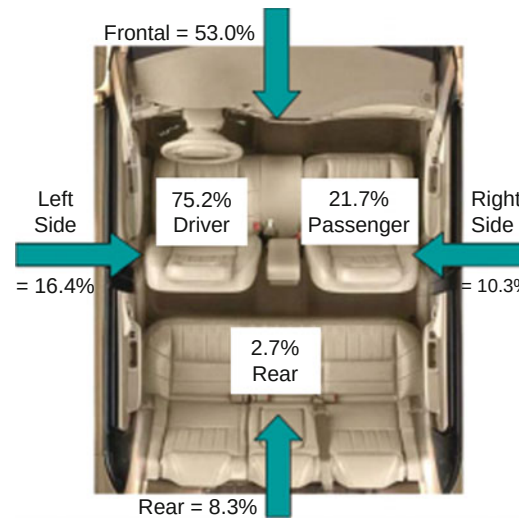

Fig. 10.8 Occupant seating position and impact direction distributions for pregnant occupants [156]

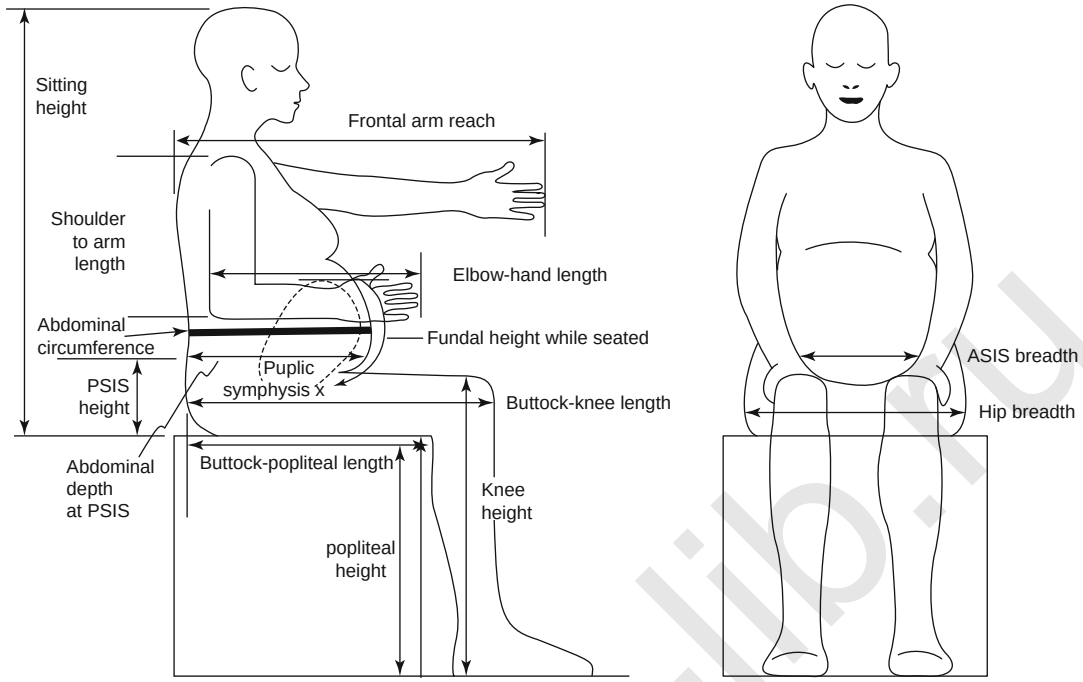

Fig. 10.9 Illustration of anthropometric measurements. *ASIS* anterior superior iliac spine, *PSIS* pubic symphysis [43]

the evaluation of the effectiveness of safety improvements for pregnant occupants has been the absence of a pregnancy surrogate for crash testing. In 1996, the first pregnant crash dummy was developed as a feasibility project [157]. Although that project was an important first step in developing a pregnancy surrogate, the design has numerous limitations. In particular, the first-generation pregnant crash test dummy does not provide for assessing the likelihood of fetal loss as a result of separation of the placenta from the uterus, which is believed to be the most common cause of fetal loss from abdominal trauma. In addition, the abdomen of the first-generation pregnant crash dummy does not have a realistic external contour and is too stiff. These deficiencies are likely to cause inappropriate interactions of the pelvis and abdomen with occupant restraints and vehicle components such as the steering wheel rim (Figs. 10.9 and 10.10).

However, due to the difficulties in measuring this mechanism in the pregnant dummy, such as tissue strain and pressure, a computational model of the pregnant occupant was created [158]. This computer model has been used to evaluate frontal crashes and has shown that local uterine compression is a critical factor in predicting placental abruption [159].

10.2.2.3 The Seat Belt for the Prevention of Maternal-Fetal Injury

The seat belt was developed by Lavenne in France in 1903 for use in airplanes; it was then adopted for use in motor racing [160] and later widely introduced for occupant protection in the United States in the 1960s [161]. Studies of automobile accidents from the 1960s have shown that the major single cause of fatal injury is ejection from the vehicle [162]. When the body is ejected, injury occurs as it strikes the ground or is crushed by the vehicle. Huelke and Gikas estimated that 80 % of fatally injured automobile accident victims would have survived had they been wearing lap belts [162]. As a result of such studies, lap-type seat belts become standard car equipment in the 1970s [143].

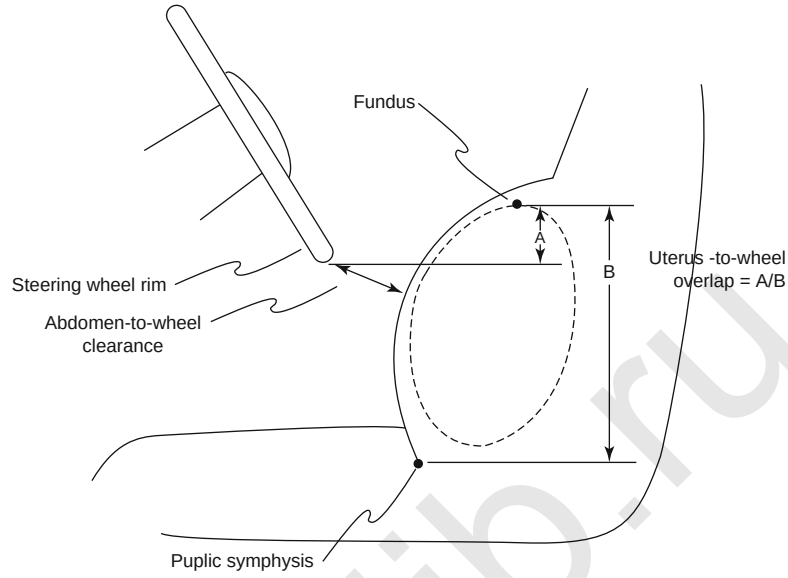

Fig. 10.10 Illustration of abdomen-to-wheel clearance and uterus-to-wheel overlap [43]

Herbert concluded that lap belts reduce injury 35 % and diagonal belts 80 % [163]. Lister found that seat belts could reduce injuries by 51 % in England [164], and in Michigan, Huelke and Gikas predicted that 80 % of fatal accidents would have survived if they had been wearing only the lap belt [162]. Garrett and Braunstein calculated that there were 35 % fewer major, fatal injuries in seat belt wearers [165]. Lindgren and Warg [166] in Sweden studied injuries in people wearing diagonal-type belts and they concluded that this type of belt reduced by 60 % the number of major injuries that would have occurred without the use of belts. The outcome for the fetus is improved by the use of shoulder restraints. Crosby et al., in a study of 22 baboons in the third trimester of pregnancy, used an impact sled with a decelerative force of 24.5–29.0 G-force to compare the effectiveness of lap belts and shoulder harnesses [147]. They found a significant difference in the fetal death rates, which were 8 % when a shoulder harness was used and 50 % when a lap belt was used. There were no maternal deaths or instances of uterine rupture. Those investigators suggested that the improvement in fetal survival with the use of a shoulder harness was due to the greater surface area over which the decelerative force was dissipated as well as the prevention of forward exion of the mother.

Seat belt use has been shown to reduce the risk of adverse maternal and fetal outcomes in several large population-based studies [29, 42, 45]. In 1983, the *American College of Obstetricians and Gynecologists* (ACOG) issued a recommendation that the three-point restraint system (that places the lap belt under the abdomen and across the upper thighs and the shoulder belt between the breasts) should be used by pregnant occupants for maximum protection of the mother and fetus [167].

> The three-point restraint system (that places the lap belt under the abdomen and across the upper thighs and the shoulder belt between the breasts) should be used by pregnant occupants.
>
> *American College of Obstetricians and Gynecologists*, 1983

Using the seat belt prevents hitting the windshield with the head and the chest cage in the steering wheel. When a vehicle attacks a barrier with a speed that is realistic in the road traffic, the vehicle in a short time will void its speed and the untied traveler will continue to move in almost the same direction and speed; during the

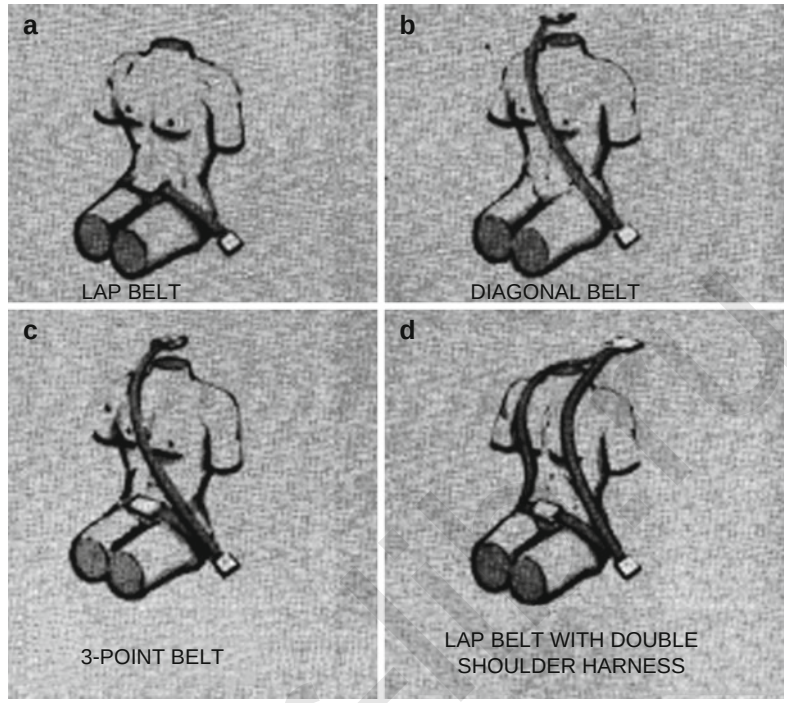

Fig. 10.11 Four basic restraint systems currently used in automotive vehicles [143]. (**a**) A *2–point belt* attaches at its two endpoints. (**b**) A "sash" or *shoulder harness* is a strap that goes diagonally over the vehicle occupant's outboard shoulder and is buckled inboard of his or her lap. (**c**) A *3–point belt* is a Y–shaped arrangement, similar to the separate lap and sash belts, but unitized. Like the separate lap-and-sash belt, in a collision the 3–point belt spreads out the energy of the moving body over the chest, pelvis, and shoulders. (**d**) *Lap belt with double shoulder harness* is improved 3–point belt which further spreads out the energy of the moving body over larger body area

mentioned attack – inside the vehicle – serious or fatal injury can occur. The safety belt is designed to keep the human body in the seat during the crash, meaning that it does not allow the body to strike inner parts of the vehicle or ejection of the body from the vehicle under the in uence of created forces. Safety belts are most effective in frontal collisions or when a vehicle attacks the barrier. Researchers have shown that under the crash speed of about 50 km/h, the front is shortening by 50 cm, and a significant part of the load is taken by seat belts. In the sidelong collisions the safety belts are much less efficient, and such collision leads to injuries of the head while hitting the side glass.

There currently are four principal configurations of seat belts in automotive use: the lap belt, the single diagonal belt, the three-point (or combination of lap and diagonal), and the double parallel combination of lap and double shoulder harness (Fig. 10.11).

Lap belt refers to a single belt across the anterior aspect of the pelvic structure; *seat belt* refers to any combination of lap and torso restraint. There are numerous variations of the types, such as five-point, double vertical belts without lap belt, and shoulder belts with inertia reels. Diagonal seat belts that run over the shoulder cause injuries that are primarily confined to the upper part of the trunk such as bruised chest, fractured ribs or sternum, and lacerated liver. There are fewer head and neck injuries with this type of belt than with the lap type. Injuries to the pelvis, lumbar spine, and abdomen are found with the lap-type belt. Bone injuries consist of fracture of the pubis, separation of joints, and compression fracture of the lumbar spine, the so-called fulcrum fracture [168]. The use of a lap belt alone may allow enough forward exion and subsequent uterine compression to rupture the uterus. If the lap belt is worn too high, the force of the impact is transmitted directly to the uterus and likewise may rupture it [169].

It was shown that the three-point belt and the four-point belt were superior in protecting the pregnant occupant by reducing the movement toward the far-side door and therefore eliminating the head-strike potential. However, this resulted in some force being applied through the abdomen and therefore it increased the risk of

fetal injury. This is an acceptable trade-off given the most important factor in saving the fetus' life is keeping the mother alive. The reason that the four-point belt is better than the three-point belt with respect to abdominal loading is that some of the overall load is applied through the mother's neck and therefore less is applied to the abdomen in order to restraint her for the same given crash speed. The belt contact loads through the neck were below published injury thresholds [156]. Overall, the results indicate for all frontal and side impacts that it is safest for the pregnant occupant to ride in the passenger seat while wearing a three-point belt, or four-point belt if possible, and utilizing the frontal airbag when appropriate [158]. Study by Klinich et al. found that the odds of adverse fetal outcome, including fetal loss, preterm delivery, placental abruption, and uterine laceration, after an MVA were 4.5 times higher among women who were not properly restrained compared with those who were properly restrained at the time of the crash [170].

The Seat Belt Syndrome

Distinctive injuries caused by safety belt due to traffic accidents were first described as the *seat belt syndrome* coined by Fish and Wright [171]. These injuries were described even before [165, 172]. They noted two cases of rupture of the pregnant uterus caused by seat (lap) belts. Rubovits in 1964 first reported the traumatic rupture of a 6-month pregnant uterus in a woman whose car was struck at 56 km/h by another vehicle head-on front quarter, when the other vehicle jumped a divider. There was avulsion of the uterine musculature at the site of the seat belt impact. This was attributed to the force of the belt at the anterior uterine wall being transmitted to the fetus, which was then blasted through the left uterine wall [145]. This was fatal to the fetus. As in the case reported above, absence of sign of shock or intraperitoneal hemorrhage precluded diagnosis for 2 days. Therefore, the disadvantages of using seat belts are most often related to injuries that it can cause during a collision. Previous researches [173] have shown that injuries caused by the seat belt are most likely as follows:

- Abdominal organ damage
- Bowel rupture
- Abdominal wall injuries
- Ruptured liver
- Blood vessel trauma
- Chest trauma
- Fractured sternum
- Myocardial contusion
- Spine fractures

There are countries like Japan where the pregnant women while driving are exempted of use of the belt [107] due to possibility of fetal injury during sudden braking. It is important that pregnant women wear their seat belt to prevent secondary collision with interior structures of the vehicle or sudden ejection, to dissipate the force of an impact [174], and to provide both the mother and the fetus with maximum protection. But the seat belt must also be worn correctly to prevent potential significant harm to both the mother and fetus. Women are reported to be at an increased risk for intra-abdominal injuries or uterine rupture if restraints are improperly positioned at the time of collision [175]. In 1992, ACOG recommended that all women receive seat belt counseling from prenatal care providers [176]. Nevertheless, many pregnant women report uncertainty about the safety and use of seat belts during pregnancy [177] and lack of information regarding proper seat belt use and its role in protecting the fetus [178]. If women regularly and correctly wear their seat belts, prenatal counseling on seat belt use during pregnancy would not be an important public health issue, but that is not the case. A 2004 study of women attending prenatal clinics by McGwin et al. reported that only about 45 % always wear their seat belts (both before and during their current pregnancy) even though 72.5 % of subjects were able to demonstrate the proper way to wear a seat belt [178]. In addition, only 58 % thought that seat belts would have a positive effect if they were in a MVA during pregnancy, 34 % were unsure of the effect, and 8 % thought the seat belt would cause them to get hurt [178]. When asked if a seat belt would help protect their baby in the event of a crash, only 55.3 % of the women thought that the seat belt would help, 10.7 % said it would do harm, and 34 % were

unsure [178]. The women who thought a seat belt would help protect them were significantly more likely to report always wearing a seat belt versus the women who were unsure or thought negatively of the seat belt (84.4 % vs. 64.6 %) [178]. Considering this finding, it seems that knowledge and belief in the effectiveness of the seat belt could help motivate women to use a seat belt. Therefore, prenatal care providers should take the opportunity that prenatal visits provide to educate women on the importance of proper use of seat belts during pregnancy to protect both the mother and fetus and the hazards of crashes during pregnancy [179], as well as clear up any misconceptions that a woman may have about seat belt use. However, several questions remain. For instance, what percentage of women are actually receiving seat belt use counseling, how many wear their seat belts during pregnancy, and how many report being hurt in a MVA?

Seat Belt Use Counseling

In summary, reported prenatal care provider counseling for seat belt use occurred in 48.7 % of prenatal visits; women aged 20–29, nonwhite, Hispanic ethnicity, and less educated were the most likely to report being counseled on seat belt use; women who were 30 or older and had a greater than high school education were more likely to report always wearing seat belts in the last trimester; and on average, 2.3 % of respondents reported being hurt in a "car accident" during pregnancy. Women less than 20 years old, of black race, and less educated were the most likely to report being hurt in a crash during pregnancy. It is encouraging that this study determined that black women are the most likely to report being counseled on seat belt use during pregnancy, because this study also determined that black women were more likely to report being hurt in a crash. To further support this finding, from 2001 to 2005, black women of reproductive age (15–44) were more likely to be involved in a nonfatal MVA than white women [180]. Although there are groups of women who are more at risk for experiencing a crash during pregnancy, it has been demonstrated that less than half of women always wear their seat belt (including before and during pregnancy) [178]. For this reason, all women should be counseled on the importance of seat belt use and how to properly wear a seat belt during pregnancy regardless of age, race, ethnicity, or education. Extrapolating from the reported *Pregnancy Risk Assessment Monitoring System* (PRAMS) rates in 2001 to the US population, it is estimated that at least 92,500 pregnant women (rate = 2.3/100 live births) are hurt in MVAs each year in the United States. This finding is important because it is one of the few such estimates available from population-based multi-state data sources. The only previous estimate came from analysis of crashes reported by the NASS/CDS from the period 1955 to 1999 [107]. The latter reported only about 33,000 pregnancy-related crashes (not injuries) annually. The current PRAMS data portrays the magnitude of the level of underreporting in the NASS data system, because by definition, pregnancy status is 100 % complete in PRAMS. The findings regarding seat belt counseling were similar to the findings of earlier studies. The percentages of women who reported being counseled were 48.7 % in 22 PRAMS states, 53 % in 14 PRAMS states during 1997 and 1998 [181], and 48 % in 19 PRAMS states in 2000 [179]. The consistently low prevalence of seat belt use counseling during pregnancy suggests that this issue has not yet been properly addressed. Interventions needs to be put in place to ensure that women are educated and counseled on the importance of and proper use of a seat belt during pregnancy. Prenatal counseling is a time where topics related to the health of the mother and the baby are discussed and proper seat belt use should be included. It is important to note that the literature is not unanimous on whether prenatal counseling is the best way to increase the use and proper use of seat belts during pregnancy. It is particularly important among those women identified as being more at risk for adverse pregnancy outcomes (young women who smoke, do not begin prenatal care during the first trimester, and have not completed high school).

One issue with seat belt counseling during pregnancy is that some women have been reported to forget some of the topics that were discussed during prenatal counseling, including seat belt use. Tyroch et al. did a follow-up survey in pregnant women after their initial prenatal visit

and showed that 73 % of the women did not recall having received advice on seat belt use even though they received brief counseling by a clinician and a pamphlet on seat belt use during pregnancy during their initial visit [182].

The authors suggested that new teaching methods such as audiovisual aids, mannequins, or having women demonstrate proper seat belt use to the health-care provider may increase knowledge retention [182]. However, among the population in general, some research suggests educational initiatives have been ineffective at increasing seat belt use when compared with successful legislative and enforcement efforts [183].

On the other hand, several studies have reported positive effects due to prenatal counseling. For instance, Pearlman and Philips administered a survey to women who consecutively presented for their first prenatal visit and readministered the survey at their second visit (28–32 weeks gestation) to assess the attitudes toward and usage of lap and shoulder belts. The authors showed that women who received seat belt use instructions were more likely to use restraints and properly identify restraint position than those who received no information [184]. Similar findings were reported by Johnson et al. for pregnant women who recalled being advised on correct placement [160]. Thus, studies show that education by prenatal care providers increases the number of pregnant women correctly using seat belts [46, 160, 184]. Therefore, instruction by health-care providers is an important component to solving the problem of incorrect seat belt placement [160] and lack of use among pregnant women. This study is not without several limitations due to the way that PRAMS collects data. The first limitation is potential misclassification. Since it has been shown that some women forget about counseling [182], it is possible that some women are misclassified as never having received prenatal counseling on seat belt use in the PRAMS data, when in fact they did. Another limitation is potential recall bias due to the fact that PRAMS collects data from women within 2–6 months postpartum. This means that some women are asked to recall counseling information and topics that were provided or discussed potentially over a year before the data were collected and those who had uneventful pregnancies may be less likely to remember specific counseling topics. However, this is a common limitation with retrospective studies, and as discussed, perhaps a more impressionable counseling approach would increase the number of women who use and correctly use their seat belts during pregnancy and consequently are better able to recall counseling. Future research is needed to determine the effectiveness of different educational strategies [173].

Another limitation of this study is that out of the 22 states in this study, only Maryland and Vermont collected data on seat belt use during pregnancy and the data they collected is only for the last three months of pregnancy. This limits the generalizability of the seat belt use data not only for women in those two states but also to only women in their third trimester of pregnancy. Seat belt use might change as a woman's pregnancy advances due to the growing abdomen and increasing level of discomfort, but with incomplete and limited PRAMS data on seat belt use throughout pregnancy, these practices cannot be adequately measured. Nevertheless, the sample from these two states was large enough to provide useful results on these issues and can show other states the usefulness of adding these variables to their PRAMS surveys.

Comparison of Belted and Unbelted Pregnant Women

There is only one study by Hyde et al. with comparison of belted and unbelted pregnant population during MVAs with short- and long-term follow-up [42]. The main findings are that nearly 3 % of births linked to MVAs during pregnancy and that pregnant women in crashes in which the mother wore her seat belt were not significantly more at risk for adverse fetal outcomes than pregnant women not in crashes. Pregnant women who did not wear seat belts during a crash were more likely to have:

- Low birth weight infant
- Excessive maternal bleeding
- 3× higher incidence of fetal death

Authors found that 2.8 % of all live births in the state were from mothers who were exposed to a driver-related MVA during pregnancy. Considering the absence of data on nondrivers and

nonreported crashes, this suggests that in Utah more than 3 % of all live births are from mothers exposed to a MVA. The only other study known to estimate the rate of MVA exposure during pregnancy reported it as 1 % based on investigator reports from the NASS/CDS and was thought to have underestimated [107]. Although belt use has been shown to be effective in reducing morbidity and mortality for the mother and the fetus when comparing belted and unbelted pregnant women [45, 147, 185], this study extends these findings by showing that belted pregnant women in crashes were not significantly more at risk for adverse fetal outcomes than pregnant women not in crashes. No other studies have compared crash-related pregnancy outcomes with a non-crash population. Schiff et al. [186] found that, compared with uninjured pregnant women, injured pregnant women were at increased risk of several adverse outcomes, including placental abruption, prematurity, low birth weight, fetal distress, and fetal death. However, Schiff et al. only included women who had been hospitalized for their injuries and delivered during their hospital stay, which would indicate an overall greater severity of injuries than the study by Hyde et al. Because the Schiff et al. study also focused on all injuries, and not just MVA, the authors were not able to control for severity-reducing countermeasures such as seat belt use. Lack of seat belt use has previously been associated with low birth weight by Wolf et al. [45], who also documented an increased risk of delivery within 48 h of the crash. There is no increased risk of immediate delivery. Unbelted pregnant women were nearly three times more likely to experience fetal death than belted pregnant women in crashes. Even though the small numbers of fetal deaths in the study by Hyde et al. limited the ability to more completely describe the effect of MVA risks on fetal death, the crude OR of 2.8 was an indication that the unrestrained pregnant women were much more likely to lose their fetus in a MVA than restrained women. Wolf et al. [45] found no statistically significant increase in the risk of fetal death associated with lack of seat belt use, despite their larger parameter estimate (4.1 vs. 2.8). Another population-based study [185], published over 40 years ago, reported that lap belt use was associated with a reduction in maternal death and maternal injury, but there was no association with fetal loss. The authors concluded, however, that lap belts were preferable to no restraint. The majority of fetal deaths (51 %) were linked to crashes that occurred during the first trimester, even though all of the fetal deaths occurred during the second and third trimesters. This may be a result of the fact that first trimester crashes have up to 36 weeks to result in a fetal death, whereas the other trimesters have correspondingly less time to do so. Essentially, there was a longer exposure period of gestation in which fetal deaths could occur, whether or not those fetal deaths were related to the crash. Another possibility is that the last trimester may be offset by an increased likelihood of these infants being born through trauma- or physician-induced labor, which may have resulted in deaths not recorded in the fetal death file. Finally, the finding may suggest that the first trimester represents a sensitive period of fetal development and vulnerability to crashes but that the fetal deaths do not occur (or are not noticed) until a few weeks later in development. Further research is warranted to better determine how gestational age impacts fetal death due to crashes. Also there is increased risk of fetal death for unbelted crashes that occur during the later weeks of gestation. When comparing gestational age and the time of fetal death, the unbelted group had sharp increases of fetal deaths between 31 and 38 weeks' gestation. This may be indicative of a period of increased vulnerability to fetal death from MVA among unbelted drivers. One might believe that this increase is a result of more crashes during the third trimester. However, linkage of all births involving unbelted MVA showed that only 25 % of crashes occurred during the third trimester, the lowest percentage of any trimester. On the other hand, 55 % of fetal deaths among the unbelted group linked to third trimester crashes. Therefore, this pattern is probably a result of something different than increased crash risk. These findings have implications for health providers as well as researchers involved with crash dummy development. For instance, crash dummy testing has mainly focused on the 28–30-week gestational age period for designing

Table 10.6 Reported seat belt use before pregnancy and current use among 880 pregnant women in Japan, shown by gestation period; results in absolute numbers and % [196]

	<20 weeks		20–29 weeks		30 weeks +	
Location/seatbelt use	Before	Current	Before	Current	Before	Current
Driver's seat						
Always	172 (82.3)	129 (62.3)	211 (83.4)	127 (51.4)	229 (78.4)	108 (37.9)
Often	14 (6.7)	22 (10.6)	17 (6.7)	30 (12.1)	31 (10.6)	32 (11.2)
Sometimes	19 (9.1)	34 (16.4)	22 (8.7)	42 (17.0)	29 (9.9)	58 (20.4)
Never	4 (1.9)	22 (10.6)	3(1.2)	48 (19.4)	3(1.0)	87 (30.5)
Front passenger's seat						
Always	164 (76.3)	118 (55.1)	190 (72.0)	108 (41.4)	208 (67.3)	89 (29.2)
Often	19 (8.8)	35 (16.4)	24 (9.1)	36 (13.8)	45 (14.6)	26 (8.5)
Sometimes	25 (11.6)	33 (15.4)	41 (15.5)	57 (21.8)	42 (13.6)	81 (26.6)
Never	7 (3.3)	28 (13.1)	9 (3.4)	60 (23.0)	14 (4.5)	109 (35.7)

Total number (in driver's seat) is not equal to the number of pregnant women (with driver's license) due to missing data
Seat belt use before pregnancy was not significantly different across gestation periods, whereas the difference in current use was significant across gestation periods

the physiological characteristics of a pregnant woman and the fetus [43, 157]. It is important to design dummies representing a few weeks later in gestation to more appropriately target the population that may be at the greatest risk for fetal death. Despite substantial research on the protective value of seat belts, many women still do not wear them during pregnancy. Previous research indicates that the leading reasons for lack of seat belt use during pregnancy include forgetting, discomfort or inconvenience, no seat belt available, and fear that seat belts may cause injury to the fetus or mother [187]. It is worth noting that some countries exempt pregnant women from seat belt laws, which may be promulgating misconceptions about seat belt use during pregnancy. Studies also show that many women are simply unaware of the correct usage and positioning of seat belts [160, 167].

Factors associated with low seat belt compliance – younger age, lower education, lower socioeconomic status, seating location (passengers), and longer annual distance traveled – are also important factors during pregnancy [188–193]. Seat belt use during pregnancy has gone unnoticed in Japan because expectant mothers are exempted from seat belt legislated requirements [194]. Compared with seat belt use before pregnancy, seat belt use during pregnancy was reduced for both drivers and front-seat passengers. This trend is contrary to the finding in California that seat belt compliance significantly increased during pregnancy (79 % before pregnancy vs. 86 % during pregnancy) [182]. A study in New Mexico, where seat belt use was generally low, found that seat belt use increased from 27 to 42 % during pregnancy [187]. If concerns associated with the gestation period dissuade maternal seat belt use, then gestation period would be a major determinant for nonrestraint use during pregnancy. However, a recent study in the United States reported that trimester status has relatively little effect on seat belt use [107].

It is interesting to note that seat belt use was consistently higher among drivers than front-seat passengers despite discomfort of the steering wheel. Since front-seat passengers are less likely to wear seat belts than drivers among the general population (88.1 % for drivers vs. 75.2 % for front-seat passengers) [195], it is possible that the same trend would be seen in pregnant women. A large majority of the respondents in studies in the United Kingdom and the United States, where pregnant women are encouraged to continue wearing seat belts, reported that seat belt use is beneficial for both pregnant women and their fetuses [160, 182]. In contrast, only one-third of respondents acknowledged this. Seat belt use was less among pregnant women who knew of the current exemption (Tables 10.6 and 10.7) [196].

None reported that their obstetricians had given this information perhaps because Japanese obstetrics textbooks do not address this issue. In other industrialized countries, obstetricians take an important role in disseminating maternal seat belt use information and pregnant women who reported receiving this information were more likely to wear seat belts and do so correctly [160, 184]. Daily car users were less likely to wear seat belts despite their longer exposure to the risk of traffic injuries. This suggests that frequent car use may lower risk perception [188, 191].

Table 10.7 Number and proportion of pregnant women who reduced seat belt use after pregnancy, shown by gestation period (%) [196]

Location	20 weeks	20–29 weeks	30 weeks
Driver's seat	25.7	41.1	55.6
Front passenger's seat	27.4	45.2	58.9

The limitation of Japanese study [196] is that authors did not examine whether pregnant women wear seat belts correctly, and it is likely that incorrect use is similar to that reported elsewhere [160, 182, 184]. Current recommendations still support the use of three-point restraints (i.e., lap and shoulder belt) for all pregnant women [197, 198]. The lap belt should be placed as low as possible, beneath the bulge of the uterus, and the shoulder belt should lie to the side of the uterus and run between the breasts and over the midportion of the clavicle (Fig. 10.12).

The Airbag as a Passive Factor of Safety of Road Vehicles

The airbag is passive safety system of vehicles, which is nowadays more and more found in standard equipment of vehicles. In a crash, the airbag is opened by means of sensors within 30–50 ms and is rapidly filled with gas, usually nitrogen,

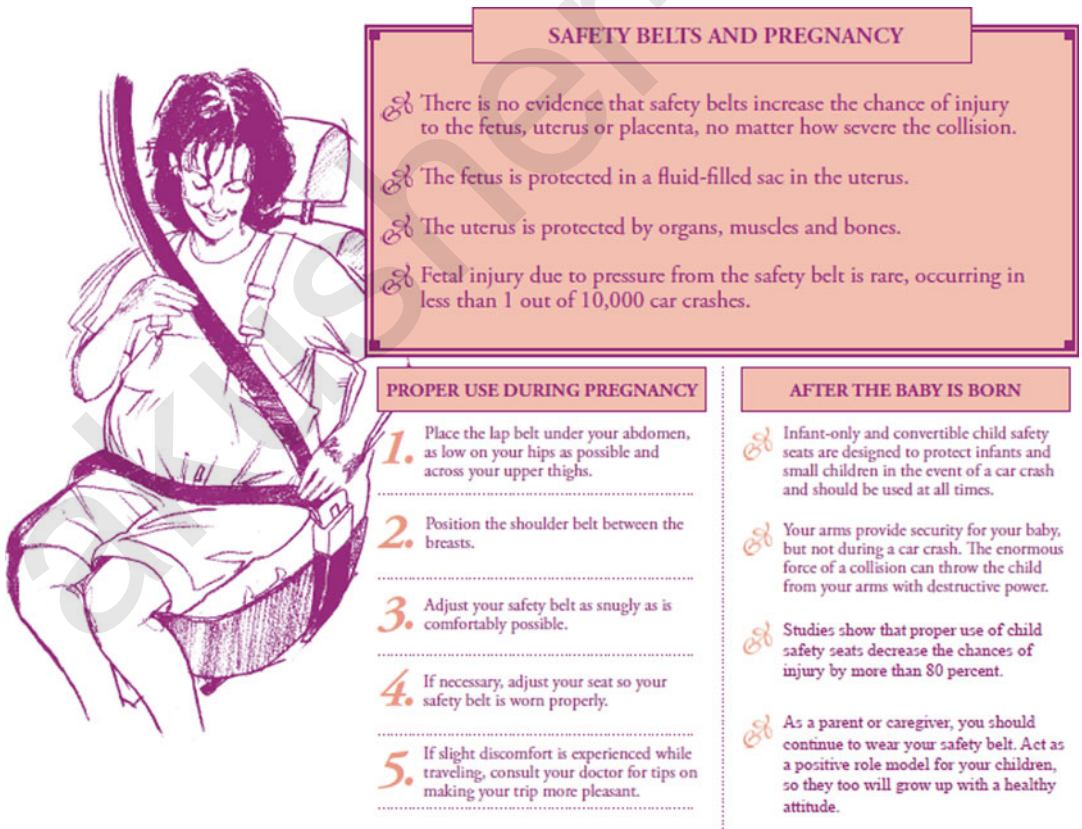

Fig. 10.12 Lea et about proper position of seat belt in pregnancy (Ohio Department of Public Safety)

to softly await the body of passengers and in that way to absorb inertial force of the body. Airbag for driver and passenger should protect against head injuries and chest in the frontal crash. For the full effect, airbags should works in combination with safety belts that are tied at three points. In the collision of the head and upper body, the airbag must not constitute a strong barrier to maintain constant pressure. The body hitting the bag pushes gas filling through the exhaust openings from the airbag. The basic elements of the airbag are:

- Bag of multilayered composites based on polyamide
- Gas generator
- Contact board with an initiative capsule
- The electronic control unit with a sensor system

To ensure active filling of the airbag, the two sensors are mainly built in a vehicle, in a bumper, and in the divider between the engine parts and space for passengers. Sensor system, a few milliseconds after impact, transmits an electronic signal that activates the initial capsule with approximately 8 g of plastic explosives. The explosion lits the initial mixture in the generator gas, whose combustion releases nitrogen to fill the airbag. The airbag is, after in ated and depreciated the impact of driver, blown out, and the whole cycle takes about 150 ms. Due to the cases when the electronic trigger did not worked at the time of the accident, the mechanical activation of the airbag has been introduced. The negative effect of opening the airbag and a loud burst with strength of 140–160 dB should not pose a threat to human hearing because the impact of vehicle alone into another vehicle or object creates a louder noise.

The biggest imperfection of airbags is their ability to activate when they are simply not expected. Except with failure in the system that may cause the opening of the airbag, there is a risk that the airbag opens in collisions when a vehicle has low speed and airbag is not needed to absorb the body impact to the steering wheel. In such cases, due to low speed, the body does not come into contact with the interior of the vehicle because of its small inertia forces, but it reinforces the seat belt in the vehicle seat. If the airbag is activated, in such cases, it can cause head and chest injuries, which would not emerged if the airbag is not activated.

Such injuries are especially dangerous for pregnant women because they can cause death of the fetus. Such phenomena are trying to be solved in a way that airbags do not open up to a certain vehicle speed or up to specific vehicle body deformation. The European cars are built with two types of airbags:

- 35 l “eurobag”
- 67 l “bull size”

Although the “euro” airbag adds significantly to the safety, measurement results conducted on the dummies in crash tests showed significantly less stress in the critical part of the cervical vertebrae and smaller injuries when using a large “bull-size” airbag. Newer-generation airbags like the French SRP system (System de Retenue Programmee) function in a way that they are programmed to strain safety belts with pyrotechnic strainer that work in combination with the new generation of airbags. These bags can bend from top to bottom and sideways, which allow regular distribution of tensions in the chest, and have specially calibrated valve that regulates the throughput power and exhaust of gas. Such combined protection proved to be much more successful than previous ways of functioning, so chest injuries are 70 % less.

10.2.2.4 Maternal Pelvic Trauma

Despite the occurrence of pelvic and acetabular fractures among women of childbearing age, literature specifically addressing patients who sustained pelvic or acetabular fractures in pregnancy is scarce. In a recent review, Leggon et al. [199] examined 101 cases of pelvic fractures (11 acetabular and 89 pelvic) in pregnant women. Overall, maternal mortality was 9 % and fetal mortality 35 %. Automobile-pedestrian collisions had a statistically higher maternal mortality rate than pregnant women involved in vehicular collisions which had a statistically significant trend toward a higher fetal mortality rate, as compared to falls. Most maternal deaths occurred from associated injuries, in particular from acute hemorrhage [199]. Injury severity in uences

both maternal and fetal outcomes. Increasing injury severity (minor to moderate to severe) and associated injuries significantly increased both maternal and fetal death rates. Direct injury to placenta, uterus, or fetus accounted for fetal deaths in 52 %, while maternal hemorrhage (with or without maternal death) accounted for 36 % of the non-surviving fetus. These observations are similar to predictors of fetal death after severe trauma in pregnancy in general. Predictors of fetal death in trauma in pregnancy include automobile-pedestrian collisions [38], motorcycle collisions [38], lack of restraints [38], maternal ejection during trauma [38, 57], and increased injury severity score (ISS) [57, 200].

The close association between concomitant abdominal and pelvic injuries and fractures of the acetabulum or pelvis re ects the kinetic injury dissipated with the initial impact. Reported incidences of associated injuries in series of pregnant patients with pelvic fractures include the following rates: abdomen, 42 % (bladder 13 %, kidney 6 %, liver 6 %, spleen 5 %, urethra 5 %); closed-head injury, 37 %; thorax, 25 %; and most frequently, additional orthopedic injuries (fractures) in 48 % of patients with pelvic fractures [200]. Overall, outcome of patients with pelvic fractures in pregnancy due to blunt trauma correlates with the severity of associated injuries and physiological derangement on admission rather than with characteristics, or the type, of pelvic fracture. Occurrence of pelvic fractures in young patients requires transmission of significant amounts of kinetic energy and should therefore be regarded as an index injury mandating a thorough search for other occult visceral injuries.

Fetal Injury

Pelvic trauma in the third trimester of pregnancy should alert the trauma surgeon and obstetrician of direct injuries to the fetus. If the mother survives, fetal loss occurs in the majority of cases because of placental abruption, while direct injury to the fetus in the absence of uterine injury is a relatively infrequent event [197]. Direct injury of the fetus is usually associated with trauma occurring late in pregnancy and most commonly involves fracture of the fetal skull [197]. This is especially likely during the third trimester when the fetal head is engaged low in the pelvis trapped between the anterior pelvic ring and the sacrum. The vast majority of in utero skull fractures have been related to severe maternal injury involving pelvic fractures [201]. Fetal skull fractures should be regarded as an index injury for severe maternal trauma. Vice versa, multiple pelvic fractures in pregnant women require a thorough sonographic and radiographic examination of the uterus and fetus.

10.2.3 Falls

Falls accounted for more than half of classifiable reported maternal injuries during pregnancy, and about 3 % of all mothers reported at least one fall during pregnancy. Falls are also the leading cause of nonfatal injury among women of childbearing age (15–44 years) in the United States, although they account for only 20 % of nonfatal injuries among this more general population [202]. Falls may be a more common mechanism of injury during pregnancy, particularly in the second and third trimesters, because of [203]:

- Weight gain
- Shift in the center of gravity to accommodate the expanding uterus
- Increased joint mobility experienced during pregnancy

Increased levels of relaxin result in softer ligaments, cartilage, and cervix allowing the tissues to spread during delivery. The pubis symphysis – cartilage joining the pubic bones – and sacroiliac joint, where the hips attach to the spine, become unstable during pregnancy to aid delivery. The occurrence of falls becomes more likely as pregnancy progresses, with nearly 43 % of reported falls occurring during the third trimester [204, 205]. Although extensive clinical guidelines exist for physician counseling about the importance of fall prevention in the elderly (*American Geriatrics Society*, *British Geriatrics Society*), clinical guidelines for counseling about fall prevention for pregnant women are limited to warnings against strenuous physical activities with high risk for falls, such as horseback riding and skiing. In the injury descriptions, falls during

pregnancy most often occurred during normal daily activities.

10.2.4 Social Violence

Throughout the world, many studies have been performed to assess the prevalence of domestic violence in pregnancy. The reported rates of abuse vary significantly, from 5.4 to 27.7 % [206–211]. This re ects both a genuine diversity in the occurrence of violence and in definitions of abuse used by researchers. The prevalence of interpersonal violence during pregnancy ranged from approximately 2.0 % in Australia, Cambodia, Denmark, and the Philippines to 13.5 % in Uganda among ever-pregnant, ever-partnered women; half of the surveys estimated prevalence to be 3.9–8.7 %. Prevalence appeared to be higher in African and Latin American countries relative to the European and Asian countries surveyed. In most settings, prevalence was relatively constant in the younger age groups (15–35 years), and then appeared to decline very slightly after age 35 [212]. Parker et al. noted that as many as 20.6 % of pregnant teenagers and 14.2 % of pregnant adult women were physically abused during pregnancy [213]. Interpersonal violence has been emphasized as an etiology of trauma only during the past few decades. Sexual or physical abuse occurs in up to 17–32 % of pregnancies, and 60 % of those abused reported multiple episodes of abuse [26, 214]. In one study 75 % of the women who were hospitalized twice during the same pregnancy had domestic abuse as the cause of the trauma. It was also noted that one patient was seen for trauma from a domestic violence encounter during two separate pregnancies [215]. Abuse often begins or escalates during pregnancy or the immediate postpartum period. Most often the abuser is known to the patient, frequently her husband or partner. In addition to acute trauma during pregnancy, it should be noted that probably these women are exposed to repeating violence. Because many women seek medical attention only when they become pregnant, health-care providers of pregnant women play a crucial role in discriminating women who are abused. Because the woman has her unborn child's safety in mind, she may be more motivated to seek assistance and she may speak more freely during pregnancy. Among 15 studies addressing pregnancy outcomes and exposure to violence, five have reported a positive association between intimate partner violence and low birth weight or preterm birth [216–220]. Rates of low birth weight among battered women were 1.5–2.5 times higher [216–218] than those among nonbattered women, and rates of preterm birth were 2.5–4 times higher [216–218, 221]. Among 10 studies reporting no association of abuse with adverse pregnancy outcomes, one did not report outcomes separately for women exposed to verbal and physical abuse [222]. Others lacked sufficient power to address most pregnancy outcomes assessed [223–226]. One study ascertained exposure status through a mailed survey [227], whereas the others interviewed study subjects. A number of studies have reported increased rates of low birth weight, reduction in mean birth weight, or preterm labor in bivariate analyses, but the associations became nonsignificant when adjusted for use of tobacco and other substances [228–231], only one being population based [227].

> Pregnant patient presenting with blunt trauma not from traffic should be examined in detail for the signs of older trauma which could lead to chronic violence.

Adverse pregnancy outcomes after minor trauma occur at a rate 1–5 % [232]. Because more than 90 % of all injuries to pregnant women are the result of minor trauma, most pregnancy losses associated with trauma occur in cases of minor trauma [233]. The rate of fetal mortality after maternal blunt trauma is 3.4–38.0 % [2, 9, 26, 37, 38, 53, 57, 120, 234], mostly from placental abruption, maternal shock, and maternal death (Table 10.1) [2, 16, 37, 38, 40, 234–238]. Fetal loss can occur even when the mother has incurred no abdominal injuries [37, 53]. Among pregnant trauma victims, head injury and hemorrhagic shock account for most deaths [239, 240]. Serious injuries do not result in a higher mortality rate in pregnant women compared with

nonpregnant women. However, splenic and retroperitoneal injuries and hematomas are more frequent in pregnant victims of blunt abdominal trauma due to increased vascularity during pregnancy. Conversely, bowel injury is less frequent [133, 239]. Regardless of the apparent severity of injury in blunt trauma, all pregnant women should be evaluated in a medical setting [2].

As previously stated domestic violence occurs in up to 25 % of pregnant women [17, 48], but physicians detect only 4–10 % of cases [26]. It is important for physicians to screen all patients for domestic violence and to be familiar with the community resources for helping patients who experience domestic abuse [17]. As with any trauma patient, the entire body needs to be examined, looking for hidden injuries under clothes, makeup, jewelry, or wigs. Injuries range from cuts, bruises, and black eyes to miscarriage, bony injuries, splenic and liver trauma, partial loss of hearing or vision, and scars from burn or knife wounds. Injuries to the breast, chest, and abdomen are more common in battered women, as are the presence of multiple old and current injuries. Defensive injuries are common. For example, fractures, dislocations, and contusions of the wrist and lower arms result from attempts to fend off blows to the chest or face. Injuries inconsistent with the patient's explanation of the mechanism of injury should also raise suspicion of abuse. The presence of these patterns of injury should raise concern about abuse during evaluation in the emergency room (Table 10.8).

Table 10.8 Warning signs of domestic abuse [17]

Mixture of old and new injuries
Characteristic injuries (multiple soft tissue injuries, fingernail scratches, cigarette and rope burns, areas usually covered by clothes – breast, chest, abdomen, genitals)
History of prior domestic abuse
Isolating behavior of partner
Behavior of patient: depressed, poor eye contact, fearful, withdrawn
Pregnant patient: trauma to breast and abdomen; no prenatal care; unexplained spontaneous abortion, miscarriage, or spontaneous labor
Family income below $10,000/year

10.2.5 Obstetric Consequences of Blunt Trauma

10.2.5.1 Mode of Delivery

Pelvic Fractures

The recommended method of delivery for pelvic fractures during pregnancy depends on the presence of initial fetal and maternal distress, the degree of fetal maturity, the maternal injury severity, the displacement of the pelvic or acetabular fracture, and the eventual course of labor. Because these fractures tend to heal within 8–12 weeks, vaginal delivery should not be contraindicated after fractures that occurred earlier in pregnancy. Pubic ramus fractures adjacent to the urethra or bladder, severe lateral compression fractures, and acute fractures of the pelvis with marked displacement may be relative indications for Cesarean delivery if labor starts in a viable pregnancy. In the recent review by Leggon et al., vaginal delivery was successful in 75 % of pelvic fractures that occurred in the third trimester [199].

10.2.5.2 Placental Abruption

Incidence

Over 70 % of fetal losses following blunt abdominal trauma result from placental abruption [54, 55, 133, 232, 241]. Studies suggest that the incidence of abruption is approximately 5 % [118, 185, 239]. Clinically evident placental abruption occurs in up to 40 % of severe blunt abdominal trauma and in 3 % of minor trauma with direct uterine force [239, 241]. In 1942, VanSante reported a case in which blunt trauma to the maternal abdomen resulting from a fall off a stepladder was followed by spontaneous delivery of a stillborn infant and a placenta showing a clean laceration through both the fetal and the maternal surface at the area of insertion of the umbilical cord [242].

Pathophysiology

The mechanism of placental abruption resulting from trauma is based on the fundamental differences in tissue characteristics between the uterus and the placenta. The uterus consists of a significant proportion of elastic fibers

whereas the placenta is largely devoid of elastic fibers. Thus, when an external deforming force is applied to the uterus, its inherent plasticity allows deformation. At the same time, the placenta cannot undergo similar deformation and a shearing effect is created at the uteroplacental interface. It is also thought that concomitant increases in amniotic fluid pressures propagate this shearing effect, further separating the placenta from the underlying decidua. Experiments have been conducted on pregnant baboons, which were subjected to decelerative forces (~20G) typical of MVAs [243]. Such forces produce very high intrauterine pressures (~550 mmHg).

Because most blunt abdominal trauma occurs to the anterior uterine wall, one would expect that if the mechanism of separation were just displacement from the striking object, the risk of abruptio placentae would be greater when the placental location is anterior. However, the pathophysiological mechanism of separation just described does not explain the finding that an anterior placental location does not appear to be a risk factor for abruptio placenta resulting from trauma [118]. Two alternative possibilities should be considered. Firstly, the contained mass within the amniotic fluid (i.e., the fetus) can either strike the placenta in any location and thus create a potential shear or, alternatively, pull the placenta by transmitting force via the umbilical cord. A second possibility that could explain the lack of importance of placental location on the likelihood of abruptio placentae is that traumatic deformation may set up a fluid wave within the uterus. In this case, a force striking the anterior uterine wall would cause elongation and narrowing of the uterus as the contained amniotic fluid is non-compressible. The fluid wave would then "rebound" and expand horizontally causing a shortening and widening of the uterus. Again, because of the fundamental tissue differences between the uterus and placenta, a shearing effect of this interface could occur completely independent of placental location [55, 133]. Placental abruption risk is independent of whether placental location is anterior or posterior.

Clinical Presentation

Traumatic placental abruption may occur even when there are few other signs of trauma. Clinical findings may include vaginal bleeding, abdominal cramps, uterine tenderness, amniotic fluid leakage, and maternal hypovolemia out of proportion to visible bleeding. Only 35 % of clinically significant placental abruptions had vaginal bleeding [99]. Up to 2,000 ml of blood can accumulate in the uterus, and this can be a cause of maternal shock. In a patient with intrauterine hemorrhage, the uterus may be larger than normal for gestational age. Changes in fetal cardiotocography, such as bradycardia, loss of beat-to-beat variation, or sinusoidal patterns, may also indicate placental injury, fetal hypoxia, or fetal blood loss.

10.2.5.3 Placental Tear

History and Incidence

Traumatic laceration of the placenta following blunt abdominal trauma is even more infrequent than placental abruption. The first case published was by VanSante in 1942 when he reported a case in which blunt trauma to the maternal abdomen resulting from a fall off a stepladder was followed by spontaneous delivery of a stillborn infant and a placenta showing a clean laceration through both the fetal and the maternal surface at the area of insertion of the umbilical cord [242]. In 1969, Peyser and Toaff reported a similar case following a MVA in which a radial tear involved the whole thickness of the placenta; the fetus subsequently bled to death in utero [244]. Spontaneous laceration of a placental vein resulting in intraamniotic hemorrhage has also been described [245]. The uterus, umbilical cord, and fetus were completely intact in all of these cases and in the two patients reported by Stuart et al. [246].

Pathophysiology

There are two mechanisms of placental injury. The placental injury may be mediated by either a contrecoup or a direct force depending on the location of placental implantation and the direction of abdominal injury/deceleration. Following disruption of the placental circulation, the fetus bleeds to death in utero.

Contrecoup Mechanism

If the placenta is implanted posteriorly in the uterus and deceleration starts, a contrecoup mechanism similar to that in closed-head injuries occurs. Although the initial decelerative force is applied to the anterior abdominal and uterine walls, the incompressible amniotic fluid immediately anterior to the fetus would have retarded the forward movement of the fetus. The sudden anterior force to the uterus momentarily causes the posterior uterine wall and the placenta to move away from the fetus, the result being a "vacuum" between the fetus and the posterior wall. When the anterior decelerative force was no longer applied to the uterus, the posterior wall would have stopped moving and the vacuum would have caused the fetus to be projected against the placenta on the posterior uterine wall. In this situation the amniotic fluid, instead of acting as a buffer for the fetus, is operating as a vehicle for fetal movement, allowing sufficient mobility for a contrecoup injury of the placenta. This is analogous to injury of the occipital region of the brain following a frontal blow, when the cerebrospinal fluid acts as the vehicle for contrecoup movement of the brain.

Direct Placental Injury

When the placenta is implanted anteriorly in the uterus, the initial decelerative force applied to the anterior uterine wall causes the fetus to be propelled forward. The amniotic fluid, though incompressible, allows the fetus to travel forward with sufficient momentum to apply a sudden force to the surface of the placenta implanted on the anterior uterine wall, causing a "bursting" or irregular laceration of the fetal surface of the placenta (Fig. 10.13).

10.2.5.4 Preterm Labor

The true incidence of preterm labor following trauma during pregnancy is not known. It appears to be under 5 % [99, 118]. Traumatic injury to the uterus may result in destabilization of lysosomal enzymes that can initiate prostaglandin production. This is the mechanism presumed to cause preterm labor associated with trauma.

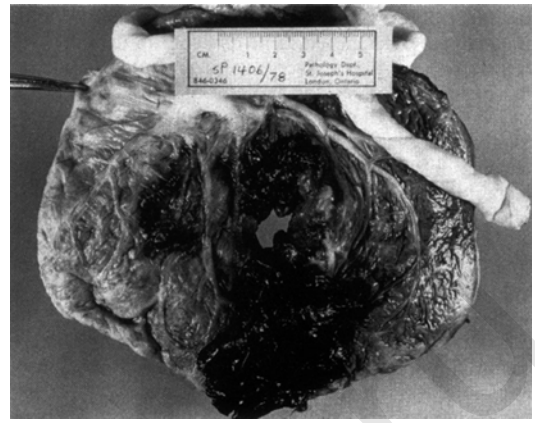

Fig. 10.13 Approximately 3 cm from the insertion of the umbilical cord was an elliptical laceration of the placenta through both the fetal and the maternal surfaces; it measured 6.5 × 2.8 cm. The cotyledons were intact, but there were masses of clot adherent to the fetal surface. Microscopically the placenta and the umbilical cord were normal [246]

Another possibility is that trauma may cause preterm premature rupture of membranes and preterm birth. Administration of slow-released progesterone should be considered in all women with contractions after trauma in pregnancy to decrease the rate of preterm birth and the risks of prematurity [247].

10.2.5.5 Fetal Injury

Direct Fetal Injury

Direct fetal injuries and fractures complicate less than 1 % of severe blunt abdominal trauma in pregnant women, since the maternal soft tissue, uterus, and amniotic fluid absorb energy and diminish the force delivered to the fetus. Most cases, with severe injuries, occur during late pregnancy [133, 239]. Cranial injuries are the most frequently reported category of direct fetal injury after blunt abdominal trauma. Fetal brain and skull injuries may be more common in cases with fetal head engagement in which maternal pelvic fractures occur [142, 248]. Deceleration injury to the unengaged fetal head may also occur [63–65, 133, 239]. Isolated fractures of the mandible, the clavicle, the vertebrae, and all the long bones have been reported [249]. In these direct injuries either the maternal abdominal wall is

struck by a blunt instrument or the maternal abdomen strikes the car's dashboard, steering wheel, or other area. Such injuries may not be diagnosed at the time of the accident, and the pregnancy may well continue to term in the absence of concomitant placental or uterine injuries. Intrauterine fetal fractures may spontaneously heal in utero, as evidenced by callus formation at the fracture site [249].

Indirect Injury of the Fetal Viscera

Indirect injury of the fetal viscera – that is, injury in the absence of external evidence – has been reported, but one can only speculate on the mechanism of injury. Connor and Curran reported a case in which the fetus suffered hepatic, renal, and adrenal contusions and hemorrhage without showing external evidence of trauma [250]. They suggested that the injury was due to rapid compression and impact of the organs during deceleration, but whether it resulted from a contrecoup effect within their attachments or was secondary to a shearing force within the organs could only be conjectured [251].

10.2.5.6 Uterine Rupture

Uterine rupture can be spontaneous (see Chap. 16) or is a rare complication of blunt abdominal trauma, complicating about 0.6 % of traumatic events during pregnancy [239]. The first published paper found was by Lazard and Kliman from 1936 [252]. Authors proposed classification of traumatic uterine rupture:

- *Complete*, through the entire uterine wall, with complete or partial extrusion of the uterine contents into the abdominal cavity.
- *Incomplete*, where the rupture is not through the entire uterine wall. As to location, the tear may be in the upper or in the lower uterine segment, usually the upper when due to external trauma.

Incidence

In a review of the literature, by Estor and Pueck (referred to by Jaroschka, Medizinische Klinik, 1929), up to and including 1929, 40 cases were found. Additional cases in the 1930s were described by Orthner [253], Lazard and Kliman [252], Ruder and Moore [254], and Smilow [255].

Etiopathogenesis

Traumatic Uterine Rupture

While a trauma of sufficient force may cause a rupture in a healthy uterus, the presence of a weakened point caused by preceding disease, such as hyaline degeneration of muscle fibers resulting from multiparity, previous curettages, placenta previa, intramural fibroids, etc., would undoubtedly increase the probability of rupture resulting from external violence.

Orthner gives the following explanation of the mechanics of the injury [253]: as to whether the blow or the resultant fall is the principal factor, one can assume that whichever is of the greater intensity is the chief factor, i.e., with a slight blow and a fall from a great height, the latter is the main factor; with a severe blow and a short fall to the oor, the blow in all probability is to blame. It is not possible, as a rule, to determine the kind and direction of the force from the location of the uterine rupture, as this usually occurs by contrecoup.

The rupture is always the result of a sudden increase of the intrauterine pressure, caused by the sudden compression of the abdominal contents. In accordance with the laws of hydrodynamics, this pressure spreads equally in all directions in the uterine cavity filled with amniotic uid. The tear occurs at the weakest point of the uterine wall. At the end of pregnancy, that point is at the fundus, which, moreover, lacks the protection of the bony pelvis. In many cases it appears that the placental site is especially weak because of the increased vascularity.

The site of rupture bears a direct relationship to the site where direct traumatic or contrecoup forces are applied mostly involving the uterine fundus (Fig. 10.14), although other locations and

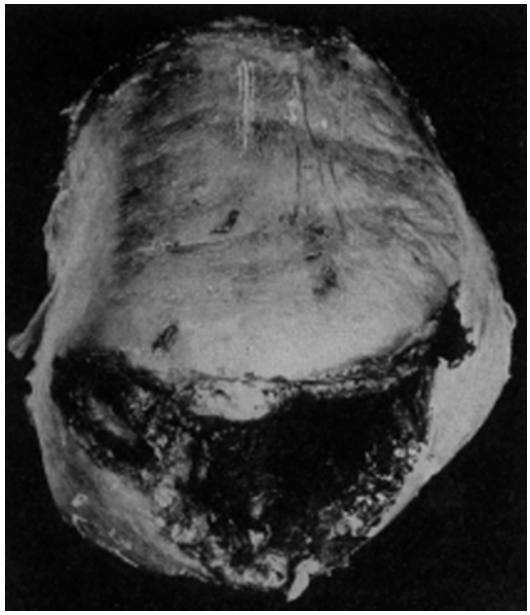

Fig. 10.14 Ruptured uterus. Transverse rupture on the posterior surface of the fundus after falling down on steps [252]

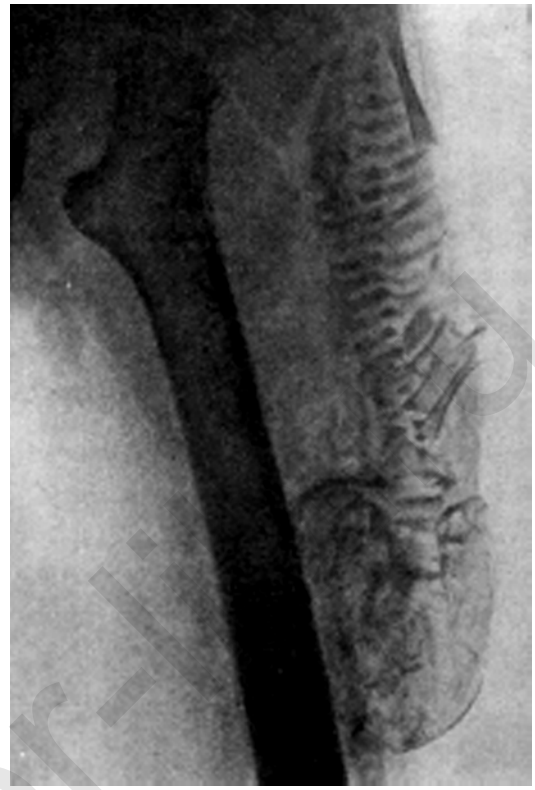

Fig. 10.15 A vertical incision was made on the upper anterior surface of the right thigh, extending up to the groin, and the fetus was found lying just under cover of the skin and superficial fat [257]

degrees of uterine rupture from other causes have also been reported [133, 239, 256]. This is because amniotic uid transmits high pressures efficiently; "blast injuries" can follow blunt trauma, resulting in rupture of the uterine fundus mostly.

Fetal Injury

Traumatic uterine rupture is commonly associated with fetal injury. In extreme situations (mother hit by a truck) the fetus was found on mother's thigh (Fig. 10.15). Coutts explain two possible mechanisms [257]:

1. The bus struck the woman on her left side, throwing her on the ground, and went over her; the pressure of the tires and counter-pressure of the ground ruptured the uterus, and the pressure continuing downward and to the right forced the fetus down into the thigh (the fetus was about 23 weeks old, so the uterus would be above the brim and nearing the level of the umbilicus).
2. The original blow and pressure were on the right side and stripped the skin and superficial fascia off the thigh, detaching the inguinal ligament from its attachments and the abdominal muscles from the anterior third of the iliac crest; the same force, continuing to act, tore the peritoneum and ruptured the uterus. On release of the pressure, the uterus rebounded forward and squeezed out the fetus, which passed out under the skin of the right thigh along the line of least resistance.

Clinical Presentation

The classic description of uterine rupture includes the following: severe uterine pain and tenderness, profound shock, palpation of fetal parts outside the uterus, and vaginal bleeding. These complex findings, however, often are not present [258–260]. Consequently, the diagnosis is often delayed or not considered at all. Uterine blood ow increases from nongravid rate of 60 cm^3/min up to 600 cm^3/min at term [239]. A loss of

Table 10.9 (Pregnant) uterus injury scale [261]

Grade[a]	Description of injury	AIS-90
I	Contusion or hematoma (without placental abruption)	2
II	Superficial laceration (<1 cm) or partial placental abruption <25 %	3
III	Deep laceration (≥1 cm) in second trimester or placental abruption 25–50 %	3
	Deep laceration (≥1 cm) in third trimester	4
IV	Laceration involving uterine artery	4
	Deep laceration (≥1 cm) with >50 % placental abruption	4
V	Uterine rupture	4
	Second trimester	5
	Third trimester	4–5
	Complete placental abruption	

[a]Advance one grade for multiple injuries up to grade III

blood volume such as that seen with trauma is compensated in part by an increase in uterine vascular resistance and decreased uterine blood flow [57]. Hemodynamic stability in the mother, therefore, is maintained at the expense of uterine blood flow, putting the fetus at risk [40, 197]. As a consequence, fetal distress may be the first indicator of unsuspected maternal hemorrhage. The presence of maternal hypotension is a late and ominous sign.

Treatment

The diagnosis of uterine rupture warrants immediate surgical intervention. As to therapeutic procedure, much depends on the location of the rupture and the degree of injury (Table 10.9). Total abdominal hysterectomy is considered the operative intervention of choice, although subtotal hysterectomy or simple suture repair may be reasonable alternatives [258, 260, 262]. If it occurs in the fundus, a repair of the laceration is quick and is done with less shock. If the tear is located in the lower segment, transverse hysterectomy is indicated. Palliative measures must be considered and might be lifesaving, such as the application of the Momberg belt or clamping the uterine arteries through the cervix until the patient can be relieved of shock and prepared for surgery.

Prognosis

Uterine rupture tends to occur only in the most serious accidents involving direct abdominal trauma. This event can be catastrophic for both the mother and her unborn fetus, especially when there is a delay in the diagnosis, since initial symptoms may be variable. With traumatic rupture, fetal mortality approaches 100 % and maternal mortality close to 10 % with most maternal deaths due to concurrent injuries [124, 239, 263, 264]. At first glance, it is striking that most of the patients reported have survived. However, a reason for the survival is to be found in the fact that the blood vessels constrict and thus the bleeding rapidly diminishes or even stops entirely. The uterine contents (the placenta, the amniotic sac, etc.) are immediately emptied into the abdominal cavity, whereupon the uterus contracts as it would following Cesarean section. Since the blood supply at the midline (where the rupture usually occurs) is scanty, these contractions of the uterine muscle practically stop the bleeding. This consideration suggests that in cases where the placenta is inserted more toward the parametrial region, where the contractibility is less and the blood vessels are much larger, the trauma would result in fatal exsanguination.

10.2.5.7 Fetal-Maternal Hemorrhage

Fetal-maternal hemorrhage (FMH) occurs four to five times more frequently in injured pregnant women than in uninjured controls, and the volume of transfused blood is also greater in injured women [44, 99, 118, 133]. A direct correlation between the incidence of FMH and the severity of maternal injury has not been demonstrated [55, 239]. Pearlman et al. [118] found that neither the severity of injury nor the presence of uterine activity was predictive of FMH. However, an anteriorly positioned placenta and the presence of uterine tenderness did correlate with FMH. Complications of FMH include rhesus (Rh) sensitization in the mother, neonatal anemia, cardiac arrhythmias in the fetus, and fetal death from exsanguination [239]. The Kleihauer-Betke acid elution assay is one method used to detect FMH and should be considered in every woman, in order to determine the Rh immune

globulin dose necessary to be administered to women who are Rh- and suffered a massive transfusion [54, 55, 118, 239]. The amount of FMH sufficient to sensitize Rh- mothers is far below the level detected by most laboratories. In a study by Pak et al., none of the patients had a positive Kleihauer-Betke test result, which indicated the absence of significant FMH [215]. This differs dramatically from 8 % to 30.6 % FMH rates reported by other investigators [44, 99, 239]. This difference in the rate is likely due to the fact that the study by Pak et al. included only those with noncatastrophic trauma, whereas other studies included patients with catastrophic trauma. Although Mostello et al. [265] suggest that the Kleihauer-Betke test is not indicated in the Rh+ woman without symptoms, quantification of FMH is still recommended for all patients with abdominal trauma regardless of their Rh status by several other studies [44, 99, 118]. Until more sensitive diagnostic tools for detection of placental abruption and subsequent FMH are available to the obstetrician, continued use of the commonly available screening tests for all pregnant women who have abdominal trauma is recommended.

10.2.5.8 Traumatic Rupture of Membranes

Rupture of membranes (ROM) secondary to trauma in pregnancy is seldom an isolated injury. A thorough search for concomitant injuries is mandatory and prolonged continuous fetal monitoring strongly advocated. In the absence of maternal or fetal compromise, management is usually not different from spontaneous ROM.

10.2.5.9 Urinary Bladder Rupture

If bladder rupture is suggested by clinical findings (e.g., severe abdominal pain, board-like rigidity of the anterior abdominal wall, blood on the external meatus, gross hematoma) or by radiologic findings (e.g., pelvic ring disruption, obliteration of pelvic fat planes), then a cystogram with a maximally distended bladder and a post-evacuation film, as a minimum, should be obtained. To do this procedure, one may place in a retrograde fashion at least 250–300 ml of contrast material into the urinary bladder as much as the alert patient will tolerate. If an upper abdominal contrast-enhanced CT evaluation is necessary, some radiologists may be tempted to perform a CT cystogram instead of a routine cystogram. Goldman and Wagner consider this inadequate because the bladder may not be completely distended with contrast material [266]. Furthermore, oral contrast material should be given for bowel opacification to obtain an adequate abdominal CT study. However, this contrast material may obscure and confuse the findings if a subsequent plane-film cystogram is needed. The one exception is the potentially unstable patient, where the contrast should be diluted to 5 % and instilled into the bladder before any CT cuts are obtained. Air can be used as a substitute bladder contrast agent.

10.2.5.10 Traumatic Rectus Sheath Hematoma

There is a case with suspected blunt abdominal trauma during pregnancy with verified rectus sheath hematoma after delivery. Therefore, it is not known whether the cause is abdominal trauma or the process of delivery with straining itself [267]. Possible mechanism is that during distension of the abdominal wall in pregnancy causes elongation of the inferior epigastric artery. Blunt trauma to that region possibly causes further distension of inferior epigastric artery beyond its elastic modulus making it prone to tears and lacerations. Rectus sheath hematoma is described in detail in Sects. 11.6 and 11.6.8 in Chap. 11.

10.2.6 Diagnosis

10.2.6.1 Laboratory Findings

- *Base deficit (BD)* >-6 has probability $\geq$95 % for the absence of intra-abdominal bleeding.
- *BD* ≤-6 and *increased pulse rate* indicate that there is a markedly enhanced risk for intra-abdominal bleeding.

Decreased BD and/or increased pulse rate was highly sensitive for detecting patients with internal bleeding [268–270], although both of these research focused on BD and one of them [268] chose a BD of ≤ 4. BD ≤ 6 had sensitivity of approximately 88.2 % compared with ultrasonography, 76.5 % [270]. The latter is due to the fact that ultrasonography is not likely to detect most retroperitoneal or pelvic injuries [271]. However, ultrasonography has a positive predictive value of approximately 100 % and nearly equal negative predictive value with BD for detecting free uid [272]. Finally, BD correlates well with blood transfusion and laparotomy requirements (68.4 % of patients with BD ≤ 6 indicated for blood transfusion compared with only 1.2 % of patients with BD > 6 and 57.9 % of patients with BD ≤ 6 indicated for laparotomy compared with only 1.2 % of patients with BD > 6). Therefore, patients with blunt abdominal trauma whose BD is ≤ 6 are more prone to laparotomy and blood transfusion [270, 273]. The same results and conclusions are confirmed in pregnant women who we often do not want to expose to radiation. All of these patients whose BDs were ≤ 6 had intra-abdominal bleeding and undergone blood transfusion. This fact shows the importance of BD in pregnant patients [270]. A normal BD does not exclude intra-abdominal injury in blunt trauma patients, but the presence of a BD ≤ 6 should be considered a strong indication for abdominal evaluation. The results of the study demonstrated that a BD of ≤ 6 has high sensitivity and specificity for detecting free intraperitoneal uid in patients with blunt abdominal trauma, as well as a high transfusion requirement and laparotomy in these patients.

Placental Abruption

There has been a great interest in using laboratory markers in aiding the diagnosis of placental abruption. Elevated D-dimer levels and fibrin-split products (FSP) are early markers for accelerated fibrinolysis in beginning disseminated intravascular coagulopathy (DIC). Although often found to be elevated in cases of placental abruption, most studies failed to demonstrate clinical usefulness as a screening test [41, 274]. Although placental abruption is frequently found in association with FMH, screening for fetal blood cells in the maternal circulation with Kleihauer-Betke tests has a low specificity and is currently for this purpose not recommended [10, 47].

10.2.6.2 Focused Abdominal Ultrasound for Trauma

Focused abdominal sonography for trauma (FAST) performed by radiologists, sonographers, trauma surgeons, and emergency physicians is an important method of evaluating patients with blunt trauma worldwide and has been extensively studied. Previous investigators have reported sensitivities for the detection of free uid with this method that ranges 42–100 % [271, 275–279]. Goodwin et al. reported a sensitivity of 83 % in their retrospective study of 208 pregnant patients, although they did not directly compare sonography results in pregnant patients with those in nonpregnant patients [19]. One explanation for the marked number of false-negative results is that FAST is performed relatively early in the resuscitation process, at a time when hemoperitoneum may not have accumulated to a detectable amount. In the study from 2004 [279], a marked number of false-negative results (27.5 %) were observed in patients with bowel and mesenteric injuries; this finding is consistent with findings of previous studies involving both sonography and CT [280].

Miller et al. [278] suggested that all hemodynamically stable patients who have sustained blunt abdominal trauma should undergo CT scanning rather than FAST to prevent the possible underdiagnosis of intra-abdominal injury. This may be a difficult concept to apply in the assessment of pregnant patients because the risk of teratogenesis from CT radiation exposure, however minor, may be unacceptable. Further consideration should be given to the gestational age of the fetus, because radiation exposure in early pregnancy would have a more deleterious effect than radiation exposure in later pregnancy [281]. In one series at a large trauma center [119], only 7 % of pregnant patients with trauma underwent CT scanning; this is comparable to the 8.2 % of patients who underwent it in the study

by Richards et al. [279]. It appears that the decision to perform a CT examination is arbitrary and may depend on the presence of equivocal objective findings that might result in an unnecessary laparotomy.

Although not as sensitive as CT, FAST has a distinct advantage over CT in the rapid triage of unstable patients with blunt trauma who cannot safely travel to the CT suite. Detection of free uid and/or parenchymal abnormality in this setting results in safer and faster disposition to the operating room than could be accomplished with either CT or diagnostic peritoneal lavage. If no free uid is detected, the patient may be transferred to the labor and delivery area for fetal monitoring and potential delivery. With this method, the possibility of teratogenesis from the ionizing radiation at CT and the risk of an allergic reaction to intravenous CT contrast material are avoided. In the future, sonography performed with contrast material may be a viable alternative to CT. In one small, blinded study with 15 patients with abdominal trauma that involved comparing CT with power Doppler, there were no false-positive or false-negative examination results in the Doppler arm [282].

Pelvic Free Fluid

Physiological free uid (FF) in the pelvis of normal women was first described by Novak in 1922 [283]. Since then, many have investigated the characteristics, etiology, and typical volume of physiological FF. Varying amounts of FF have been detected during the menstrual cycle, with the greatest volume detected during ovulation [284–286]. This FF is presumed to serve the teleological purpose of transporting the ovum by wave motion [285–287]. Prevalence of transient physiological FF on transabdominal ultrasonography in reproductive women has been estimated to range from 36 % to 40 %. The estimated mean volume ranges from 5 to 21 ml [284–286, 288–293]. This phenomenon has been attributed to:

- Fluid secondary to follicular rupture [284]
- Ovarian uid exudation secondary to increased capillary permeability under the in uence of estrogen [284, 289]
- Blood secondary to retrograde menstruation [294]

The amount of peritoneal FF seemed to decrease significantly after the peak, near menstruation [284, 289]. In study by Ormsby et al. [295], detection of FF in (a) both the abdomen and pelvis had the highest association with intra-abdominal injury, followed by (b) FF isolated to abdomen, then (c) isolated to pelvis, and the least is (d) when there was no FF. Sirlin et al. [296] have reported that FF most often occurs at the site of organ injury and also within the pelvis. Another study of women of reproductive age, in which 8 % were pregnant, compared the FF location to injury rate [297]. The conclusion was that there was no difference in injury rate between those with isolated pelvic FF and those without FF and that isolated pelvic FF was not likely to be associated with intra-abdominal injury. These findings differ from Ormsby et al. in that isolated pelvic FF had a statistically significant higher injury rate than those without FF in pregnant and nonpregnant women. The discrepancy between previous findings by Sirlin et al. [297] and findings by Ormsby et al. regarding isolated pelvic FF among nonpregnant patients may be due to several factors. Sirlin et al. had only 8 % of pregnant patients. In study by Ormsby et al. [295], there was a larger sample size with 16 % of pregnant women. Physiological FF is detected mostly during ovulation and a few days after ovulation in 36–40 % of nonpregnant women, according to previous studies [285, 286]. Therefore, outside of their ovulation period, these women would not be likely to have sonographically detectable amounts of physiological FF. Unfortunately, authors did not query the menstrual history of their study subjects. Therefore, it is impossible to know if there were a greater percentage of women who were anovulatory and/or were in a time period of their menstrual cycle when physiological FF is less likely to be seen.

Transabdominal sonography is less sensitive than transvaginal sonography in detecting pelvic FF [290, 293, 298, 299]. Von Kuenssberg Jehle et al. [300], in their study on the sensitivity of the pelvic view on transabdominal ultrasound imaging for the detection of FF, administered intraperitoneal uid directly to both male and female patients until the uid was identified on pelvic view. They reported that the mean minimal

volume of uid detectable by pelvic ultrasound by the examiner and reviewer was 157 and 129 ml, respectively, with the lowest volume detected by examiner to be 73 ml. This is much larger than the average 7–21 ml of physiological uid aspirated from the cul-de-sac of women [284, 288–293]. Thus, any trace FF in the pelvis on FAST exam in the setting of blunt abdominal trauma may indicate the FF level is not physiological. It might then be more difficult to attribute pelvic FF detected by FAST of women who are anovulatory or using oral contraceptives as physiological, since the average volume is much smaller in these patients [284, 289].

Transvaginal sonography is more sensitive in detecting FF in the cul-de-sac [290, 293, 298, 299]. Although more likely to detect small volumes of pelvic FF, it is impractical, as it would be difficult to perform in the active trauma resuscitation setting. Furthermore, trauma patients undergoing FAST do not always have the benefit of having a completely full bladder. Therefore, FAST would not be expected to reliably detect small amounts of FF that would be detected during a detailed comprehensive transvaginal ultrasound examination. Of interest, there were three patients in the study by Ormsby et al. who had ruptured ectopic pregnancies, one of whom had FF isolated to the pelvis and the other two cases with FF in both the pelvis and abdomen. Additionally, of the 53 total patients with isolated FF in the pelvis, 87 % underwent further tests (CT, exploratory laparotomy, and/or diagnostic peritoneal lavage) compared to the 49 % with isolated FF in the pelvis in the study by Sirlin et al. [297]. This may also explain the difference between these two studies. In pregnant patients, small amounts of pelvic FF may be missed due to a mass effect of the enlarging uterus [301]. It was previously described that ultrasound was less sensitive for detection of intra-abdominal injury in pregnant versus nonpregnant female patients [279]. In that study authors did not address the perplexing problem of isolated FF detected in the pelvis of traumatized female patients. However, Sirlin et al. [296] did address the question of location of FFs in this patient population. Another possible explanation of missed pelvic FF is adequate bladder distention during ultrasound. Sirlin et al. [297] have noted that using a full bladder technique increased detection of pelvic FF that is of minimal amount and often physiological. One study has reported that a significant cause for missing pelvic FF was the bladder not being distended enough to provide an adequate acoustic window [302]. Patients with blunt abdominal trauma often have a Foley catheter, which decompresses the bladder. Without a full bladder as an acoustic window, FF in the pelvis may be overlooked with transabdominal ultrasound. This may explain why some patients had false-negative FAST in the group without FF in the study by Ormsby et al. Of the nine false-negative cases in pregnant patients, 67 % were due to placental abruption. It has previously been reported that ultrasound is not sensitive for detection of placental abruption [303]. For these patients, careful clinical correlation such as gestational age, significant vaginal bleeding, fetal distress, and/or severe abdominal pain should be made. If placental abruption were excluded for the group comparison, pregnant patients in a group without FF would have an injury rate of 1 % with no change for the group where the uid was isolated to pelvis. Also, as Sirlin et al. [297] used a full bladder, this could explain why their detection of FF in trace amounts was probably physiological. Without a full bladder, only larger amounts of FF would be detected. These amounts may be more significant than small amounts of uid.

Isolated pelvic FF was the second most common true-positive uid accumulation pattern observed in the study by Richards et al. [279]. The ability to distinguish between physiological FF and FF resulting from injury has been addressed in a previous study: Sirlin et al. [297] reported isolated FF in the cul-de-sac in 56 patients, and only two had injuries, but they made no distinction between pregnant and nonpregnant patients. Their conclusion was that isolated FF in the pelvis was likely to be physiological and not due to injury. In another study, 54 % of the false-positive US examinations in pregnant and nonpregnant patients combined revealed isolated FF in the pelvis [279]. Also of interest in the same study are the three patients with undiagnosed ectopic pregnancies that ruptured after their traumatic events. The incidence of ectopic pregnancy

has steadily increased over the past 3 decades, and these patients are seen more frequently in the acute care setting [304]. Transvaginal US has been the imaging study of choice for detecting ectopic pregnancy, but less is known regarding transabdominal US for this indication [305]. US assessment of FF in the three patients in the study by Richards et al. [279] revealed isolated pelvic FF in two patients and FF in the Morison pouch and the pelvis in one patient. On the basis of these findings, isolated FF in the pelvis cannot necessarily be discounted as being physiological in the pregnant patient. Sirlin et al. [296] analyzed the results of 2693 US examinations for blunt abdominal trauma and determined that FF present in the left upper quadrant, in both upper quadrants, or diffusely was significantly associated with splenic injuries. In one study, all pregnant patients with splenic injuries had FF in the left upper quadrant [279].

The dynamics of ow in the abdomen are of interest in that FF tended to ow from the left to the right upper quadrant rather than down the left paracolic gutter into the pelvis. One explanation for this may be that hemorrhage from the spleen first accumulates in the left and then progresses to the right upper quadrant because the phrenocolic ligament acts as a relative barrier to the movement of uid to the left gutter [306]. It also appears that uid from the right upper quadrant owed down the right paracolic gutter rather than toward the left upper quadrant, perhaps because of the gravity dependence of the right paracolic gutter and pelvis. In the study by Richards et al. [279], the most common pattern of FF accumulation in pregnant patients with fetuses of all gestational ages was a pattern of accumulation in the left and right upper quadrants and the pelvis (Figs. 10.16 and 10.17). However, US depicted pelvic FF in pregnant patients in the third trimester, and the sensitivity of focused abdominal US for trauma was the highest for patients who were in the first trimester of pregnancy. One possible explanation for this may be that the compression of intra-abdominal structures, specifically the paracolic gutters, by the expanding uterus may make it more difficult to detect FF in the paracolic gutters and pelvis [307].

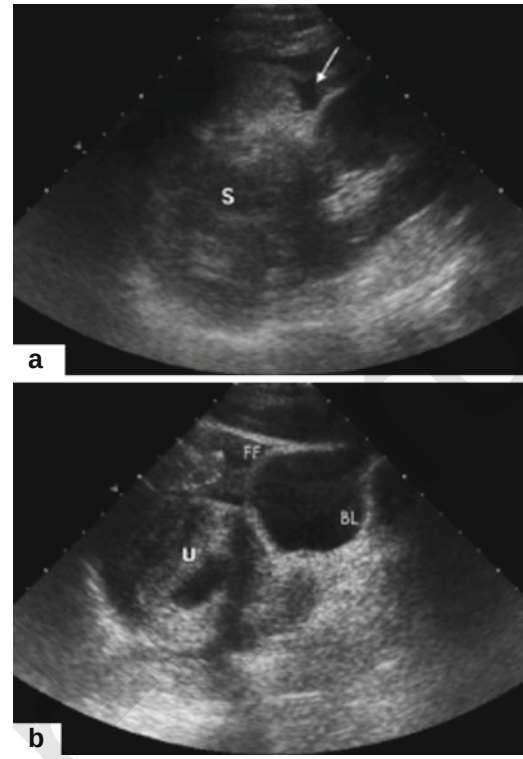

Fig. 10.16 Images in a 22-year-old woman in the first trimester of pregnancy who had sustained blunt abdominal trauma and subsequent splenic laceration in a motor vehicle collision. After US was performed, the patient was taken immediately to the operating room for laparotomy. (**a**) Longitudinal US image of left upper quadrant reveals perisplenic free uid (*arrow*) and abnormal-appearing splenic parenchyma (*S*). (**b**) Longitudinal US image of pelvis shows free uid (*FF*) superior to the bladder (*BL*) and gravid uterus (*U*) [279]

It has been suggested in the past that the fetus is well protected against injury from blunt trauma because it is encased in a uid-filled structure [308]. It was shown that intra-abdominal injuries in pregnant patients were most common to the spleen or placenta, necessitating precipitous delivery or resulting in fetal demise [279]. Thus, the shear forces present in even low-force injuries such as falls cannot be discounted, and it is recommended that US, as well as fetal monitoring for patients whose fetuses are past 20 weeks' gestation, should routinely be used in pregnant patients with trauma. Continuous fetal monitoring is more sensitive but is less specific than US for the detection of placental abruption [118].

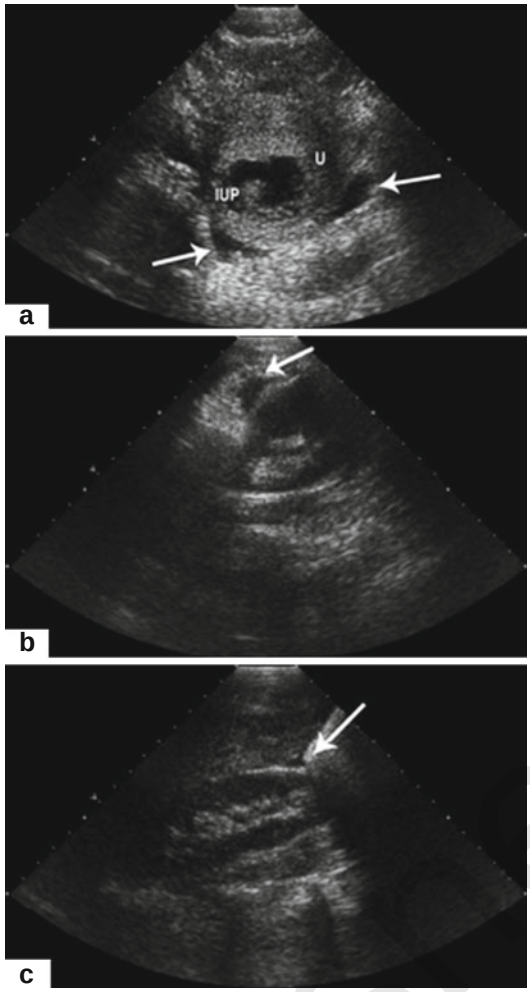

Fig. 10.17 A 19-year-old pregnant female in her first trimester involved in a high-speed motor vehicle accident with spleen laceration. (**a**) Transverse scan of the pelvis with empty bladder shows early intrauterine pregnancy and bilateral free uid (*FF*) (*arrows*) adjacent to the uterus. (**b**) Transverse scan of the left upper quadrant demonstrates FF (*arrow*). (**c**) Longitudinal scan of the right upper quadrant demonstrates FF (*arrow*) in the hepatorenal fossa. *IUP* intrauterine pregnancy, *U* uterus [295]

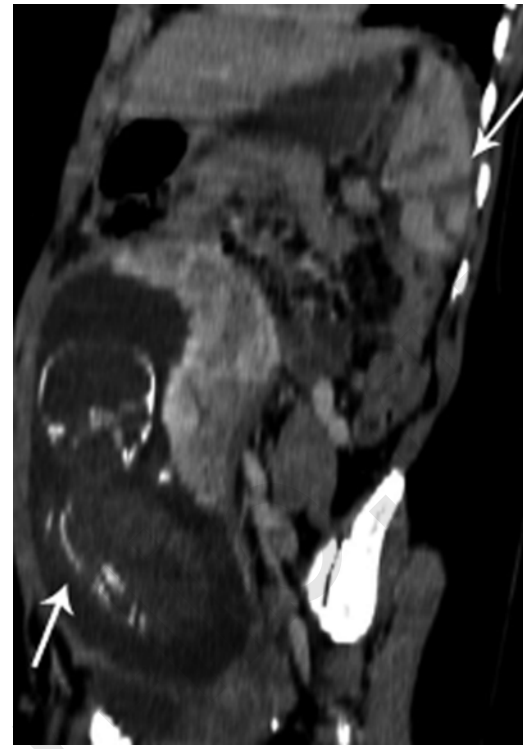

Fig. 10.18 An oblique sagittal reformatted CT scan image showing traumatic splenic laceration (*right arrow*) and the 26-week fetus (*left arrow*) [309]

Spleen

The spleen (Fig. 10.18) and liver are most likely to be damaged in later stages of pregnancy, as they are displaced by the expanded uterus closer to the chest wall. Although there are no guidelines on the management of specific injuries in the pregnant patient, there is experience with successful nonoperative management of stable patients in the gravid state [310]. With concomitant head injury, intervention with either embolization or splenectomy is recommended (see Chap. "9" where further discussion is found in Sect. 9.1). This approach is designed to prevent hypotension and instability, which would worsen the prognosis of their head injury. Likewise, one could argue that the risk to the viable fetus from ongoing hemodynamic instability may warrant adopting a more aggressive approach in the management of traumatic injuries in the mother.

Placental Abruption

Ultrasound examination of the pregnant abdomen to detect FF is much more useful than clinical examination. The sensitivity of sonography to identify post-traumatic abruption is only 40–50 % [41, 118]. Therefore, the absence of visualization of subchorionic hemorrhage or a retroplacental clot (Figs. 10.19 and 10.20) on ultrasonography in the presence of clinical symptoms like abdominal pain mandates further

continuous fetal monitoring with a low threshold to intervene should signs of fetal distress appear.

10.2.6.3 Cardiotocography

Ultimately, complete placental separation and fetal demise will occur as the process of placental abruption continues. Depending on the size of the initial clot, placental abruption might not be infrequently asymptomatic in its early stages. Owing to the high thromboplastin concentration in the surrounding trophoblastic tissue, local DIC is likely to develop leading to expansion of the clot. With expansion of the retroplacental clot, uterine activity will usually emerge. With more than eight registered contractions per hour and in the absence of reassuring fetal monitoring, there is a 25 % chance of finding placental abruption in pregnant women after blunt abdominal trauma [118].

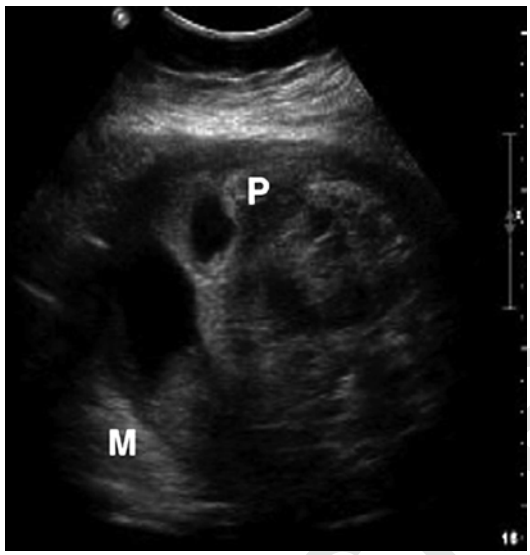

Fig. 10.19 Placental abruption. Emergency ultrasound performed in the trauma bay reveals presence of anechoic pockets representing hematoma separating the placenta (*P*) from the myometrium (*M*) [309]

10.2.7 Treatment

10.2.7.1 Observation

There is much controversy regarding the optimum duration of observation needed in the gravid woman who has had any form of trauma. The controversy results from the fact that the frequency and onset of adverse outcomes are uncertain. This uncertainty has led to the development of many different protocols for the management of the pregnant patient with trauma. Over three-quarters of women were admitted for only 1 day following MVA. Although the optimal length of time necessary to monitor women in hospital with minor or no obvious injuries following a MVA cannot be determined in one study, it would suggest that 1 day is sufficient in most cases, without any adverse impact on complication rates [3].

The management of pregnant trauma patients may be assisted if we stratify injured women into four groups [54]. The first is comprised of injured women who are unaware that they are pregnant.

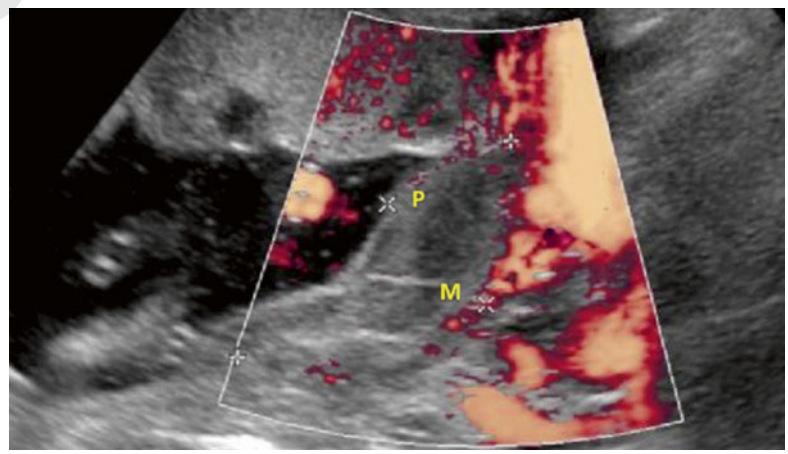

Fig. 10.20 Placental abruption. A 21-week pregnant patient. A heterogeneous collection is seen interposed between the placental edge (*P*) and the myometrium (*M*). The collection lifts the placental edge away from the underlying myometrium [309]

Since routine radiographic studies have the greatest teratogenic potential in early pregnancy, a pregnancy test should be obtained from all trauma patients of reproductive age. The second group is pregnant women of less than 24–25 weeks of gestation where the primary focus is aimed solely at the mother, since the fetus has not yet reached the border of viability. The third group consists of pregnant women at a gestational age beyond the border of viability. For this group, monitoring, support, and clinical consideration are aimed at two patients, the mother and fetus. The fourth group is comprised of severely injured women who present in a perimortem state. In these patients early Cesarean section may facilitate maternal resuscitation and increases the chance of fetal survival.

10.2.7.2 Radiologic Interventional Techniques

Classified as zone 3 of the retroperitoneum, hemorrhage into the pelvis is difficult to control operatively and is usually managed with interventional embolization if pelvic fracture is not present that mandates fixation (see section "Pelvic fracture treatment") which, apart from bone stabilization, also stabilizes retroperitoneal hematoma. The radiation dose required for interventional radiologic procedure(s), however, can be prohibitive.

10.2.7.3 Surgical Treatment

Initial Stabilization

A systematic approach to initial stabilization and management should be used after blunt trauma in pregnant women (Fig. 10.21) [37, 38, 47].

Rapid maternal respiratory support is critical; anoxia occurs more quickly in advanced pregnancy as functional residual capacity may be significantly reduced, leading to more rapid respiratory decompensation, particularly with chest trauma so supplemental oxygen should be administered early (Fig. 10.21) [312–314].

Evaluation of the fetus should begin only after the mother has been stabilized. Supplemental oxygen and intravenous fluids are administered initially and are continued until hypovolemia, hypoxia, and fetal distress resolve [47]. These measures maximize uterine perfusion and oxygenation for the fetus [47]. In animal studies, improvement in fetal partial pressure of arterial oxygen or fetal heart rate is slower with the use of saline or lactated Ringer's solution than with blood replacement attesting to the importance of restoring oxygen-carrying capacity as well as blood volume [57, 61, 315].

Because of the increased blood volume late in pregnancy, the mother may not show typical signs of hypovolemia, even with loss of a large volume of blood (up to 2,000 ml). However, uterine perfusion still may be compromised.

> Uterine blood flow may decrease by up to 30 % before the mother demonstrates clinical signs of shock. Therefore, blood transfusion should be initiated when significant blood loss has occurred or is suspected.

It is important to recognize that significant blood loss can occur in the uterine wall or retroperitoneal space without external bleeding. After 20 weeks of gestation, the uterus may compress the great vessels when a pregnant woman is supine. This compression can cause a decrease of up to 30 mmHg in maternal systolic blood pressure, a 30 % decrease in stroke volume [312], and a consequent decrease in uterine blood flow [47]. Manual deflection of the uterus laterally or placement of the patient in the lateral decubitus position avoids uterine compression [47].

Secondary Assessment

After initial stabilization, other maternal injuries are evaluated, and fetal heart tones are assessed by Doppler or ultrasonography. If fetal heart tones are absent, resuscitation of the fetus should not be attempted. There were no fetal survivors in a series of 441 pregnant trauma patients with initially absent fetal heart tones [234]. When fetal heart tones are present, gestational age is determined by fundal height, history, Leopold's maneuvers, or ultrasonography [234]. Ultrasonography is the most accurate method of determining gestational age. Determination of fetal viability is subject

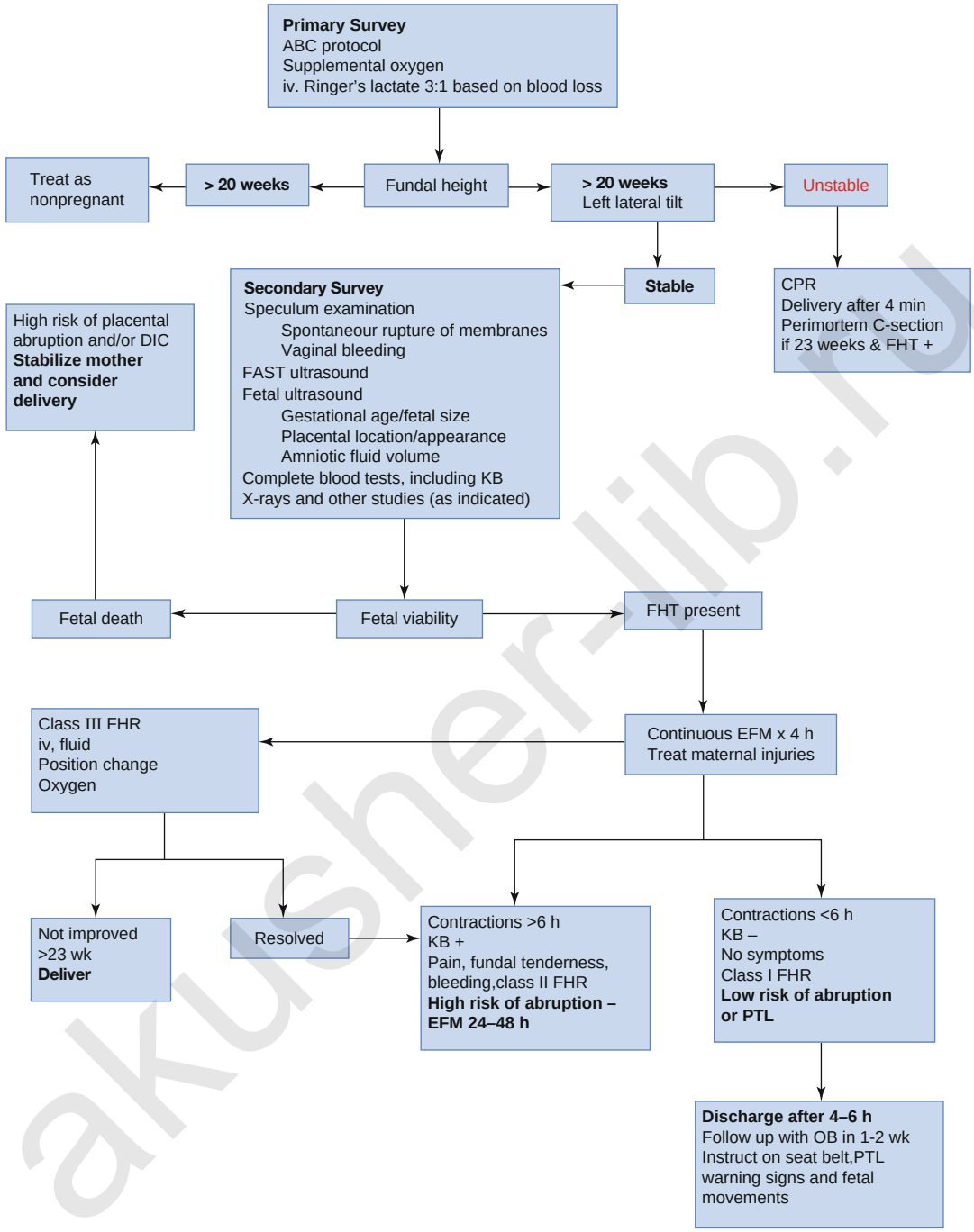

Fig. 10.21 Algorithm for the management of the pregnant woman after blunt (abdominal) trauma. Algorithm combined from the algorithms proposed by Grossman [20] and Muench et al. [311]; *KB* Kleihauer-Betke test, *FHT* fetal heart tones, *EFM* electronic fetal monitoring, *PTL* preterm labor

to institutional variation: an estimated gestational age of 24–26 weeks and an estimated fetal weight of 500 g are commonly used thresholds of viability. Only viable fetuses are monitored [234], because no obstetric intervention will alter the outcome with a previable fetus. The findings of the physical examination in the pregnant woman with blunt trauma are not reliable

in predicting adverse obstetric outcomes [10, 118]. Pregnancy induces physiological changes in women (Table 10.3) [313, 314]. For example, maternal blood pressure does not accurately re ect uterine perfusion or fetal injury [37, 40, 120, 235, 236], because pregnant women can lose up to 30 % (2,000 ml) of their blood volume before vital signs change. Blood transfusions should be administered according to standard guidelines, but the mother's Rh status must be considered. If it is unknown, Rh- blood should be administered. Invasive hemodynamic monitoring should be considered early during resuscitation to ensure adequate volume resuscitation [47]. Compared with nonpregnant persons who experience trauma, pregnant women have a higher incidence of serious abdominal injury but a lower incidence of chest and head injuries [2]. Maternal pelvic fractures, particularly in late pregnancy, are associated with bladder injury, urethral injury, retroperitoneal bleeding, and fetal skull fracture [47]. After 12 weeks of gestation, the maternal uterus and bladder are no longer exclusively pelvic organs and are more susceptible to direct injury [43]. Skull fracture is the most common direct fetal injury, with a mortality rate of 42 % [37]. Altered mental status or severe head injury after trauma in a pregnant woman is associated with increased adverse fetal outcomes [57]. Placental abruptions usually occur from 16 weeks of gestation onward [43]. Some signs of placental abruption, including spontaneous rupture of membranes, vaginal bleeding, and uterine tenderness, are infrequent after trauma [2, 39, 41, 118]. Although associated with maternal and fetal morbidity [53, 237], these signs are only 52 % sensitive and 48 % specific for adverse fetal outcomes [10].

Pelvic Fracture Treatment

Current guidelines are recommended in the hemodynamically unstable, nonpregnant patient who sustained severe pelvic trauma and has no other identifiable source of bleeding (patients with negative diagnostic peritoneal lavage and/or FAST examination) control of pelvic or retroperitoneal hemorrhage via embolization of pelvic vessels during angiography, in particular of the hypogastric arteries [316]. Although successful pregnancies after prior occlusion of both hypogastric arteries have been described, there are no reports on the safety and efficacy of angioembolization for acute pelvic hemorrhage in pregnant patients.

Pelvic and acetabular fracture surgery in pregnancy is performed infrequently [199, 201, 317, 318]. Acetabular fracture treatment was reported in 83.3 % (10/12), with skeletal traction and open reduction and internal fixation performed equally frequent [199]. Unstable fractures of the pelvic ring can be safely treated with open and percutaneous osteosynthetic techniques resulting in favorable pregnancy outcome [201, 317, 318]. A report by Loegters et al. from 2005 describes the operative treatment of a vertical unstable fracture of the posterior pelvic ring using a low-exposure technique and imaging restricted to the posterior ring [318]. External fixation of unstable pelvic fractures in pregnant patients has been described as a viable option with good outcomes [310].

Damage Control Surgery

Damage control surgery is defined as rapid termination of an operation after control of life-threatening bleeding and intestinal spillage, followed by correction of physiological abnormalities which precedes definitive management of initial injuries [319]. It is best defined as creating a stable anatomic environment to prevent the patient from progressing to an unsalvageable metabolic state when patients are more likely to die from metabolic failure than from failure to complete organ repair [320]. This modern strategy involves a staged approach to multiply injured patients. Damage control surgery is designed to avoid or correct the lethal triad of hypothermia, acidosis, and coagulopathy during or before definite injury management. The concept of abbreviated laparotomy was first described by Stone in 1983 [321]. Any laparotomy was terminated with temporizing measures when coagulopathy was noted. These involved packing of the abdominal cavity in the majority of the cases to stop bleeding and scheduled return to the operating room. The term "damage control" was popularized by Rotondo and Schwab, who in 1993 outlined a three-phase approach to patients with major abdominal

injuries [322]. Phase one consisted of control of hemorrhage and contamination with rapid techniques of intra-abdominal packing and stapling intestinal ends, followed by temporary abdominal closure. Phase two in the ICU addressed restoration of a physiological environment, in particular temperature, coagulation, and optimization of oxygen delivery. Phase three occurred, usually within 24–36 h, with removal of abdominal packs, restoration of intestinal continuity, and definitive surgery with abdominal closure. The concept of damage control was expanded further in 2001 by Johnson who added a fourth phase at the beginning called "ground zero" [323]. The principles of "ground zero" damage control include rapid transport to hospital and early decision making to facilitate hemorrhage control, prevention of hypothermia, and utilization of massive transfusion protocols. Since the early 1990s, several series have consistently demonstrated superior survival rates of patients with blunt and penetrating trauma in whom principles of damage control surgery had been employed. Damage control surgery should be considered in the following:

- Multi-system trauma with major abdominal injury
- Compound pelvic fracture with associated abdominal injury
- High-velocity gunshot or abdominal blast injury
- Penetrating abdominal injury with systolic blood pressure (SBP) <90 mmHg

Choosing the right patient for damage control is challenging. Awareness of potential triggers to initiate damage control is vital. Preemptive decision making to implement damage control should occur early rather than at a delayed point when the patient is in extremis. Accepted clinical and laboratory parameters for the application of principles of damage control surgery are the following:

- Hypotension: SBP <90 mmHg
- Hypothermia: T <34 °C
- Coagulopathy: activated partial prothrombin time (aPPT) >60 s
- Acidosis: pH <7.2 or arterial base deficit (BE) ≥8
- Major intra-abdominal vascular injury
- Associated need for management of extra-abdominal life-threatening injury (e.g., concomitant thoracic injuries)

Reports on damage control surgery in pregnancy are rare and mostly limited to liver injuries. In one of the few and largest studies to date, Smith reviewed 35 cases of hepatic rupture in pregnancy [324]. Most cases were spontaneous occurrences complicated by HELLP syndrome. The maternal survival rate with packing and drainage was 82 % compared to 25 % in patients undergoing lobectomy. Delivery by Cesarean section was carried out in nearly all cases. In case the patient required second packing due to persistent major hemorrhage from the liver at re-laparotomy, selective embolization during hepatic angiography was carried out at the conclusion of the second procedure [324]. Other more recent reviews are anecdotal case reports or case series describing successful management of liver injuries with a planned staged approach (abbreviated laparotomy and scheduled return to the operating room) [325–327]. Pregnancy should not in uence the decision to employ principles of damage control in severely injured woman. In fact, hypotension, coagulopathy, and acidosis, all which show or develop in pregnant woman at a later state, ask for a more proactive approach.

Although not addressed in the recent literature, one of the main controversies of damage control surgery in the pregnant woman concerns the timing of delivery. Since most authorities agree on the fact that delivery of the fetus in maternal extremis should be part of resuscitation because of recruitment of the uteroplacental blood volume to the maternal circulation, delivery of a term or near-term fetus should be regarded as part of the damage control approach. The situation in the severely preterm infant is more complex. Assuming that damage control surgery is exclusively employed in catastrophic

abdominal or thoracic injuries with ongoing bleeding, one would accept that the hemodynamic instability of the mother in these situations mandates the use of all possible resuscitative efforts including Cesarean delivery of a premature fetus. However, that delivery of a preterm fetus is not always mandatory in the setting of damage control surgery shows a recent report by Aboutanos et al. [328]. A fetal gestation could be safely prolonged after 28 weeks of gestation.

10.2.7.4 Obstetric Management

Fetal Monitoring

Continuous electronic fetal monitoring after trauma is the current standard of care with viable fetus [9, 38]. Monitoring is initiated as soon as possible after maternal stabilization [38, 47, 234] because most placental abruptions occur shortly after trauma [2]. Occasional uterine contractions are the most common finding after trauma in pregnant women [2, 10, 39, 118]. These occasional contractions are not associated with adverse fetal outcomes [2, 38] and resolve within a few hours in 90 % of cases [118]. The occurrence of ≥8 uterine contractions per hour for more than 4 h, however, is associated with placvental abruption [118]. With placental abruptions after trauma, there is a 67–75 % rate of fetal mortality [2, 53]. If significant placental abruption occurs, a viable fetus should be delivered immediately. In an analysis [329] of case fatality rates among pregnant women who had placental abruption subsequent to trauma, 69 % of fetal deaths were prevented by Cesarean delivery. Bradycardia or repetitive late decelerations unresponsive to intrauterine resuscitation also require immediate delivery of the fetus if the mother is stable [234]. The ideal duration for electronic fetal monitoring is unclear [10, 26, 37, 38]. A widely used protocol, as outlined in Fig. 10.21 [37, 38, 47], is based on a prospective study [118] of 60 patients at >20 weeks of gestation. This protocol has a sensitivity of 100 % for predicting adverse outcomes within 4 h. In this prospective study 70 % of patients required more than 4 h of fetal monitoring because of continued contractions (≥4/h), abnormal laboratory values, or vaginal bleeding, but all of the patients discharged at the end of 4 or 24 h had similar outcomes compared with noninjured control patients. If fetal tachycardia is present or a nonstress test is nonreactive, monitoring usually is continued for 24 h, but no studies exist to support or refute this practice. Some experts recommend prolonged electronic fetal monitoring in patients with high-risk mechanisms of injury. These high-risk mechanisms include automobile versus pedestrian and high-speed MVAs [38]. No evidence supports the use of routine electronic fetal monitoring for more than 24 h after noncatastrophic trauma [10]. Continuous electronic fetal monitoring is more sensitive in detecting placental disruption than ultrasonography, intermittent monitoring, an acid elution test (Kleihauer-Betke test to assess the amount of fetal blood in the maternal serum), or physical examination [38]. However, continuous fetal monitoring prevents few perinatal deaths [10]. It is most useful for determining reassuring fetal status and appropriate discharge [10]. Abnormal tracings (found in 3.1 % of pregnant women with traumatic injury) are not reliable in predicting adverse fetal outcomes (sensitivity 62 %, specificity 49 %) [2, 10, 330]. In contrast, a normal tracing has a negative predictive value of 100 % when combined with a normal physical examination [10].

Blunt abdominal trauma includes the possibility of the injury of every organ and description of surgical treatment would be too long. The treatment of the injuries of every organ is described elsewhere in the book.

Tocolytics (Preterm Labor)

The use of tocolytic agents for the treatment of preterm labor is controversial. Limited information exists regarding the use of tocolysis after blunt abdominal trauma. Pearlman et al. discourage any use of tocolysis in the patient with trauma on the basis of their study of 85 women [118]. In their series there were no cases of placental abruption seen among women with contractions at a frequency of <1 uterine contraction every 10 min. In that population almost 20 % of women with frequent contractions had placental abruption [118]. Because regular uterine activity after a traumatic event could result from uterine contusion or placental abruption and these two diagnoses are indistinguishable from each other, they recommend that tocolysis not be attempted

[118]. In the study by Pak et al. of noncatastrophic abdominal trauma in pregnancy, tocolytic agents were instituted in cases of persistent contractions after the maternal and fetal testing results were evaluated and found to be reassuring [215]. For patients with abdominal trauma, betamimetic tocolytic agents are not recommended. Betamimetic tocolytic agents cause maternal and fetal tachycardia, and they can mask the clinical signs of hypovolemia in both the mother and the fetus, leading to a delay in institution of the appropriate intervention. Therefore, magnesium sulfate is the tocolytic agent of choice. The preterm birth group received more magnesium sulfate tocolysis than did the term birth group (31 % vs. 7 %, respectively). However, there were no differences in the gestational age at abdominal trauma and the interval between trauma and delivery between groups. Recently cervical length, as measured by transvaginal ultrasonography, was found to be useful in predicting preterm birth [331]. In the study by Pak et al., authors did not measure serial cervical length with transvaginal ultrasonography. All patients who later delivered preterm had a closed and no effaced cervix at the time of abdominal trauma [215].

Magnesium sulfate decreases respiratory efforts and, in high doses, may lead to hypotension, respiratory collapse, or cardiac arrhythmias. Terbutaline and other β_2-adrenergic agonists cause cardiac stimulation leading to increased oxygen consumption, tachycardia, and hypotension. Such vital sign changes mimic those seen in occult hemorrhage, mandating scrutinous monitoring. Indomethacin affects platelet function and is contraindicated in patient with head injury or occult bleeding. Calcium channel blockers may produce hypotension.

10.2.8 Prognosis

10.2.8.1 Blunt Injury in General

Trauma, however, does appear to increase the rate of fetal loss and placental abruption over baseline rates in pregnant women. The actual rate of spontaneous fetal loss in the general population of pregnant women is not known. In the past, estimates have ranged 10–15 %. More recent studies that take into account early spontaneous abortions with values between 20 and 62 % [332, 333]. However, Simpson et al. reported a fetal loss of only 3 % subsequent to confirmation of a live fetus at 8 weeks' gestation [334]. Similar results have been reported by others [335, 336]. Fetal loss occurred in 4–61 % in pregnant trauma patients, depending on mechanism and severity of injury [15, 37, 185, 337–339]. Surgery for trauma has not been associated with an increased rate of fetal loss [47].

Although fetal-maternal hemorrhage occurs in 30.6 % of pregnant women with trauma compared with 8.2 % of pregnant women without trauma, and the amount of fetal-maternal hemorrhage is four times as large on average in cases of trauma, these two patient groups have similar outcomes [118]. Evidence of disseminated intravascular coagulation requires immediate intervention because it is associated with poor fetal outcomes [9, 235]. In a retrospective study [40] of 76 % patients with blunt trauma, the maternal bicarbonate level at admission was found to be predictive of fetal outcomes.

In one series [337] of 103 cases of blunt trauma in pregnancy, 24 % sustaining a major injury died. Major injury in this series was defined as documented shock at time of admission, skull fracture, cerebral contusion or intracerebral hemorrhage, spinal column fracture and/or injury, chest injury necessitating thoracotomy or tube thoracostomy, injury of the abdominal viscera or genitourinary tract treated operatively, or a pelvic fracture. Crosby and Costiloe [185] reported a 7 % maternal mortality in serious automobile injuries and a 14 % injury rate in surviving mothers. Head injury is the most common cause of maternal death, followed closely by abdominal injuries [340].

The main cause of fetal death is maternal death. Maternal shock due to major trauma has an 80 % fetal mortality rate [112, 337]; therefore, an all-out effort must be made to sustain maternal life for survival of the fetus.

10.2.8.2 Motor Vehicle Accidents

MVA in pregnancy is associated with a perinatal death rate of approximately 3–6/100,000 live births in high-income countries [341]. Injury severity, associated abdominal and pelvic trauma, and gestational age during a MVA have been shown in part to predict pregnancy outcomes after MVA [342]. MVAs during pregnancy caused 1.4 maternal fatalities per 100,000 pregnancies and a fetus/neonate mortality rate of least 3.7/100,000 pregnancies. The incidence of maternal major injury was 23/100,000 pregnancies [341].

During the MVA admission, the majority of women who had no adverse outcomes were admitted for 1 day and were discharged home undelivered. However, for those requiring delivery (≥20 weeks of gestation) during the MVA admission, the rate of pregnancy complications was significantly higher than women who did not have a MVA during pregnancy. Over a quarter had a placental abruption, and over half delivered <37 weeks of gestation [3]. The fetal/neonatal outcomes in the pregnancies that are delivered during the MVA admission, either spontaneously or in the context of a pregnancy complication such as a placental abruption, were poor. About a third ended in a perinatal death. Whereas some of these perinatal deaths would have been as a result of spontaneous preterm birth, the high rate of Cesarean section (61.1 %) in the group who delivered during the MVA admission suggests a significant number underwent emergency delivery for maternal or fetal indications (e.g., placental abruption or abnormal fetal heart rate pattern on cardiotocography). The low overall perinatal death rate of 1.4 %, during the admission immediately following a MVA in pregnancy ≥20 weeks, is reassuring [3]. What is also reassuring is that for women who did not require delivery during the MVA admission, the rate of pregnancy and delivery complications, as well as perinatal deaths, was the same as for women who had not had a MVA during pregnancy [3].

Elliott reported 39 cases of MVA trauma sustained in pregnancy [142]. Eight women died and each had multiple injuries. The primary cause of death was uncontrollable hemorrhage, and the author suggested that the increased vascularity associated with pregnancy accounted for the large number of deaths due to hemorrhage. In one study from Saudi Arabia pregnancy loss was significantly greater in older, non-urban, employed women and in women with family income >6,000 Saudi riyals (>1,600 US$). It appears as new prognostic factor and higher family income could be a proxy for the presence of high-powered, luxury cars, which may encourage fast driving [343].

Table 10.10 Types of injuries, by women hospitalized for a motor vehicle accident in Washington State, 1989–2001 [29]

Injury classification	Nonsevere injury (%)	Severe injury (%)
Fractures, dislocations, sprains	53.4	81.0
Intracranial injuries	9.7	25.0
Internal injury of chest	0	26.2
Internal injury of abdomen	2.9	20.2
Internal injury of pelvis	1.0	2.4
Open wound	17.5	41.7
Blood vessel injury	0.3	3.6
Superficial, contusion, crushing injury	53.4	26.2
Nerve and spinal cord injuries	0.3	1.2

Seat Belt Use

Studies conducted in the period 1989–2001, in the State of Washington (Table 10.10), have shown that pregnant women (nonsevere, $n = 309$; severe, $n = 84$) who were not tied with a seat belt have three times higher possibility of infant death and it is two times more likely to have complications during pregnancy than women who were tied at the time of accident [29].

Airbag Use

By analyzing the available research (Table 10.11), it is obvious that activation of the airbag during traffic accidents caused higher percentage of preterm childbirth and fetal mortality. These results indicate that the airbag negatively affects pregnant women during traffic accidents, but because of the large differences in the number of pregnant women (three times more when an airbag was not activated than it was), which were included by research, the possibility of certain deviation is included which reduces differences in the impact of airbag to pregnant women. It is possible to

Table 10.11 Obstetrics and Gynecology, Washington State (2002–2005): maternal and perinatal outcomes associated with airbag deployment among pregnant women in a motor vehicle accident [344]

	Airbag (%)	No airbag (%)
Maternal outcome		
Preterm labor	15.7	10.3
Placental abruption	2.0	1.6
Cesarean delivery	31.9	21.6
Cesarean delivery	26.8	24.1
Perinatal outcome		
Gestational age <37 week	11.1	10.0
Birth weight <2,500 g	8.7	8.2
Small for gestational age	11.6	9.8
Meconium at delivery	6.5	5.7
Fetal distress	5.6	6.0
Respiratory distress	2.5	1.6
Fetal death	1.0	0.3

conclude that the airbag has no negative impact on pregnant women during traffic accidents. It should be noted that, in this analysis, there was no available data on how many of the pregnant women involved in traffic accidents were tied with the safety belt. For vehicles that have airbags (mainly the front seats), in order to absorb the shock of activating the airbag in the body of pregnant women, the seat should be set back as much as possible, preferably a seat can be partially lowered.

Pelvic Trauma

Pelvic fractures can be particularly difficult to manage and life threatening to the mother and the fetus and are the most common injury resulting in fetal death with rate as high as 25–35 % [199, 340]. Mortality rates of women who sustained pelvic trauma in pregnancy were not affected by the fracture classification (simple vs. complex), the fracture type (acetabular vs. pelvic), the trimester of pregnancy, or the era studied by the review of literature [199, 200].

10.2.8.3 Repeated Blunt Abdominal Trauma

The rate of emergency room visit for blunt abdominal trauma was 5.4/1,000 deliveries encompassing 270 pregnant women with one or more noncatastrophic abdominal trauma during the second and third trimesters due to traffic accidents, falls, and assaults. There is only one study with an analysis of repeated blunt abdominal trauma with only 1.9 % (5/270) of women that sustained more than one blunt but direct blow to the abdomen due to falls during the second and third trimesters [345]. The time between the events ranged 1–4 weeks. The median hospitalization time per admission was 2 days, while all five patients together stayed in the hospital for 27 days in total during pregnancy. Extension to more than 24 h surveillance was exclusively due to preterm uterine contractions after the incident. Preterm contractions were noted in 60 % (3/5) of patients and one of which delivered at 34 weeks. Repeated blunt abdominal trauma occurs rarely in gestation. No premature rupture of membranes, pregnancy and does not warrant clinical management vaginal bleeding, placental abruption, intrauterine growth different from that for single-event cases. Restriction or antepartum death was encountered. The time between the last trauma and the delivery ranged 2–10 weeks. All patients delivered spontaneously. One patient, an epileptic woman, suffered from an increase of partial seizures with disturbances of motor function. Lack of compliance with the prescribed antiepileptic drug regimen could not be ruled out contributing to the rationale for the four extended hospital stays of that patient following the seizures. The Kleihauer-Betke test was positive in that patient only after multiple trauma events and negative in the rest of the patients including patient who delivered preterm after two trauma events 1 week apart.

Repeated blunt abdominal trauma is rare but could induce preterm uterine contractions and labor. Delayed severe complications such as placental abruption have been reported as rather infrequent after noncatastrophic abdominal trauma due to fall [41, 124] and did not appear to be a more prominent issue after a second such event with a time lag of 1 week or more as in these series of five cases [345]. The Kleihauer-Betke test was not useful as a predictor of early or delayed complications after repeated blunt abdominal trauma but should be performed in all D-negative trauma patients to determine the appropriate dosage of D-immunoglobulin to be

administered (300 mg/30 ml fetal blood transfused). After a visit, careful evaluation following repeated abdominal trauma and costly routine hospitalization for 24 h or more appears to be dispensable as in single-event cases [41]. Patients without premature uterine contractions or abdominal tenderness and with normal findings in the clinical evaluation, in the screening ultrasound, and in the continuous 4 h nonstress test may safely be sent home along with instructions for a proper follow-up in the outpatient clinic.

10.3 Penetrating Trauma

10.3.1 Incidence

Of all abdominal traumas in pregnancy, penetrating trauma is present in 9–16 % [346, 347] with predominantly gunshot wound in excess of 70 % of cases [347] and stab wounds around 20 %. The incidence of maternal visceral injury during penetrating injuries is 19–38 % in five series [348]. Penetrating trauma in pregnancy, generally due to gunshot or stabbing, has a different injury pattern to blunt trauma. The size of the uterus in pregnancy makes it the most likely organ to be injured, followed by the fetus and placenta. The gravid uterus may act to protect the abdominal viscera – only 18 % of women with gunshots sustain visceral injury [349]. Buschbaum explains this on the basis that the uterine muscle acts as a buffer to absorb missile energy and so prevent injury to the viscera beyond the uterus [350]. Although the gravid uterus protects other viscera, stabbings into the upper abdomen can cause serious injury, especially to compressed loops of bowel or to the overlying diaphragm. The latter is particularly dangerous in pregnancy if unrecognized, because of the possibility of subsequent bowel strangulation, which has much higher mortality rates in pregnancy (25–60 %) than in the nonpregnant patient (16–20 %) [243].

10.3.1.1 Gunshot Wounds to Uterus

The first report of a gunshot wound to the uterus is from the 1600s by Ambrose Pare and the first recorded case of gunshot wound of the pregnant uterus appeared in 1845 [351]. A subsequent review, 10 years later, uncovered a total of 45 reports since 1845 [352]. In 1968, there were 16 additional cases, for a total of 61 in the world literature [249], and several more during the last several decades [353, 354].

10.3.1.2 Stab Wounds to the Uterus

Reported instances of uterine stab wounds during pregnancy are even rarer. There are 4 reports up to 1961 by Guadagnini (1930), Badia and Charlton (1940), Wright et al. (1954), and Bochner (1961) [355–357] (Table 10.12).

10.3.2 Clinical Presentation

Clinical presentation depends on the number, extension, and type of organs involved. During examination entrance and exit wound (if exist) should be noted (Fig. 10.22). These can predict the bullet path and possible intra-abdominal injuries. If the uterus is damaged, continued or intermittent vaginal bleeding can be found [359]. Traumatic anhydramnios may be caused by a leak due to rupture of membranes with vaginal drainage or into the peritoneal cavity with penetrating wounds of the uterus. The latter can be strongly suspected with the presence of FF in the abdomen and pelvis.

Table 10.12 Data of reported cases of stab wounds of the pregnant uterus [357]

Author	Year	Pregnancy (months)	Time before delivery	Mode of delivery	Fetal weight (g)	Fetal outcome
Guadagnini	1930	8 ½	Several hours	Spontaneous vaginal	Unknown	Stillborn
Badia and Charlton [355]	1940	7	Term	Spontaneous vaginal	2,280	Live
Wright et al. [356]	1954	4 ½	Term	Spontaneous vaginal	2,810	Live
Bochner [357]	1961	7	38 days	Induced vaginal	900	Stillborn

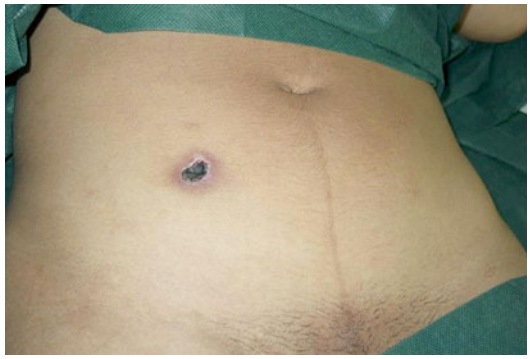

Fig. 10.22 Maternal entry gunshot wound healing [358]

10.3.3 Diagnosis

10.3.3.1 Laboratory Findings

After trauma occurs in a pregnant woman, complete blood count, blood type, and Rh status should be determined. Additional blood tests may be indicated in patients with more severe injuries.

Previously the Kleihauer-Betke test was used to determine whether fetal blood has entered the maternal circulation (fetomaternal transfusion). Fetal red blood cells containing fetal hemoglobin are identified by erythrosine staining; maternal red blood cells remain unstained (ghost cells). The Kleihauer-Betke test can be helpful in Rh- mothers to roughly quantify the volume of maternal-fetal hemorrhage. All Rh- patients with a positive test should be treated with Rh- immune globulin (300 μg initially and a positive test should be repeated in 24–48 h to investigate continuing fetomaternal hemorrhage). In Rh- pregnant women, administration of Rho(D) immune globulin (Rho-GAM) is unnecessary after insignificant superficial injury confined to an extremity. After any other trauma, the immune globulin should be administered within 72 h to all Rh- women, including those who are at less than 12 weeks of gestation and those who have minimal injuries [47]. One dose (300 μg) of the immune globulin is sufficient in 90 % of cases of FMH, because most FMH are less than 30 ml of blood [47]. Additional dose of 300 μg for each 30 ml of estimated fetomaternal hemorrhage is administered to reduce the risk of isoimmunization. Therefore, Kleihauer-Betke test is unnecessary [41, 47, 53, 360], unless a FMH needs to be quantified for accurate dosing of the immune globulin [10, 47]. A Kleihauer-Betke test is not predictive of fetal outcome [10, 41, 47, 53, 118].

Table 10.13 Radiation exposure for the unshielded uterus in various imaging studies

Imaging study	Uterine radiation dose (rad)
Plain film radiography	
Abdomen (AP)	0.133–0.92
Abdomen (PA)	0.064–0.33
Cervical spine	Undetectable
Chest (AP)	0.0003–0.0043
Chest (PA)	<0.001
Femur (AP)	0.0016–0.012
Hip (AP)	0.01–0.21
Pelvis (AP)	0.142–2.2 (mean 0.2)
Full spine (AP)	0.154–0.527
Lumbar spine (AP)	0.031–4.0
Thoracic spine (AP)	<0.001
Computed tomography	
Upper abdomen	3.0–3.5
Entire abdomen	2.8–4.6
Head	<0.05
Pelvis	1.95–5.0
Thorax	0.01–0.59

In urban medical centers, 13 % of pregnant patients admitted for trauma have detectable levels of alcohol, and 12 % have positive toxicology screening results [57]. Therefore, alcohol levels and toxicology should be obtained during diagnostic workup.

10.3.3.2 Radiography

Fetal Radiation Exposure

Patients and physicians commonly are concerned about fetal exposure to radiation, but adverse effects are unlikely at less than 5–10 radiation-absorbed doses (rads) [47, 236, 361, 362]. Less than 1 % of trauma patients are exposed to more than 3 rads (Table 10.13) [39, 47, 360, 362, 363]. However, the risk to the fetus of a 1 rad (1,000 mrad) exposure, approximately 0.003 %, is >1,000 times smaller than the spontaneous risks of malformations, abortions, or genetic

disease. Intrauterine exposure to 10 rad does not appear to cause a significant increase in congenital malformations, intrauterine growth retardation, or miscarriage but is associated with a small increase in the number of childhood cancers. Poor growth, mental retardation, central nervous system defects, and microcephaly are the most common adverse events associated with extremely large doses of fetal radiation [236, 361]. The relative risk (RR) of childhood cancers is greatest when a fetus is exposed to radiation in the first trimester (RR 3.19) and is especially high when exposure occurs before 8 weeks of gestation (RR 4.60) [360]. In a study of 19,889 children exposed to radiation in utero and 35,753 children without such exposure, radiation exposure was not found to be linked to childhood cancer [364]. In another study of 39,166 children with in utero radiation exposure, a lower rate of leukemia was found among the exposed children than in the age-matched general population [365]. When the results of these and four other studies were combined, the overall RR of in utero radiation was not statistically different from that of the general population [360]. After 15 weeks of gestation, fetuses are unlikely to be affected by radiation [360, 361]. Fetal doses from identical procedures vary among pregnant women and are lower in obese women [366].

Use of Intravenous Iodinated Contrast

Intravenous iodinated contrast crosses the placenta and is therefore classified as a US Food and Drug Administration category B drug. Its known risk is free iodine uptake by the fetal thyroid gland early in pregnancy, with the potential risk of inducing a hypothyroid state. Animal studies with intravenous iodinated contrast have shown no fetal risk, but no controlled studies on pregnant women have been performed and theoretic risks remain [367].

Roentgenogram

Roentgenogram of the abdomen can show pneumoperitoneum if the shallow viscera are injured through visceral wall. Also bullet or fragments of the bullet (Figs. 10.23 and 10.24) can be found.

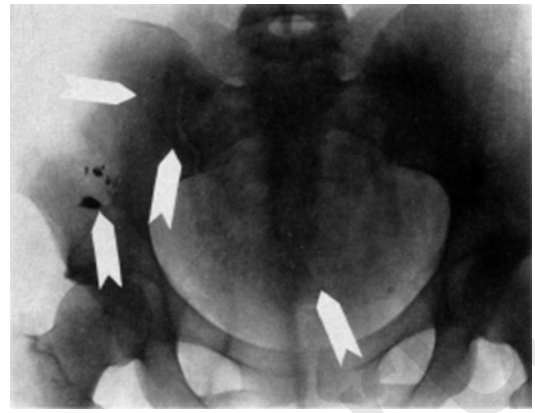

Fig. 10.23 A small fetus lying transversely across the pelvis and metallic fragments adjacent to the right iliac bone [359]

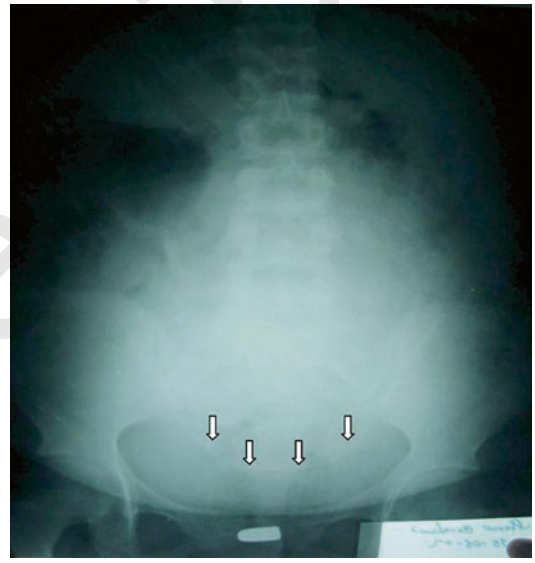

Fig. 10.24 Bullet inside the uterine cavity and the fetal head in vertex position [358]

10.3.3.3 Ultrasonography

Maternal Status

Ultrasonography misses 50–80 % of placental abruptions [38, 118, 237, 368], but rapidly and safely determines fetal heart tone, placental location, gestational age, and amniotic fluid index [41, 313]. Ultrasound examination is particularly helpful with maternal tachycardia, when the fetal and maternal heart rates may be difficult to distinguish with Doppler. Based on limited data,

most obstetric ultrasonography results that are obtained after trauma are normal [39, 41, 53, 118, 215]. Few fetuses survive when ultrasonography detects evidence of fetal trauma (Fig. 10.25a) [39, 41, 53, 118, 215]. The benefit of a biophysical profile after trauma is unknown [215]. The accuracy of ultrasonography greatly depends on operator experience and maternal body habitus. Maternal pulsation can mimic fetal bradycardia or cause fetal movement, leading to unnecessary emergency deliveries in cases of fetal demise. Ultrasonography commonly is used to reassure the mother after noncatastrophic trauma, but this practice has not been studied.

Fetal Status

Doppler ow measurements of the umbilical artery may reveal high placental resistance associated with intrauterine growth retardation [369]. Oligo- or anhydramnios in this setting would raise suspicions of a diagnosis of placental insufficiency. All fetal organs should be examined and evaluated (Fig. 10.26).

10.3.3.4 Abdominal CT Scan

It is used when the ultrasound examination is not diagnostic and unequivocal. The risk and benefits should be weighed on every pregnant patient. Sometimes abdominal ultrasound shows free intraperitoneal uid without obvious cause, and if the primary cause of the FF dictates the indication for the operation, CT is performed (Fig. 10.25b, c).

10.3.3.5 Peritoneal Lavage

If needed, open diagnostic peritoneal lavage, in which the peritoneum is visualized directly, or fistulogram is safe and accurate in pregnant women and was previously used more in the conservative management of stable lower abdominal penetrating injury during pregnancy before the era of modern imaging techniques [7, 37, 47, 133, 371].

The complete diagnostic algorithm is presented on Fig. 10.27.

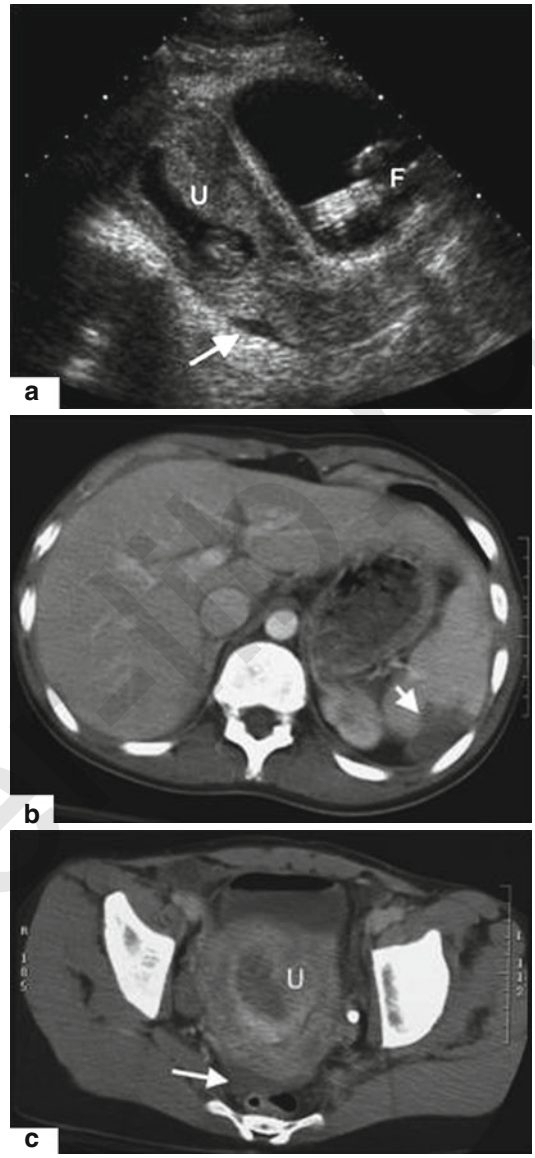

Fig. 10.25 Images in a 20-year-old woman in the first trimester of pregnancy who was involved in a high-speed motor vehicle accident that resulted in splenic laceration that was managed without intervention. (**a**) Longitudinal US image of pelvis shows free uid (*arrow*) in cul-de-sac and an intrauterine (*U*) pregnancy. A Foley catheter (*F*) is present within the bladder. (**b**) Transverse helical CT scan of abdomen shows laceration (*arrow*) in posterior aspect of spleen but no substantial free uid. (**c**) Transverse CT scan of pelvis shows an enlarged uterus (*U*) with gestational sac and free uid (*arrow*) in the cul-de-sac [279]

10.3.4 Treatment

10.3.4.1 General Principles

Liberal administration of oxygen and uids when the bicarbonate level is low improves tissue perfusion and fetal oxygenation [37, 40].

Tetanus Prophylaxis

Tetanus is a rare, potentially fatal disease caused by the anaerobe *Clostridium tetani*. Wounds that are crushed, devitalized, or contaminated with dirt or rust are considered to be tetanus prone. Open fractures, punctures, and abscesses are also associated, but severity of the wound does not determine the risk. All wounds should be cleaned and debrided if necessary. Tetanus toxoid should be given if the last booster was more than 10 years prior. If a vaccination history is unknown, tetanus toxoid can be considered when convenient. If the last immunization was >10 years ago, then tetanus immune globulin should be given. The tetanus toxoid dose is 5 IU i.m., while tetanus immune globulin prophylaxis dosing is 250 or 500 units i.m. (in opposite extremity to tetanus toxoid) [47].

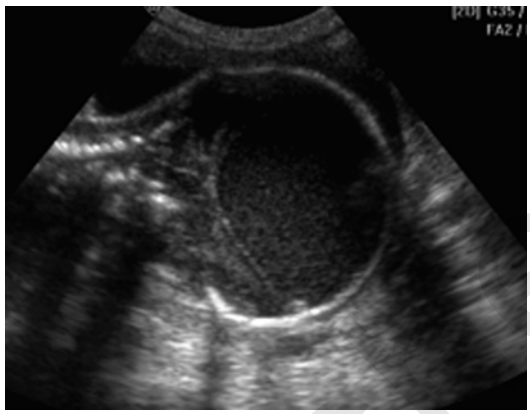

Fig. 10.26 Ultrasonographic finding demonstration of fetal intracranial hemorrhage after maternal physical abuse [370]

10.3.4.2 Gunshot Wounds

Proposals for management of such patients vary widely. In 1941, Bost indicated that the uterus should be emptied by Cesarean section, at almost any stage of pregnancy [372]. Eckerling and Teaff in 1950 stated categorically that the injured gravid uterus must be emptied by Cesarean section, irrespective of the viability of the fetus, and particularly if the injured woman was in labor [373]. Their rationale was to avert the possibility of a ruptured uterus with labor and also to spare the injured patients of the additional heavy physical strain of labor and delivery, during the early postoperative period.

Conservative Treatment

Traditionally the presence of penetrating abdominal trauma necessitates surgical exploration. Mandatory explorative laparotomy for all gunshot wounds to the abdomen has been challenged first by Shaftan [374]. Accumulating data suggests

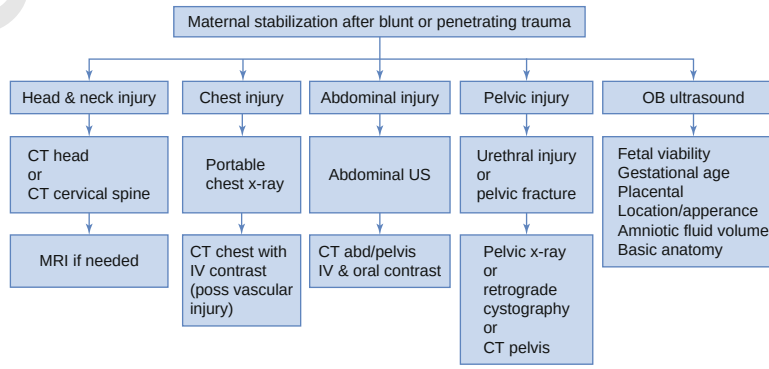

Fig. 10.27 Diagnostic imaging options for maternal blunt and penetrating trauma patients [311]

a more selective approach [133, 353, 371, 375] but high-velocity gunshot wounds to the abdomen universally require exploratory laparotomy, given the high likelihood of intra-abdominal injury to the mother.

A distinction is made between upper and lower abdominal penetrating wounds. In general, explorative laparotomy for all upper abdominal wounds is advocated. A major reason is that compression of bowel into the upper abdomen increases the likelihood of visceral injury. Another reason is that diaphragmatic lacerations must be ruled out [371]. Awwad et al. [353] suggested conservative management of anterior abdominal entry wounds below the level of the uterine fundus. Iliya et al. [376] found a low incidence of life-threatening injury in pregnant patients and proposed the following criteria for conservative management:

- Fetus is dead.
- Entrance wound is below the level of the fundus.
- Bullet is radiographically shown to be in the uterus.
- Maternal evaluation is reassuring.
- Hematuria or proctorrhagia must be absent.

Medications

Regular contractions may signify placental abruption. Administration of tocolytics could compromise the fetus by delaying the diagnosis of placental abruption and consequently delaying delivery [Evidence level B] [118, 215].

Surgical Treatment

Kobak and Hurwitz recommended that all such patients should be subjected to immediate laparotomy as in the case of any patient with a gunshot wound of the abdomen [377]. The subsequent treatment depends upon several factors. If the fetus is dead or previable and the uterine damage is not extensive, the uterus may be sutured and a vaginal delivery allowed. The uterus is capable of a satisfactory, normal labor if the wound is small and well repaired, without danger of rupturing. Extensive uterine damage would be an indication for Cesarean section or possibly hysterectomy. Bowel perforation at that time did not carry higher mortality because all patients underwent laparotomy and all bowel lesions were repaired.

Obstetric Management

Carugno et al. noted that labor, whether spontaneous or induced, was almost always well tolerated by wounded patients as also confirmed by others [358]. On the other hand, if the fetus is viable (i.e., ≥28 weeks or ≥1,000 g) and alive, immediate abdominal delivery is the treatment of choice [377–379]. Goff and Muntz favor prompt Cesarean section delivery of viable fetuses that survive the initial injury after maternal stabilization, with the aim of reducing the risk of delayed intrauterine death from occult trauma to the fetus or placental bed [380]. Browns et al. suggest that Cesarean section is absolutely indicated if the fetus is alive and near term, if the diagnosis of placenta hemorrhage is made or suspected, and if maternal injury necessitates laparotomy [381].

If there is an indication for Cesarean section, the baby should also be examined and all injuries noted. Figure 10.28 shows the newborn with superficial wound 8 cm long over his left scapula.

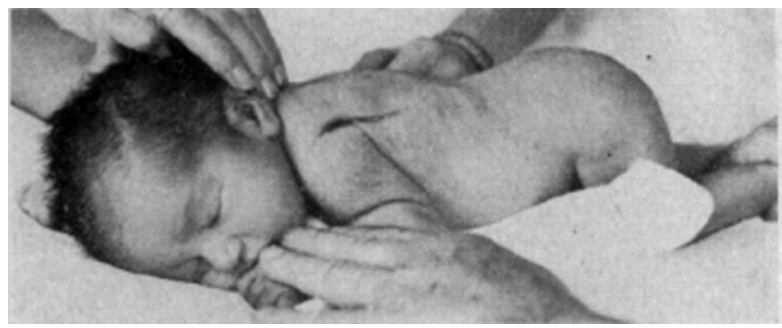

Fig. 10.28 Photograph of newborn infant showing superficial wound over the left scapula [359]

The extremities of the wound were healed, but its central portion was open for a distance of about 2.5 cm and was filled with healthy granulation tissue. There was no evidence of skeletal injury. Figure 10.29 shows similar case with the superficial wound over scapula due to gunshot wound to the pregnant abdomen.

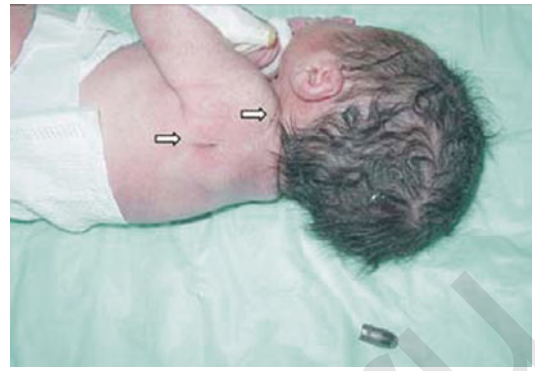

Fig. 10.29 Superficial wounds on baby's left scapular area and left shoulder (*arrows*) [358]

10.3.4.3 Stab Wounds

Conservative Management

Most stab wounds without maternal hard signs, such as hypotension, evisceration, hemorrhage, or peritonitis, can be managed nonoperatively (Fig. 10.30). Local wound exploration

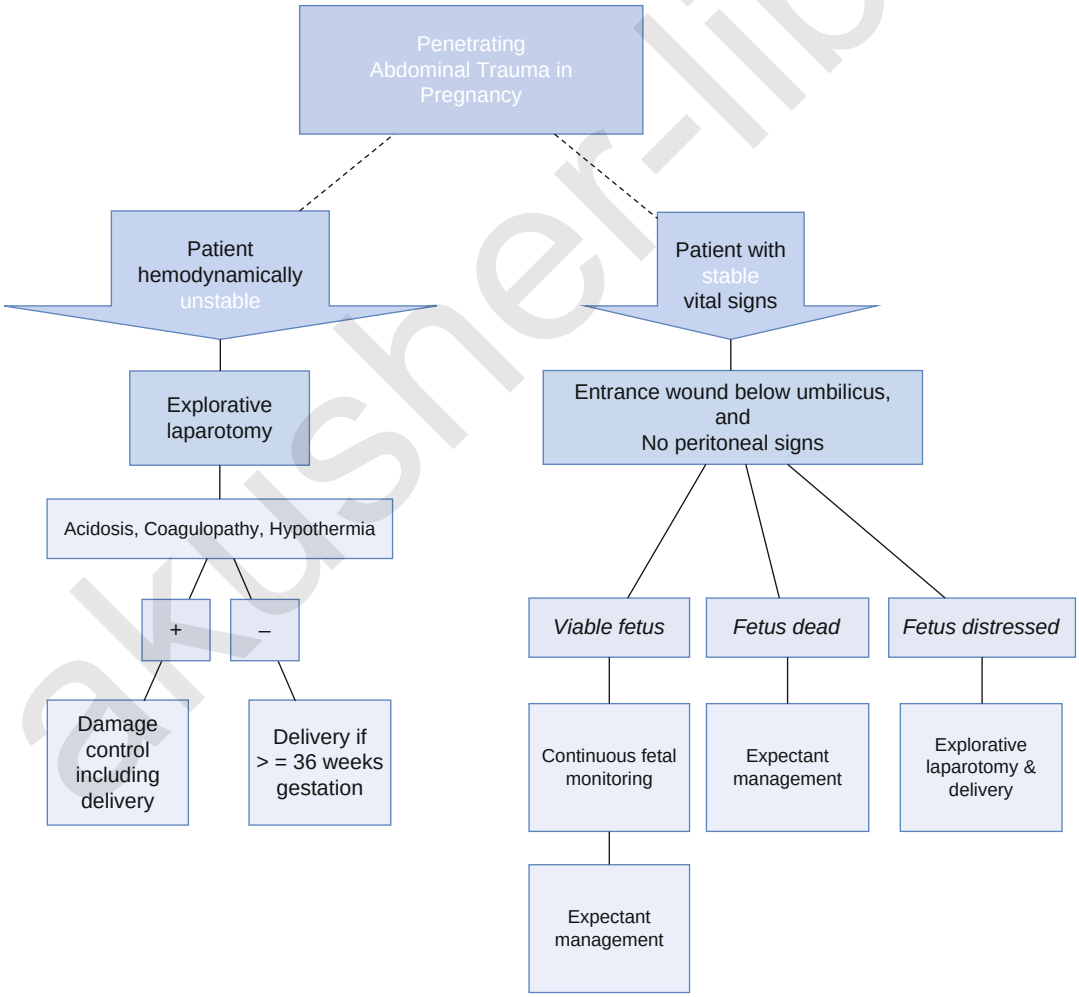

Fig. 10.30 Treatment algorithm for *penetrating* abdominal trauma in pregnancy [382]

and diagnostic laparoscopy are other options to diagnose intra-abdominal injury resulting from a low-velocity stab wound.

Obstetric Management

Fetal trauma after stabbing injuries to the uterine cavity occurred in 93 % (13/14) of such cases reported by Sakala and Kort, and 47 % (9/19) of fetuses died after stabbings to the maternal abdomen [371]. Kaloo et al. therefore recommend that third trimester fetuses subjected to stabbing injuries should therefore be delivered promptly [383].

Brief observation (4–6 h external fetal monitoring):

- Maternal trauma is minor.
- Mother is hemodynamically stable.
- Primary evaluation negative.
- FAST-US negative for intra-abdominal uid.
- No obstetric complaints.
- <6 contractions per hour.
- Class I FHR pattern.
- Normal examination and laboratory data.

Prolonged observation (24–48 h EFM):

- Multiple or severe maternal injuries.
- Mother hemodynamically unstable.
- Obstetric symptoms are present (bleeding, ROM).
- >6 contractions per hour during first 4–6 h.
- Abnormal FHR pattern or deceleration on CTG.
- Abnormal examination (e.g., fundal tenderness).
- Abnormal laboratory data (e.g., +KB, abnormal fibrinogen).

Surgical Treatment

Treatment algorithm for penetrating abdominal trauma is presented on Fig. 10.30. Surgical exploration for an abdominal penetrating wound is not an absolute indication for the removal of the fetus from an uninjured uterus. The performance of a Cesarean section significantly increases blood loss and operative time. The risk of precipitating labor after explorative laparotomy is negligible, if proper care is taken [375]. Emptying an uninjured uterus is justified only if the uterine size limits either adequate abdominal exploration or repair of extrauterine injuries or in the presence of non-reassuring fetal status. It should be stressed that Cesarean sections may have beneficial effects on maternal resuscitation due to elimination of the low-resistance uteroplacental circulation [7, 54]. In patients with fetal death, it is advisable to afford delivery by induction of labor rather than uterine evacuation at the time of laparotomy [133, 371, 375]. In the rare occurrence of patients who present in the perimortem state with a viable fetus, Cesarean section should be considered (see next section "Emergency cesarean section").

10.3.4.4 Emergency Cesarean Section

Emergency Cesarean section performed at >25 weeks of gestation for specific indications following trauma is associated with 45 % fetal survival and 72 % maternal survival [234].

Cardiac Arrest and Perimortem Cesarean Section

The difficulty in performing cardiopulmonary resuscitation in pregnant women in the third trimester is that the uterus is in the supine position and occludes the vena cava. Cardiopulmonary resuscitation is described in detail in Sect. 10.1.6. Optimization of cardiac output and perfusion of the uterus via left thoracotomy and open cardiac massage along with emergency Cesarean section should be considered. By the time the mother has suffered a cardiac arrest from trauma, the fetus has already experienced severe hypoxia. Cesarean delivery may be indicated if it can be performed within 5–15 min after loss of pulse in the mother perhaps even later, if fetal vital signs persist. Cardiopulmonary resuscitation must be continued until delivery is accomplished. Delivery has also been reported to allow

successful maternal resuscitation. The decision to proceed with postmortem delivery must be made quickly by the traumatologist and obstetrician; hemostasis and antisepsis become secondary issues. Neonatologists must be available.

Perimortem Cesarean section rarely is required [234] but is an ethically difficult decision for emergency medicine resuscitation teams. The procedure covers emergency delivery during the ongoing maternal cardiopulmonary resuscitation where the mother has no sign of recovery afterward with or without infant survival [384].

Historically, the first data about perimortem Cesarean section was the Roman decree (*Lex Cesare*, or law of Caesar). The purpose of this ancient law was based on religious rituals rather than attempts for survival of either the newborn or mother. According to the law of Caesar, the unborn infants should be separated from their mothers' bodies after death. Some infants did survive. It was reported that several mythological and ancient historical figures had been born in this fashion, including the Greek physician Asklepios [125]. The first modern approach to perimortem Cesarean deliveries was reported by Katz et al. in 1986 [312, 385]. Up to 2011 there were 38 case reports of perimortem Cesarean section published and the most common causes of maternal arrests included trauma, pulmonary embolism, cardiac causes, sepsis, and eclampsia [385, 386]. Perimortem Cesarean section is an extremely emotional and often futile exercise and should only be considered for gestations >24 week. If the mother has had cardiopulmonary resuscitation for >4–5 min, perimortem Cesarean section is unlikely to result in a viable normal infant. Therefore, although supporting data are limited, consideration should be given to performing emergency Cesarean delivery after 4 min of cardiopulmonary arrest, both to increase the chances of fetal survival and to aid effective maternal resuscitation (Fig. 10.31) [47, 312]. In cases of emergency center thoracotomy, recall that the aorta is often cross-clamped, further adding to the time of uterine hypoperfusion and decreasing the likelihood of a favorable outcome [25].

Perimortem Cesarean section must not be delayed for ultrasonography. Before making the abdominal incision, the surgeon must ensure that fundal height is several fingerbreadths above the umbilicus, ensuring adequate gestational age. The appropriate incision for a perimortem Cesarean section is from the xyphoid to the symphysis pubis through all layers of the abdominal wall and peritoneum. When the uterus is identified, a vertical uterine incision is made, and if the placenta is anterior, it should be incised as well. To deliver the infant, the gynecologist/surgeon opens the uterus, clamps and cuts the cord, and begins infant resuscitation. Efforts at maternal resuscitation should continue simultaneously, as there are reported cases of maternal survival after the delivery of the infant [387].

Before 23 weeks' gestational age, delivery of the fetus may not improve maternal venous return. Therefore, aggressive maternal resuscitation is the only indicated intervention [311]. Even a case of perimortem Cesarean section after 7 min of unsuccessful maternal cardiopulmonary resuscitation is published with the delivery of the newborn with Apgar 0. The newborn was intubated; ventilation and external chest compressions were started. After 5 min of neonatal cardiopulmonary resuscitation, cardiac activity was regained and improvement in skin color observed. There is no data about further newborn progress except that it was in neonatal intensive care unit with uncertain neurologic outcome [386].

Salvageable Infant

The most important finding is the definition of a subgroup of infants who are potentially salvageable. In this group of patients, defined by an estimated gestational age ≥26 weeks and the presence of fetal heart tones (FHTs), the survival rate was 75 %. Survival was independent of maternal distress but clearly related to the presence of fetal monitoring and early recognition of fetal distress. There were no survivors in fetuses having no FHTs. This supports the premise that fetal viability is directly related to the presence or absence of FHTs on admission. As such, the presence of FHTs is a simple, rapid, reproducible, and profoundly important marker of fetal viability. The recommendation is that the Doppler assessment of FHTs is a component of the primary

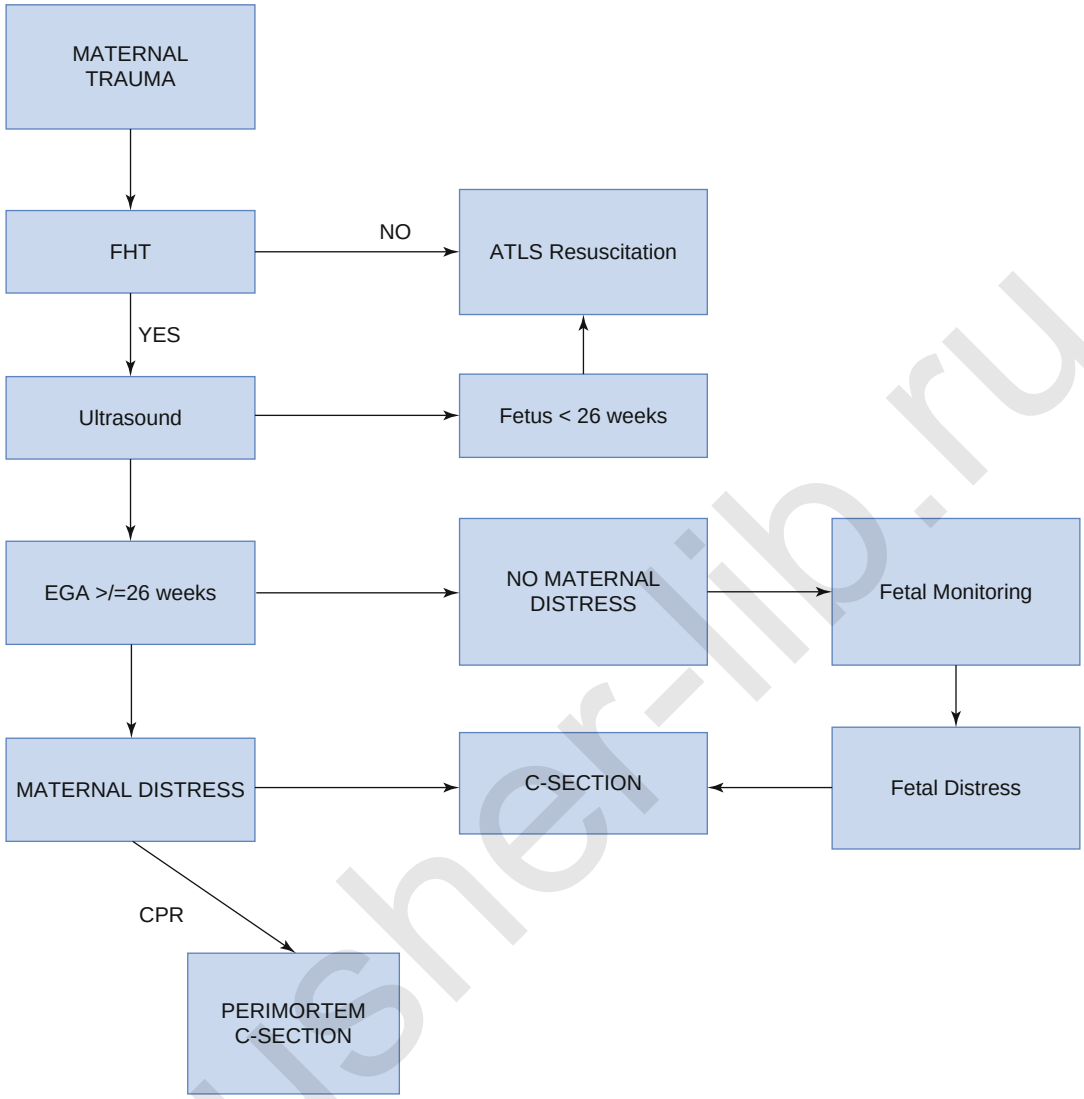

Fig. 10.31 Clinical algorithm for emergency Cesarean section and perimortem Cesarean section. The pregnant trauma patient is assessed for fetal heart tone (*FHT*) and estimated gestational age (*EGA*). If FHT is present and EGA is ≥26 weeks, fetal monitoring is required. Fetal or maternal distress mandates emergency Cesarean section. Perimortem Cesarean section is performed if cardiopulmonary resuscitation is in progress [234]

survey performed on trauma patients during the third trimester of pregnancy. This should be accomplished simultaneously with the assessment of maternal circulatory integrity during the ABCs of the trauma resuscitation [388]. If FHTs are absent, the pregnancy should be ignored and treatment directed solely at maternal survival.

Data from leading neonatal centers in the non-traumatic setting show that survival of infants born from 23 to 25 weeks' gestation increases with each additional week of gestation [389, 390]. However, the overall neonatal survival rate for infants born during this early gestational period remains less than 40 % [234]. Of those who survived, 6–40 % have moderate to serious disabilities and many have neurobehavioral dysfunction and poor spontaneous school performance [391].

As noted previously, high admission FHR values may be expected for patients arriving at the ED soon after the start of maternal hemorrhage. Furthermore, obstetric practice in the nontraumatic setting has documented baseline FHR to be less predictive of fetal stress than baseline variability and periodic change assessment of the FHR [392]. Lack of knowledge of baseline FHR prior to trauma and the wide variability (20/min) of FHR under normal physiological conditions [393] further degrade the predictive utility of admission FHRs.

Although it is ideal to inform the prospective parents regarding fetal outcome and the financial and emotional consequences of profound prematurity, this is not possible in the trauma setting where the patients are often critically ill or sedated, families are unavailable, and the decision-making process is obscure. Consequently, it is recommendation that fetal viability in the trauma patient should be defined at age 26 weeks. This recommendation changes the previous recommendations in the literature from 28 weeks [394], because 80 % of infants with an estimated gestational age of 26–28 weeks survived in series by Morris et al. [234]. This study also shows that even in the most profoundly injured mother, manifested by an ISS >25, fetal survival was 78 %. This same critically ill population had a maternal survival rate of only 44 %, illustrating the need for emergency Cesarean section at the first indication of fetal distress. Recognition of fetal distress is critical. In this study, fetal distress was defined as a FHR < 100, prolonged deceleration for more than 60 s, or recurrent late decelerations. Although maternal survival in the presence of a <16 was 100 %, fetal survival was only 73 % [234], supporting previously published reports that even minor maternal injury can result in death of the fetus [259]. Of more concern was the finding that 60 % of these infant deaths occurred in mothers with minor injury and delayed Cesarean sections in the presence of fetal distress. This may well represent delayed recognition of fetal distress or delayed Cesarean section in a misguided belief that the intrauterine environment is superior to delivery.

Table 10.14 Indications for emergent Cesarean section in gunshot wounds of the abdomen in pregnancy

Surgical
Pregnant uterus mechanically limits exploration or surgical repair
Fetal
Hemorrhage
Interference with fetal-maternal exchange
Infection

ACOG has published guidelines on performing Cesarean sections for mothers in extremis following medical disasters, i.e., amniotic uid embolism, cardiac arrest, etc. (www.acog.org). These could be extrapolated to similar physiological insults to a pregnant trauma patient. Fetal survival rates of 70 % have been reported for fetuses of at least 25 weeks of gestation who are delivered within 5 min of maternal death [312]. Incidentally, these authors revisited their 1986 recommendations in 2005 and documented 38 cases of perimortem Cesarean section with all fetuses surviving initially but 4 dying of complications from prematurity and anoxia [385]. All mothers survived except for one, who died of complications of her amniotic uid embolism.

Gunshot Wounds

Algorithm is somewhat different in gunshot wounds. While exploration is the management of choice in bullet wounds of the abdomen, Cesarean section is not mandatory and indications are listed in the Table 10.14 [395]:

Since infants have been born alive with soft tissue and visceral injuries, the hazards of prematurity must be weighed against the potential benefits of operation to the injured premature infant delivered by Cesarean section. When fetal weight approaches 2,500 g, these hazards are greatly diminished. Vaginal delivery, even in the immediate postoperative period, has been shown to have no deleterious effect on the mother [373, 377, 378].

Conservatism could be exercised in the management of the uterine wounds, since pregnancies have followed repair of extensive traumatic wounds [352, 373, 377].

10.3.5 Prognosis

10.3.5.1 Maternal Outcome

The maternal mortality rate from gunshot and stab injuries to the abdomen is less than that of nonpregnant women, due to the protective effect of the uterus [133, 353, 371, 375, 380]. The gravid uterus during late pregnancy acts to shield other abdominal viscera as well as to displace and compress the small bowel. The uterus also diminishes the velocity of a missile and thereby decreases its ability to penetrate other organs. The musculature of the pregnant uterus is relatively dense and most of the traumatic force is transmitted to the muscle. Moreover, the amniotic uid and the fetus also contribute to slowing the bullet. Hence, injury to other organs is relatively rare [375].

The mortality rate of abdominal gunshot wounds in general population is proportional to the number of organs injured [396–398]. Associated injury occurred in only 24 % [377], 27 % [352], and 38 % [399] of the victims in three series of gunshot wounds of the pregnant uterus. Maternal mortality rate is 7–10.5 % [347, 400]. Half of these maternal deaths were due to severe head injury, the result similar to other previous reports [15, 185, 337]. Six patients were admitted with evidence of shock resulting in 4 maternal and 4 fetal deaths (66.6 %) [400]. The penetrating trauma group had a longer hospital length of stay (7 ± 9 vs. 4 ± 8) as compared to the blunt trauma group [347].

Thirty-three cases of gunshot wounds of the pregnant uterus were reported by Kobak and Hurwitz during 1845–1954 [377]. There were three maternal deaths, all of which occurred before 1912. Fetal mortality was 55 % among those patients who were judged to have a viable fetus at the time of injury. There were 15 vaginal deliveries among the 33 cases reported, in all of which labor commenced within a few hours up to 17 days after the accident.

10.3.5.2 Fetal Outcome

Pregnancy loss was significantly greater in women in the second trimester of pregnancy compared to the first trimester. Some studies have reported that the second trimester represented the most vulnerable period for all types of fetal trauma because the gravid uterus ascends out of the bony pelvis in the cephalad direction to reach the level of the umbilicus by 24 weeks; here the gravid uterus may sustain direct traumatic injury. In the third trimester, the fetus is well protected by the amniotic uid [24, 343, 401]. However, in both gunshot and stab wounds, as pregnancy progresses, the fetus presents a larger target and is more likely to sustain injury [133, 353, 371, 375, 380]. Usually, the fetus has a worse prognosis than the mother, with an injury rate of 59–80 % and a perinatal mortality rate of 41–71 % [348, 402, 403]. The perinatal mortality for the years 1957–1967 was 71 % [399], unchanged from the period 1845 to 1964 [352]. This figure is considerably higher than the 59 % of infants who sustained intrauterine injury or damage to the cord and placenta in the series in the years after 1967 [399]. In the period 1845–1954, fetal mortality was 55 % among those patients who were judged to have a viable fetus at the time of injury [377]. In the same period the fetal mortality among those who had vaginal deliveries was 66 %; among those who had abdominal deliveries, it was 46 %.

According to some reports, fetal injuries are in range of 60–90 % and gunshot wounds commonly lead to fetal death, with a perinatal mortality of up to 70 % [133, 350, 375]. Fetal trauma after stabbing injuries to the uterine cavity occurred in 93 % (13/14) of such cases reported by Sakala and Kort with fetal mortality of 47 % [371]. Others found fetal mortality rate of 73 % after penetrating maternal abdominal trauma [347].

Maternal Injuries and the Risk of Birth Defects

Few studies have examined the association between maternal injuries and birth defects. A 1969 case-control study reported an increased incidence of birth defects among women who experienced “accidents” (not further defined) in the first trimester [404] and noted that defects of the central nervous system (CNS), in particular, appeared to be associated with experiencing an accident in early pregnancy. Limited data from more recent case-series studies also suggest that

maternal trauma may be associated with CNS damage in the fetus, especially hydrocephaly [152, 153, 405]. The results stratified by intention suggest that three of the associations observed when all injuries were considered, those for longitudinal limb deficiency, gastroschisis, and hypoplastic left heart syndrome, might be driven by intentionally in icted injuries [30]. The majority of the intentional injuries reported in *National Birth Defects Prevention Study* were the result of intimate partner abuse and these types of injuries could be more stressful for the mother. Associations have been observed between maternal stress during pregnancy and several birth defects, including conotruncal heart defects [151, 406], neural tube defects [151, 407, 408], and orofacial clefts [151, 407, 409]. Periconceptional injuries were associated with interrupted aortic arch type B, atrioventricular septal defect, pulmonary atresia, tricuspid atresia, hypoplastic left heart syndrome, anorectal atresia/stenosis, longitudinal limb deficiency, and gastroschisis. Associations with longitudinal limb deficiency, gastroschisis, and hypoplastic left heart syndrome were stronger for intentional injuries. This analysis was hypothesis generating, with many associations tested. Further research is warranted [30].

Although any maternal injury during pregnancy could be stressful for a woman, stress due to intimate partner violence could be both acute (during an attack) and chronic, from being in an abusive relationship. Intentional injuries are also related to many other factors that might cause or be related to other causes of birth defects. In an analysis of the *National Birth Defects Prevention Study* control mothers, we observed a higher prevalence of alcohol and cigarette use during pregnancy among women who reported an intentional injury [31]. Alcohol use and cigarette use during pregnancy are associated with increased risk for birth defects [410, 411].

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Miscellaneous Conditions 11

11.1 Small Bowel Perforation

Small bowel perforation is extremely rare during pregnancy. There are several causes, the most common being perforation due to intestinal endometriosis which is the disease found in the reproductive age group.

11.1.1 Intestinal Perforation Due to Intestinal Endometriosis

11.1.1.1 Introduction

Endometriosis is defined by the presence of endometrium outside the uterus and usually affects pelvic structures including the bowel. Intestinal involvement occurs in 3–37 % of patients with endometriosis [1] and may affect the ileum, appendix, sigmoid colon, and rectum [2]. The most common nongenital manifestation is in the rectosigmoid [3, 4]. The peritoneal implantation of endometrium by retrograde menstruation or the possible metaplasia of peritoneal cells is still the most accepted etiological theory of endometriosis [1]. Intestinal endometriosis may be found in every layer of the bowel wall, but it is most commonly found within the subserosa as superficial serosal implants [5, 6]. Under cyclical hormonal influences, these implants may proliferate and infiltrate the intestinal wall and cause a fibrotic reaction with formation of strictures and adhesions, which may lead to bowel obstruction and recurrent abdominal pain [2, 7]. On the other hand, transmural bowel wall involvement is not so common and the intestinal mucosa usually remains intact, and perforation of the affected intestinal tract is a very rare complication [3, 6].

11.1.1.2 Incidence

Up till now and including the present report, only 22 cases of intestinal perforation from endometriosis have been reported, and among these, 45.5 % (10/22) occurred in pregnancy (Table 11.1); of these ten patients, 20 % (2/10) presented postpartum. One of these postpartum presenting patients with cecal perforation had a past medical history of terminal ileal and cecal Crohn's disease diagnosed 9 years previously. The histology confirmed that

Table 11.1 Summary of cases of bowel perforation secondary to endometriosis related to pregnancy

Author	Year	Site of perforation	Duration of pregnancy
Haufler [8]	1931	Jejunal	6 months
Gini et al. [9]	1981	Appendix	35 weeks
Nakatani et al. [10]	1987	Appendix	26 weeks
Faucheron et al. [11]	2008	Appendix	
Beamish et al. [12]	2010	Cecum	Postpartum
Clement [13]	1977	Sigmoid	37 weeks
Rud [14]	1979	Sigmoid	
Floberg et al. [15]	1984	Sigmoid	Postpartum (41 weeks)
Schweitzer et al. [2]	2006	Sigmoid	Term pregnancy
Pisanu et al. [16]	2010	Rectum	33 weeks

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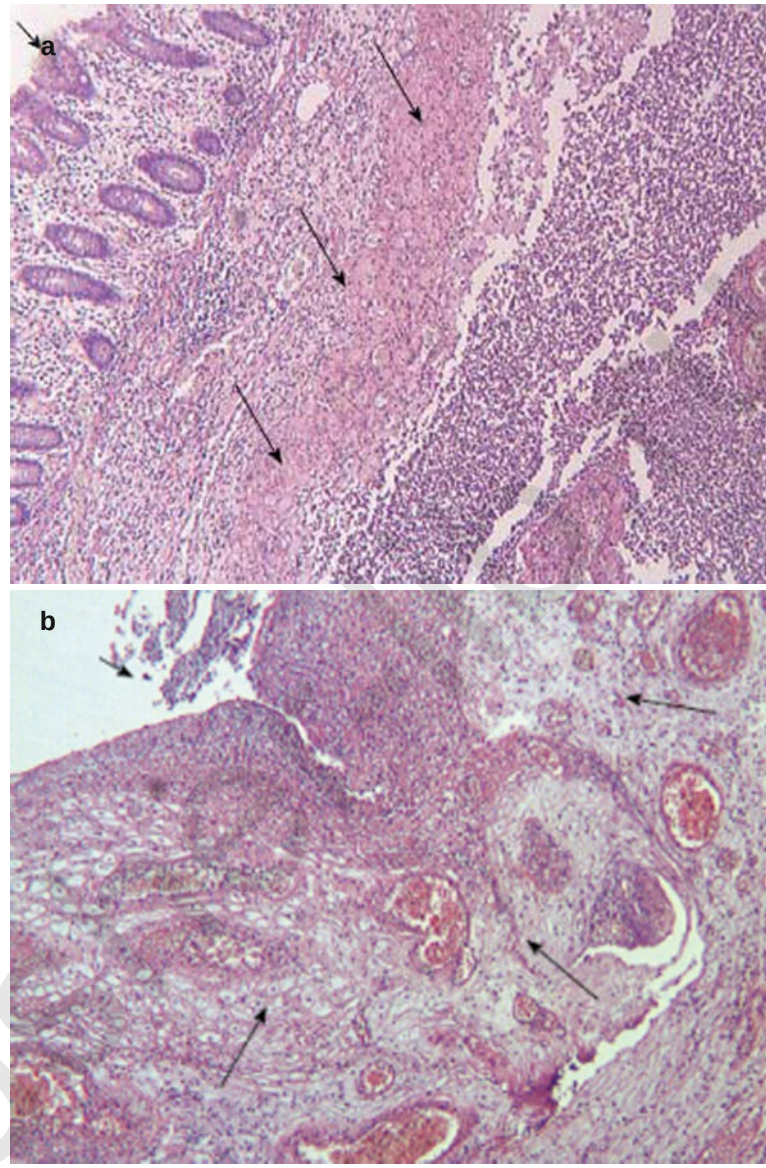

Fig. 11.1 The rectal wall. (**a**) Decidualization of the rectal wall (*long arrows*); mucosa side of the rectal wall (*short arrow*) (HE, ×40); (**b**) Decidualized endometriosis around the rectal perforation (*long arrows*); rectal perforation with necrosis at the peritoneal side of the rectal wall (*short arrow*) (HE, ×100) [16]

cecal perforation was due to decasualized endometriosis. There was no evidence of Crohn's disease [12]. Sigmoid colon is the most common site of perforation from endometriosis in general population and accounted for 55 % (12/22) published cases [12, 16].

Intestinal endometriosis typically takes the form of asymptomatic serosal implants that occasionally result in intestinal obstruction with recurrent abdominal pain [5]. Transmural involvement is not as common, and spontaneous perforation of intestinal endometriosis is a rare complication that occurred in pregnancy in almost 50 % of published cases (Fig. 11.1) [2, 3, 5].

11.1.1.3 Pathophysiology

In the third trimester and postpartum, endometrial lesions tend to contract as observed by McArthur and Ulfelder, the mechanism of which remains obscure. This contraction in an area already weakened by endometrial stromal infiltration can cause perforation as suggested by both McArthur

and Ulfelder in 1965 [17] and Garg et al. in 2009 [5]. In those patients with perforation, the entire intestinal wall is replaced by endometriotic tissue. In pregnancy, under the effect of progesterone, the area of ectopic endometrium becomes decidualized with a progressive reduction in size [11, 17]. Actually, the reduction in size of a transmural endometriotic nodule may lead to perforation, by weakening of the intestinal wall [5], particularly in the third trimester, which is the time of perforation in most reported cases [5, 16, 17]. Moreover, decidualization causes a severe inflammatory response with an increased number of natural killer cells and decidual changes, which are responsible for a higher risk of perforation [11, 18]. Additionally perforation was also facilitated by the progressive traction of the enlarged uterus on the strictly adherent sigmoid colon and, consequently, on the decidualized and weakened area of the anterior rectal wall [16]. Moreover, the absence of endometriotic foci in the cul-de-sac at final laparoscopy made rectal perforation unpredictable. Although endometriosis improves during pregnancy, the current report shows the potential occurrence of serious and unexpected complications of the disease.

11.1.1.4 Clinical Presentation

If the perforation is present, then symptoms and signs of acute abdomen are present. Before the occurrence of perforation, abdominal pain could be cyclical as is present in endometriosis. Enlargement of endometriotic nodules could aggravate constipation or initiate abdominal distension due to impaired bowel peristalsis.

11.1.1.5 Differential Diagnosis

Both the rareness of the perforation and the symptoms that are suggestive of pyelonephritis or diverticulitis may be misleading and could delay the diagnosis especially before the perforation ensue.

11.1.1.6 Diagnosis

If acute abdomen is found, clinically standard laboratory findings and plain abdominal X-rays are made. Pneumoperitoneum is found when the bowel perforation is present.

11.1.1.7 Therapy

The appropriate management of these patients may be challenging, and a good outcome is absolutely dependent on a multidisciplinary approach. The best approach is to resect, en bloc, endometriosis and perforated bowel. If the perforation is on the small bowel, anastomosis could be made (or ileostomy if prolonged peritonitis is present), and if sigmoid colon perforates, then the Hartmann's operation is the procedure of choice.

11.1.2 Spontaneous Small Bowel Perforation

Morton and Hubbard in 1959 reported seven cases of nontraumatic rupture of the small bowel during pregnancy with 85 % mortality [19].

11.2 Perforation of the Colon and Rectum

11.2.1 Colorectal Carcinoma in Pregnancy

Due to the extreme rarity of perforated colorectal carcinomas in pregnancy, an overview of colorectal carcinoma in general during pregnancy is presented. Few cases of perforated colorectal carcinoma are additionally discussed.

11.2.1.1 History

Many reports of rectal and colonic carcinoma occurring in pregnancy appear in the literature, the first being in 1835, and Cruveilhier (Fig. 11.2) reported the first case of rectal carcinoma in pregnancy in 1842.

These early reports were concerned mainly with the obstetric problems of delivering the fetus in the presence of a pelvic tumor. Robert Greenhalgh (St. Bartholomew's Hospital; consulting physician to the Samaritan Hospital for Women and City of London Lying In Hospital) in 1866 described a Cesarean section done under an ether spray on a woman with obstructed labor from a rectal carcinoma [20]. Interest in this subject lies in two effects, that of the pregnancy on

Fig. 11.2 Jean Cruveilhier 1837

the carcinoma and that of the complications of the carcinoma on the management of the pregnancy. Warren in 1957 came to the conclusion that pregnancy does not adversely affect the course of carcinoma of the rectum [21].

11.2.1.2 Incidence

Incidence of colorectal cancer in pregnancy in 1981 was 0.002 % due to the fact that incidence rises with age [22]. Up to 1949, there were 75 cases published [23, 24]. Approximately 275 cases of colon cancer associated with pregnancy have been reported in the literature up to 1998 [25]. A review of 205 of these cases performed by Bernstein et al. demonstrated that 85 % of these cancers were located below the peritoneal reflection and mean age of 31 years (range 16–48) in a review of 42 pregnant patients with colon cancer [26].

First two published cases of perforated low rectal and sigmoid cancer were by Nash in 1967 [27]. The first patient was aged 38, in her fifth pregnancy (38 weeks). Artificial rupture of the membranes was carried out, and an hour later an 8 lb live boy was born. The second patient was aged 28; in her second pregnancy, in 32nd week, she had exteriorization of the sigmoid tumor.

Most cases of CRC are discovered in late pregnancy, and 60–80 % of the patients have rectal carcinoma [28].

11.2.1.3 Pathogenesis

The main pathogenesis of CRC in pregnancy is still associated with lots of unanswered questions. Some factors including pregnancy hormones, the enzyme cyclocoxygenase-2 (Cox-2), and tumor suppressor protein p53 were mentioned to be associated with CRC. A majority of CRC cases have been found to be positive for estrogen (20–54 %) [29] and progesterone receptors (10–100 %) [30]. Maybe the increased levels of estrogen and progesterone during pregnancy stimulate the growth of tumor cells with such receptors; however, all reports did not support this hypothesis. Slattery et al. in a study found only one case with positive progesterone receptor among 156 pregnant cases with CRC [29]. The elevated amounts of Cox-2 in CRC patients have raised the hypothesis of its association with colorectal cancer; however, there are little evidences to elucidate its carcinogenic role.

11.2.1.4 Clinical Presentation

Common presenting signs and symptoms of CRC include abdominal pain, anemia, nausea, vomiting, and rectal bleeding. Because these signs and symptoms are also frequently found in pregnancy, physicians and patients often attribute them to the usual complications of pregnancy [28]. The diagnostic challenge for clinicians is distinguishing pregnancy symptoms from the warning signs of colorectal cancer (Table 11.2) [25]. Clinicians must be aware of these potential warning signs and symptoms in order to make the diagnosis at an early stage of the disease. Rectal bleeding is particularly an ominous sign and should never be attributed solely to pregnancy without a proper evaluation.

Presentation of perforated CRC is sudden and severe pain, with signs and symptoms of acute abdomen.

11.2.1.5 Diagnosis

Elective Presentation

Serum CEA is an important laboratory test used in the evaluation of pregnant and nonpregnant patients. CEA levels during pregnancy are usually

Table 11.2 Commonly confused signs, symptoms, and laboratory results between pregnancy and colorectal cancer [25]

Signs, symptoms, lab	Normal pregnancy	Pregnancy with colorectal cancer
Weight loss	In general weight gain, but women can experience weight loss in the first trimester	Pregnancy can obscure weight loss secondary to CRC, primarily in second and third trimesters
Rectal bleeding	Common in pregnancy secondary to high incidence of hemorrhoids	Often attributed to hemorrhoids without pursuing appropriate workup
Nausea and vomiting	Common in pregnancy, particularly during the first trimester	Often attributed to pregnancy, delaying workup
Constipation	Common in pregnancy	Often attributed to pregnancy, delaying workup
Abdominal mass	Natural process in pregnancy	Potential palpable masses secondary to CRC often missed secondary to changes of pregnancy
Anemia	Physiological finding in pregnancy	Anemia of pregnancy masks blood loss from CRC

normal but may be slightly elevated [31]. CEA levels obtained prior to surgery provide a baseline to monitor the response to treatment. CEA levels also have prognostic value since increased levels prior to surgery are associated with disseminated disease and increased recurrence rates [32]. However, CEA is not useful as a tool for screening due to the low sensitivity and specificity [32].

Acute Abdomen (Perforation)

Laboratory findings show elevated levels of WBC and CRP, possible microcytic anemia, and other parameters according to the duration of the perforation. The patient can present with prerenal insufficiency due to the shift of fluid in the third space. Plain abdominal X-ray shows pneumoperitoneum if the perforation is above the peritoneal fold.

11.2.1.6 Therapy

Gestational Age: Elective Presentation

Gestational age and CRC stage are important to select treatment modality. If tumor is resectable, surgical excision is recommended especially in those diagnosed in early pregnancy (before 20 weeks of gestation). In cases of more advanced pregnancy, surgery can be postponed at the earlier possible date at which fetus can be viable (around 32 weeks). In advanced stages, when adjuvant therapy is needed, elective abortion would help to save mother's life, while in greater gestational ages, it is possible to pursue adjuvant therapy after early delivery. It is important that the mother be fully informed of possible risks of each choice prior to her decision. In religious countries like Iran, there is another extra challenge for parents and clinician, since due to religious beliefs, the legal abortion is only permitted up to the week 16, and after this time there would be problems to perform the abortion legally.

One-Stage or Two-Stage Procedure: Elective Presentation

If operation is indicated in early pregnancy, then tumor resection and termination of pregnancy should be performed. It can be done in a single act or as a two-stage procedure [33]. In the first stage, termination of pregnancy is performed. After 2–3 weeks, when the uterus returns to a normal size and the pelvic venous congestion related to pregnancy decreases, oncologic resection of the colorectal cancer is performed.

Ovarian Transposition: Elective Presentation

The primary benefit of ovarian transposition is prevention or delay of premature menopause, not preservation of fertility. In fact, with "curative" doses in the range of 8,500 cGy with external beam plus intracavitary brachytherapy, the resultant endometrial damage essentially precludes successful pregnancy, either spontaneously or with in vitro technique.

Doses of radiation delivered to the ovary following successful laparoscopic oophoropexy have been determined and reported by several authors. Covens et al. [34] studied three patients in whom ovarian transposition was performed and determined the radiation dose expected to be received by the ovaries after delivery by either an external beam radiation dose of 4,500 cGy or via brachytherapy. The mean dose of radiation received by the transposed ovary was 175 cGy (range, 40–370 cGy) after a mean follow-up of 2 years. The iatrogenic menopause rate was 10 % overall, but iatrogenic menopause did not occur in any of the patients younger than 40 years of age.

Numerous studies have attempted to specify *radiation therapy tolerance doses* for the various tissues and structures of the body. Common dose definitions that are used to describe various tissue tolerances are the minimal tolerance dose, TD 5/5, and the maximal tolerance dose, TD 50/5, which refer to a severe complication rate of 5 and 50 %, respectively, with 5 years of radiation completion. For the ovary, these values are approximately 300 cGy and 1,200 cGy, with sterility being the endpoint of severe complication. Tolerance doses for other tissues are significantly higher. In clinical practice, however, the tolerance doses for the ovary and other tissues may actually be lower, given the now common treatment regimens that typically include chemotherapy or altered radiation fractionation schemes. In general, if the ovaries can be appropriately shielded from the direct radiation beam via an oophoropexy maneuver, a dose below the TD 50/5 (300 cGy) can be achieved with a reasonable expectation of ovarian function preservation posttreatment. Simply the rule of thumb for radiation and ovarian function could be applied, meaning 10 cm distance to radiation field = 10 % dose of radiation [35].

> The rule of thumb for radiation and ovarian function means 10 cm distance to radiation field = 10 % dose of radiation.

The typical outcome measure in ovarian transposition following radiation therapy is ovarian function. This is often measured by quantitative analysis of ovary-stimulating or ovary-producing hormones as well as fertility outcomes. Spontaneous pregnancies are possible if tubal function is preserved as part of the oophoropexy. Morice et al. [36] reported on 37 consecutive cases of ovarian transposition. In these cases, 43 % (16/37) of pregnancies occurred spontaneously; of these, 75 % (12/16) did not have the ovaries repositioned from the adnexa. Quantitative analysis of ovarian function has been reported by Covens et al. [34] in three patients undergoing ovarian transposition. Serum FSH was found to be normal in 67 % (2/3) of patients menstruating regularly 24–32 months after radiation. Treissman et al. [37] reported on a patient in whom laparoscopic ovarian transposition was performed before definitive treatment for an anal carcinoma. Tulandi and Al-Took [38] reported that normal menstruation returned after irradiation in a 34-year-old woman who underwent laparoscopic ovarian transposition before radiation for treatment of rectal carcinoma. Although postmenopausal symptoms and elevation of serum gonadotropins initially indicated ovarian failure, normal menstruation resumed and correlated with normal FSH levels 8 months after treatment.

The timing depends on the treatment algorithm of rectal cancer. If the operation is indicated, it can be performed during that operation for rectal cancer. If neoadjuvant chemoradiotherapy is indicated, then laparoscopic transposition can be performed prior to neoadjuvant chemoradiotherapy.

Preservation of ovarian function by laparoscopic transposition of the ovaries before pelvic irradiation has been demonstrated to be a safe and effective procedure for patients with Hodgkin's disease as well as in the treatment of a variety of gynecologic malignancies. Historically, surgical exploration of the abdomen or pelvis as part of staging or resection procedures has allowed for access to the ovaries for direct-open transposition of the ovaries for planned subsequent radiation therapy.

Techniques for ovarian transposition using a laparoscopic approach vary according to the radiation field shape, size, and location.

Medial Ovarian Transposition

Tinga et al. [39] have described transposition of the ovaries in a fixed position behind the uterus (to lie beneath an external midline block) as well as a superior transposition to the level of the iliac crest. They contend that the disadvantage of the midline oophoropexy is a higher level of internal radiation scatter, as the area is generally surrounded by in-field radiation.

Lateral Ovarian Transposition

Morice et al. [40] reported a series of 24 patients who underwent ovarian transposition to the paracolic gutters, before radiation for gynecologic malignancies. The authors concluded that this procedure was a safe and effective method of preserving ovarian function. The peritoneum of both pelvic sidewalls is incised, and the retroperitoneal spaces developed. The common, external, and internal iliac vessels are identified. The ovarian vessels and ureters are traced on both sides. Under the direct vision of the ureters, the utero-ovarian ligaments are separated with an endoscopic linear cutting stapler (Endo-GIA). The peritoneum under and lateral to the ovarian vessels are incised to an area outside of the true pelvis, under direct vision of the ureters. At this point, the ovarian vessels could be turned laterally with a sufficient angle to maintain appropriate blood supply. The ovaries and tubes are fixed high in the paracolic gutters, below the spleen and the liver, with 2-0 silk sutures, in three points, to prevent torsion. The upper and lower poles of the ovaries are marked with hemoclips. At the end of the procedure, good blood supply to both ovaries is confirmed by a small incision of the Fallopian tubes, which are cauterized. The metal clips around the ovaries help to verify that they would be out of the radiation portals on radiation verification films [35].

Perforation

The first two published cases of perforated low rectal and sigmoid cancer were by Nash in 1967 [27]. After describing the first two patients, Nash defined two possible plans of action: if the pregnancy is sufficiently advanced, labor can be induced, the uterus emptied, and the colonic condition treated in the much easier operating conditions thus afforded; if, however, the patient's condition is too poor or if she is not yet at full term, operation must be done in the presence of the gravid uterus. In these circumstances resection is very difficult, and I think exteriorization is the only possible treatment. Cesarean section via an infected peritoneal cavity seems very unwise and would appear to be indicated only if a perforated rectal carcinoma obstructs vaginal delivery.

11.2.1.7 Prognosis

Maternal Outcome

The delay leads to late diagnosis of the disease and subsequently poor prognosis. A majority of CRC cases in pregnancy present with Duck class C (44 %) in which adjutant therapies are needed to improve the surgical outcome [26]. The median survival in a review of 42 pregnant patients with CRC was less than 5 months and 56 % died by the time of the report [41].

Fetal Outcome

CRC in pregnancy represents a serious threat to both the mother and the fetus. Woods et al. reported that 78 % (25/32) of pregnancies in women with colonic tumors above the rectum resulted in healthy, live-born infants. Prematurity, intrauterine death, stillbirth, and termination were all contributors to the death of these infants [42].

Genetic Counseling

CRC occurs rarely in young patients, and as a result, this patient population is more likely to have strong predisposing factors compared to the general population of patients with CRC [43]. Such predisposing factors for CRC include hereditary nonpolyposis colorectal cancer (Lynch syndrome), familial adenomatous polyposis, Gardner's syndrome, Peutz-Jeghers syndrome, and long-standing inflammatory bowel disease. However, these increased risk groups represent only a small portion of CRC diagnosed in pregnancy [25]. A review of 19 pregnant patients by Girard et al. from 1981 demonstrated that 21 % (4/19) of patients had one of these strong predisposing factors for CRC [22]. Despite the negative result for possible hereditary nonpolyposis colon

cancer (*Amsterdam II criteria*), *Bethesda criteria* should be checked for microsatellite instability. If the microsatellite instability testing is positive, the genetic testing of the three genes associated with HNPCC should proceed. Once a mutation was identified in the family, other family members could consider predictive testing.

11.2.2 Spontaneous Colorectal Perforation

There are two causes of spontaneous perforation of the colon: stercoral and idiopathic.

11.2.2.1 Stercoral (Stercoraceous) Perforation

Incidence and Diagnostic Criteria

Stercoral perforation is rare, even in nonpregnant patients. The first case of stercoral perforation was described in 1894 [44]. A review by Maurer et al. identified only 88 cases from 1894 to 2000 [45]. These authors proposed diagnostic criteria:

- Round or ovoid perforation, ≥1 cm in diameter, antimesenteric location
- Fecaloma (hard, laminated, inspissated fecal mass) within the colon, protruding through the perforation site, or lying within the peritoneal cavity
- Typical pathohistological features (pressure necrosis or ulcer with chronic inflammatory reaction around the perforation site)
- Absence of other active colonic pathology, such as diverticulitis, carcinoma, and Hirschsprung's disease

Stercoral perforation during pregnancy is extremely rare, and there are three cases published. Women presented at 22, 36, and 41 weeks of pregnancy [46–48].

Risk Factors

Chronic constipation is the main risk factor and is present in 81 % of patients. Use of antacids, codeine-containing narcotics, nonsteroidal anti-inflammatory agents, major tranquilizers, and tricyclic antidepressants has been linked to stercoral perforation [49, 50]. These medications are all known to cause constipation.

Treatment

Treatment is surgical, and resection of the diseased segment with proximal colostomy and closure of the rectal stump or mucous fistula are the procedures with the lowest mortality rate in general population [49]. This is the recommended procedure in pregnant population as was performed in two cases [47, 48].

Prognosis

The reported mortality rate among all cases in general population of stercoral perforation is 47 %, with a 35 % mortality rate among surgically treated cases [49]. Of three pregnant patients [46–48], one died (maternal mortality of 33 %). Perinatal mortality is 66 % probably due to prolonged peritonitis. The first patient presented at 41 weeks of gestation delivered a stillborn infant and died after delivery. Stercoral perforation was diagnosed on autopsy [46]. The second patient in 36 weeks of pregnancy was explored and Cesarean section performed, with live baby, before the Hartmann procedure [47]. The third had sigmoid perforation in 22 weeks of pregnancy. One day after the Hartmann procedure, the patient delivered vaginally a dead female infant [48].

11.2.2.2 Idiopathic Perforation

The features of idiopathic perforation of the colon are as follows [51]:

- Linear perforation
- No feculent ulcer at microscopic examination
- Clear mucosal edge not extending to the serosa
- Regular broken ends of the muscular layer

There is no published case of idiopathic colorectal perforation.

Table 11.3 Possible risk and combinations of factors for *spontaneous* intestinal perforation

Antiphospholipid syndrome (macroangiopathy)
HELLP syndrome (microangiopathy)
Syphilis
Vasculitis
Low-flow states
Arrhythmia
Sepsis
Shock
Disseminated intravascular coagulation
Recent surgery/C-section
Thromboembolism per se
Ischemia caused by previous surgical manipulation [52]
Cocaine abuse [53, 54]
Valvular heart disease
Infective endocarditis
Diabetes mellitus
End-stage renal disease
Idiopathic hypertension
Oral contraceptives

11.2.2.3 Spontaneous Intestinal Perforation

Incidence

This is an extremely rare entity, and the incidence is unknown.

Risk Factors

All risk factors for "spontaneous" ischemic events in general population are also risk factors in pregnancy (Table 11.3). The difference is in incidence of different risk factors due to specific age of presentation. Also pregnancy per se is a risk factor for thromboembolic events. Combination of different risk factors could be present and should be kept in mind which aggravates the possibility of intestinal ischemia and subsequent perforation. Most spontaneous intestinal perforations are due to previously unknown but present risk factors. There are cases when women during early pregnancy (by mistake because unaware of pregnancy) [55] or early postpartum period by patient itself [56] take oral contraceptives with development of mesenteric vein thrombosis. These risk factors are the same and could include the perforation both on small and large bowel.

Prevention

It is recommended that all women with antiphospholipid syndrome should maintain antithrombotic treatment throughout their entire pregnancy and during the postpartum period. The prevention of choice is combined low-dose aspirin and full antithrombotic doses of low-molecular-weight heparin. In high-risk groups, such as history of previous thrombotic events, warfarin may be used during pregnancy, but only after organogenesis (6th–12th week) because of high risks of fetal malformations. Despite the significant risks associated with pregnancy in patients with antiphospholipid syndrome, with the correct management the likelihood of a live birth is around 75–80 % [26].

Treatment

The type of the operation depends on the extent of peritonitis and underlying ischemia. If the perforation is present without visible ischemia, resection with anastomosis is the preferred method. If there are signs of ischemia, ischemic segment is resected and anastomosis with or without stoma is performed. In long-standing generalized peritonitis, stoma is the preferred option.

11.2.3 Bowel Perforation Secondary to (Illegally) Induced Abortion

11.2.3.1 Incidence

Bowel perforation secondary to illegally induced abortion though rare and uncommon in developed world is a significant and major cause of maternal morbidity and mortality in developing or especially undeveloped countries where abortion laws are still restrictive and most abortions are performed clandestinely and illegally by unqualified personnel [57, 58]. The incidence of abortion-related complications such as bowel injuries has been reported in most developing countries to be increasing at an alarming rate [59]. Ignorance and inability to take quick decision regarding termination of an unwanted pregnancy compel a large number of women to seek illegally induced abortion in the second trimester from unauthorized person in unrecognized places. The rate of bowel

perforation as a complication of induced abortion has been reported in literature to range from 2 to 18 % of all abortion-related complications [60–64]. However, as in other iatrogenic surgical problems, many cases may have been unreported because of its medicolegal implications [65, 66].

11.2.4 Treatment

Surgical intervention is considered to be the gold standard treatment for patients with bowel perforation following induced abortion [65]. All patients underwent surgical treatment [27, 33, 34, 60, 61, 65, 67–70]. One of the many factors affecting the surgical outcome in patients with bowel perforation is time interval from perforation to laparotomy [10, 65]. Early surgery can minimize the complications, while delayed surgery leads to severe peritonitis and septic shock. The majority of patients in developing countries were operated more than 24 h after the onset of illness [4, 31, 61, 65]. Delayed definitive surgery may be attributed to late presentation due to lack of accessibility to health-care facilities and lack of awareness of the disease; as a result some patients with bowel perforation following induced abortion may decide to take medications in the prehospital period with the hope that the symptoms will abate. It is also possible that some clinicians managing the patients initially may not have considered perforation as a possible diagnosis leading to delayed referral to tertiary care hospital. The ileum and the sigmoid colon are the most common parts of the bowel affected [60, 61, 65, 67–70]. The relative fixity of these portions of the bowel has been suggested as a possible reason for this. Early surgical interference is the optimal treatment option for perforation. However, the type of surgery to be applied is controversial [65]. The surgical management of small intestinal injuries is fairly straightforward with minimal sequel. The practice in managing these patients is a simple closure in solitary perforations and segmental intestinal resection and primary anastomosis in multiple perforations or gangrenous bowel. The management of large bowel injury is more controversial [15, 65]. This is more so when the left colon is involved. A simple colostomy has been reported to be the safest approach in the management of these injuries. Other options include primary repair, resection and primary anastomosis, and repair with a proximal protective colostomy or ileostomy. A simple colostomy is easier and faster to accomplish in these poor surgical risk patients. However, the major drawback of colostomy is the need for a second operation to restore intestinal continuity, the specialized care before closure, and the attendant cost which reduces its popularity [36, 71]. The challenge is even more conspicuous in a developing country like Tanzania where resources for caring of patients with colostomy are limited. The management of stoma remains difficult in developing countries because of the shortage of suitable equipment in this respect, and peristomal ulceration remains a major problem [71]. Primary repair and resection and primary anastomosis are performed in case of viable bowel, whereas colostomy is reserved after resection of a gangrenous large bowel.

11.2.5 Prognosis

11.2.5.1 Complication Rate

The overall complications rate in the series by Mabula et al. [61] was 47.1 % which is higher compared to previous report by Thapa et al. [72]. High complication rate was also reported by Saleem and Fikree [73] in Pakistan. This difference in complication rates can be explained by differences in antibiotic coverage, meticulous preoperative care and proper resuscitation of the patients before operation, improved anesthesia, and somewhat better hospital environment. As reported by Rehman et al. [74], surgical site infection was the most common postoperative complication. High rate of surgical site infection may be attributed to contamination of the laparotomy wound during the surgical procedure. In the study by Mabula et al. [61], mortality rate was 10.3 % which is higher than that reported by Bhutta et al. [75]. High mortality rate is attributed to high gestational age at termination of pregnancy, late presentation, delayed surgical treatment, and postoperative complications.

The overall median length of hospital stay was 18 days, which is lower than that reported by Rehman et al. [75].

Self-discharge against medical advice is a recognized problem and this is rampant, especially among patients with complications of illegally induced abortions [35]. Similarly, poor follow-up visits after discharge from hospitals remain a cause for concern. These issues are often the results of poverty, long distance from the hospitals, and ignorance.

11.3 Spontaneous Liver Rupture

> *Very exceptionally lesions of the liver are observed as the result of violent muscular exertion, as in the course of parturition or epileptic seizures. In such cases it is usually necessary to assume a diminished resistance of the organ as a necessary condition.*
>
> Allesandri, 1927

11.3.1 Incidence

Spontaneous liver hemorrhage during pregnancy is uncommon and mostly associated with preeclampsia, eclampsia, or a HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). The incidence is estimated at 1/45,000 [76], and the mortality of the mother and child is high (15 and 42 %, respectively) [77]. However, spontaneous rupture in uncomplicated pregnancy, without association with previous conditions, has also been reported but is extremely rare [78, 79]. Up to 1943, there were 29 cases (the case of Vesalius included) of true spontaneous rupture of the liver (only two in pregnancy, Abercrombie in 1844 and Readmaker in 1943) [80].

11.3.2 History

Spontaneous rupture of the liver resulting from insignificant or no trauma has been noted in the literature for more than a century. The first known case was reported by Vesalius at some undetermined date. Andral, in 1829, sketchily reported two cases complicating lesions which may have been gummata or carcinomas. In many of the earliest cases, there is some possibility that gastric hemorrhage, secondary to liver disease, may have been mistaken for actual rupture of the liver. Thus, a case quoted in *Paris Medical*, in 1847, by Fauconneau and Dufresne, as reported by Latour, was undoubtedly such an instance. Abercrombie, as communicated by James Copeland, reported a case of ruptured liver complicating pregnancy in 1844 [81]. In this delightfully naive and meticulously detailed report, Abercrombie described a 35-year-old woman who, to obtain relief from "gastrodynia," took recourse to placing a silk handkerchief around her body and pulling it tight to give her relief. On this occasion a servant pulled the handkerchief so tightly that *it made me fear some injury under existing circumstances*. Labor followed and normal delivery occurred, followed by collapse some 50 min later. The crude stimulants of the time were administered, several famous physicians and surgeons were called in consultation, but the patient died 26 h after delivery. Autopsy revealed about two pounds of blood in the abdomen and two lacerated openings in the liver substance, about an inch apart. The liver itself presented a mottled appearance throughout and was unusually soft. Bleeding came from a torn branch of the portal vein. Devic and Beriel, in 1906, reviewed the literature of spontaneous rupture of the liver [82]. McEwan and McEvan and also Corriden have added more recent and excellent reviews [83, 84]. Spontaneous rupture of the liver is rare and exceptional. A number of causes for its occurrence have been described, and traumatic rupture is not rarity. Allessandri [85] stated: *Very exceptionally lesions of the liver are observed as the result of violent muscular exertion, as in the course of parturition or epileptic seizures. In such cases it is usually necessary to assume a diminished resistance of the organ as a necessary condition* [85]. Case by Rademaker, although complicating pregnancy, was not in labor [80]. Rademaker collected 28 cases in general population and found that causes other than violent muscular effort are multiple. Some associated disease or even minor trauma was present in all but three cases of 28 collected. It is no wonder that Sciacca came to the conclusion that when

rupture of the liver occurs with minimal cause, the parenchyma is probably not normal [86].

As previously stated, the first known case is by Abercrombie in 1844 [81]. He described a woman aged 35 who suffered from epigastric pain, abdominal distension, and belching at the eighth month of pregnancy. Having had frequent attacks of gastrodynia on former occasions, she, of her own accord, had immediate recourse to pressure for relief; and placing a silk handkerchief round her body she desired one of her servants to pull it as tight as she possibly could. The wish was complied with, but to an extent that made the author fear of some injury under existing circumstances. Author therefore begged for its removal. Author prescribed for her a draft composed of calcined magnesia, Liquor Opii Sedativus, Spt. ether, sulfur, and Aq. cinnamomi, to be taken immediately, and ordered hot fomentations to the epigastrium. By these mean the pain gradually abated. A few hours later labor began and was soon followed by the successful breech delivery of the fetus. An hour after the expulsion of the placenta, the patient collapsed. Hemorrhage was suspected, but there was no evidence of its coming from the birth canal. Two days later the patient died, and a postmortem examination revealed a large unruptured subcapsular hematoma on the superior and anterior surfaces of the liver. Abercrombie was of the opinion that the damage to the liver might have been caused by the tight bandaging but that hemorrhage did not occur until the pressure of the gravid uterus on the upper abdomen had been removed. He also put forward an alternative suggestion that hemorrhage took place in a liver that was already so diseased that it was readily injured by the muscular compressions of labor.

Alessandri (quoted by Rademaker, 1943), writing on this subject, agrees that rupture of the liver may occur as the result of violent muscular activity during parturition or during epileptic seizures, but he gives no case report or reference to support his views.

Rademaker in 1943 describes the case of a woman aged 32 admitted to hospital in the eighth month of pregnancy with a blood pressure of 260/160 mmHg and albuminuria [80]. After a severe bout of vomiting she collapsed, and the diagnosis of a ruptured uterus was made. At operation a rupture of the liver (the right lobe of the liver contained a vertical tear 6 in. in length, with an area of degenerated tissue which appeared to be mush and about the size of a grapefruit), with blood in the peritoneal cavity, was found. The hemorrhage was controlled by a pack, and after a stormy convalescence the patient recovered. In this case hypertension was thought to be the cause. Rademaker submits the interesting suggestion that sudden death during eclampsia may sometimes be due to a ruptured liver. It is doubtful, however, whether this speculation can be sustained, for, although scattered areas of necrosis and small subcapsular hemorrhages are not infrequently found in eclampsia, severe hemorrhages of the liver are not a feature of this disease.

Another case was by Links in 1946 during the fourth month of pregnancy. The cause of the liver damage was obscure, but Links suggests that it may have been due to a transient hypertension. Burton-Brown and Shepherd described a case 17 h after parturition [87]. Injury was the result of trauma produced by violent contraction of the diaphragm and abdominal muscles during labor. But it is interesting to note that there was also an element of toxemia, evidenced by the raised blood pressure and albuminuria.

11.3.3 Etiopathogenesis

11.3.3.1 Historical Perspective

Pathology of rupture of the liver varies with the accompanying lesion of the liver. In the past, a gumma or carcinoma may easily erode into a blood vessel causing a discharge of blood into the liver parenchyma. Again an aneurysm or hemangioma may rupture with a similar result. A vessel may rupture by reason of arteriosclerosis, as was possibly the case in Bernard's patient. A vessel may become occluded with resultant infarct, which could cause vessel rupture, as Mazel has suggested. Another mechanism, as in Rademaker's case, is rapidly rising blood pressure, with toxemia of pregnancy causing rupture of a blood vessel [80]. Devic and Beriel [82] and, later, Mazel have formulated this theory of the

pathology of spontaneous rupture of the liver: *In traumatic rupture, the rupture is the cause of hemorrhage. In spontaneous rupture, the hemorrhage is the cause of rupture. The chain of events leading to the rupture is infarct, hypervascularization at the periphery, rupture of a vessel, intra-hepatic hemorrhage with resulting rupture of the tissue and production of a subcapsular hematoma which when rupturing the capsule permits escape of blood into the peritoneum* [88].

11.3.3.2 Mechanism

In most cases, a liver rupture occurs in the third trimester of pregnancy or within the first 24 h postpartum. It occurs more often in the multiparous women above the age of 30 [89, 90]. In 75 % of the cases, it consists of a solitary injury of the right liver lobe, in 11 % of the left liver lobe, and a bilateral injury in 14 %, as shown by a study of Henny et al. [91]. The pathogenesis of a spontaneous liver rupture as a complication of hypertensive disorders of pregnancy such as preeclampsia, eclampsia, or HELLP syndrome remains unclear [92]. When hemorrhage follows delivery, one might suppose that the sudden decrease in intra-abdominal pressure or the stress of uterine contracture and the Valsalva maneuver, or both, may have encouraged the rupture. Clotting abnormalities and disseminated intravascular coagulation with focal areas of hepatic necrosis lead to spontaneous hepatic hemorrhage. Bleeding from the hepatic parenchyma results in a subcapsular hematoma that ruptures into the peritoneal cavity. Other uncommon underlying conditions associated with a liver hemorrhage are bleeding from a hemangioma, metastasis or hepatoma, trauma, infections (malaria, syphilis, rupture of amoebic abscesses), aneurysms and the use of cocaine during pregnancy.

Spontaneous hepatic hemorrhage of pregnancy is associated with the HELLP syndrome [93, 94]. In 1982, Weinstein introduced the acronym HELLP to describe a syndrome observed in severe preeclampsia consisting of hemolysis, elevated liver function tests, and low platelet counts [95]. Hemolysis is the result of shearing of erythrocytes by fibrin strands that are deposited in the microcirculation, producing schistocytes. The syndrome also has been called microangiopathic hemolytic anemia.

The histopathology of the liver in toxemia of pregnancy has been described consistently as showing fibrin plugs or strands in the sinusoids and hepatic arterioles with resultant areas of periportal necrosis [93, 96–99]. Vasospasm of the hepatic arterial circulation with resulting endothelial damage may lead to the platelet aggregation and fibrin deposition. Vascular disruption and occult parenchymal hemorrhage ensue. Coalescence of multiple focal areas of infarction and hemorrhage may progress to overt parenchymal hemorrhage and hematoma. A subcapsular hematoma, which can involve a large segment of the liver, ruptures with resultant intraperitoneal hemorrhage. In some cases, a hematoma may develop; however, the process may resolve, and the hepatic lesion may heal spontaneously without complete progression to the syndrome of spontaneous hepatic hematomas associated with pregnancy (SHHP). Several authors have reported successful nonoperative management of SHHP that have not ruptured [93, 100–103]. The spectrum of pathology is highly variable. Evidence suggests that if intraperitoneal rupture does not occur, the hepatic lesion may heal without sequel. At the minimum, these patients with hepatic hematomas that have not ruptured mandate close observation in the peripartum period for signs of hepatic rupture and the syndrome of SHHP.

11.3.4 Clinical Presentation

A study by Rinehart et al. showed that epigastric pain is present in 69.5 %, hypovolemic shock in 56 %, nausea and vomiting in 24.8 %, and shoulder pain in 20.5 % of patients with a spontaneous liver rupture [104]. On clinical examination, signs of peritonitis can be present and fetal heart sounds are usually bad or absent.

Hypovolemic shock within the first 24 h is mostly because of an excessive vaginal blood loss due to a failure of the uterus to contract after delivery of its contents. If the uterus is found to be contracted appropriately and no placental fragments are retained, a laceration of maternal

soft tissues like a cervical or vaginal tear can be the cause of persistent vaginal blood loss. If all these gynecologic causes are excluded, intraperitoneal bleeding should be ruled out next.

11.3.5 Differential Diagnosis

Because a spontaneous hepatic rupture after a normal pregnancy is extremely rare, other more common causes for a postpartum acute abdomen and/or hypovolemic shock must be excluded. Cardiovascular instability without visible blood loss can also occur due to a traumatic laceration of the blood vessels resulting in a large vulvar, vaginal, or retroperitoneal hematoma. A large pulmonary embolism can also present with sudden cardiovascular instability without bleeding. It usually occurs after a deep venous thrombosis but can also occur primarily. The risk of embolism is tenfold higher after a Cesarean birth than after a vaginal delivery.

Another cause for a hypovolemic shock is a secondary postpartum hemorrhage. This is defined as vaginal blood loss occurring at least 24 h after the end of the third stage of labor and during the following 6 weeks. The spectrum of this condition can vary from inconvenient to fatal and occurs in almost 1 % of the patients who delivered vaginally. Almost 50 % of the patients have associated lower abdominal pain and uterine tenderness.

The underlying cause is also an inability of the uterus to contract due to retained products of pregnancy and/or an intrauterine infection [105, 106].

11.3.6 Diagnosis

Ultrasound is a simple and reliable method of confirming the diagnosis of spontaneous hepatic hemorrhage [93, 107]. The familiarity with and immediate availability of ultrasound to obstetricians make this the initial diagnostic procedure of choice in patients in whom the diagnosis is suspected either ante- or postpartum.

The hemodynamic status of the patient determines the investigations to be performed. In the hemodynamically stable patient, a CT scan with contrast is the most useful investigation. This allows the surgeon to quantify the liver injury, define the underlying hepatic disorders, and determine the treatment modalities (Fig. 11.3). If the patient is hemodynamically unstable, an urgent laparotomy must be performed. This can be preceded by an urgent ultrasound, if available.

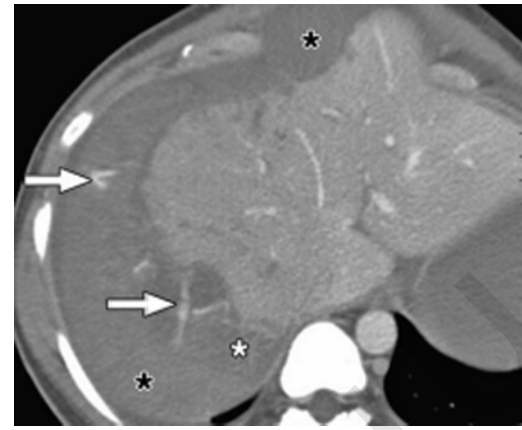

Fig. 11.3 A 36-year-old woman with toxemia of pregnancy, right upper quadrant pain, and falling hematocrit (HELLP [hemolysis, elevated liver enzymes, low platelet count] syndrome). Axial contrast-enhanced CT section shows nonenhancing hepatic foci (*white asterisk*) due to infarction and hematoma, foci of active bleeding (*white arrows*), and subcapsular and perihepatic hemorrhage (*black asterisks*) [108]

11.3.7 Treatment

11.3.7.1 Historical Perspective

In 1943, Rademaker made a review of all published cases of spontaneous liver rupture in general and pregnant population. Here are significant facts that appeared to him [80]:

- Careful observation by the family physician; otherwise, the patient would have died within a few hours.
- *Porro procedure* was the quickest means of removal of the fetus and the uterus to prevent any further bleeding from that source.
- Death of fetus as result of hemorrhage of the mother.
- Pleural effusion from pressure of the pack on diaphragm.
- Prompt multiple blood and plasma transfusions to save these desperately ill patients.

11.3.7.2 Current Recommendations

Treatment of Underlying Pathology/ Medical Treatment

There is not a specific treatment of the evolving hepatocellular pathology that occurs in the preeclampsia-eclampsia syndrome and that may lead to spontaneous hepatic hemorrhage. Systemic anticoagulation is contraindicated. The underlying preeclampsia-eclampsia syndrome should be treated by the usual methods, such as administration of magnesium sulfate and the use of antihypertensive agents. When the hepatic lesion is suspected, hypertension should be controlled aggressively to prevent further progression and hemorrhage. Intraperitoneal rupture of the subcapsular hematoma is accompanied by hemorrhage and hypovolemia. Blood volume replacement is requisite, with appropriate infusion of platelets and fresh frozen plasma. If the diagnosis is made antepartum, prompt termination of the pregnancy is mandatory, usually by Cesarean section [109].

In the postpartum period, the chosen therapy mainly depends on the hemodynamic status and the severity of the liver injury. If the patient is hemodynamically stable and there is evidence of a contained subcapsular hematoma, a conservative treatment can be started. Patient must be admitted to the intensive care unit for closely hemodynamic monitoring. Serial CT scans or ultrasounds must be performed in order to document expansion or rupture of the subcapsular hematoma. If the patient is hemodynamically unstable, two options are available: surgery or endovascular embolization of the hepatic arteries.

Interventional Techniques

Occlusion of the hepatic artery has been reported for treatment of hemorrhage due to a variety of conditions, including hepatic trauma, ruptured hepatoma, and spontaneous hepatic hemorrhage [110–116]. The hepatic artery can be occluded by surgical ligation or the interventional radiological percutaneous technique of angiographic embolization. The right and hepatic arteries, or both, can be occluded selectively by operative or radiological techniques.

Surgical Therapy

Attempts to control hemorrhage from the liver surgically, using local measures such as topical hemostatic agents and suture ligation of surface bleeders, are of limited value. Failure is predictable when dealing with hemorrhage from large areas of denuded and friable liver in patients with associated clotting deficiencies. The technique of angiographic embolization allows for the most precise localization of the site of hemorrhage and is highly successful in arresting hemorrhage (Fig. 11.4). The method applied depends mostly upon the severity of the shock and the availability of an experienced interventional radiologist. The major advantage of embolization is of course its less invasiveness.

Hepatic artery interruption has been well tolerated [112–116]. Transient elevations in the aspartate transferase and alanine transferase levels will result. In a liver with significant acute or chronic disease, the degree of hepatic dysfunction that follows hepatic artery occlusion may be accentuated. If the occlusion is proximal to the origin of the cystic artery, acute gangrenous cholecystitis may occur. Areas of focal hepatic necrosis can develop with or without secondary infection. Hypotension should be avoided after hepatic artery occlusion to maximize hepatic arterial flow. Supplemental oxygen may be administered on theoretical grounds. Hepatic perfusion through arterial collaterals may develop as little as 10 h after hepatic artery occlusion [114].

Stain et al. prefer hepatic artery occlusion as the primary therapy of SHHP rather than tamponade of the hepatic hemorrhage with abdominal gauze packing [117]. Smith et al. reviewed the available literature in the period 1976–1990 of abdominal packing for spontaneous hepatic rupture associated with pregnancy [76]. Including their four patients, they identified 27 cases, for an 82 % survival rate. Their recommendation was that abdominal packing should be the primary treatment for ruptured hepatic hematoma. The extensive experience by Feliciano et al. in treatment of traumatic hepatic hemorrhage by abdominal packing undoubtedly influenced their recommendation [118]. It should be noted that packing failed in both patients treated primarily by packing. Stain et al. could not compare their experience

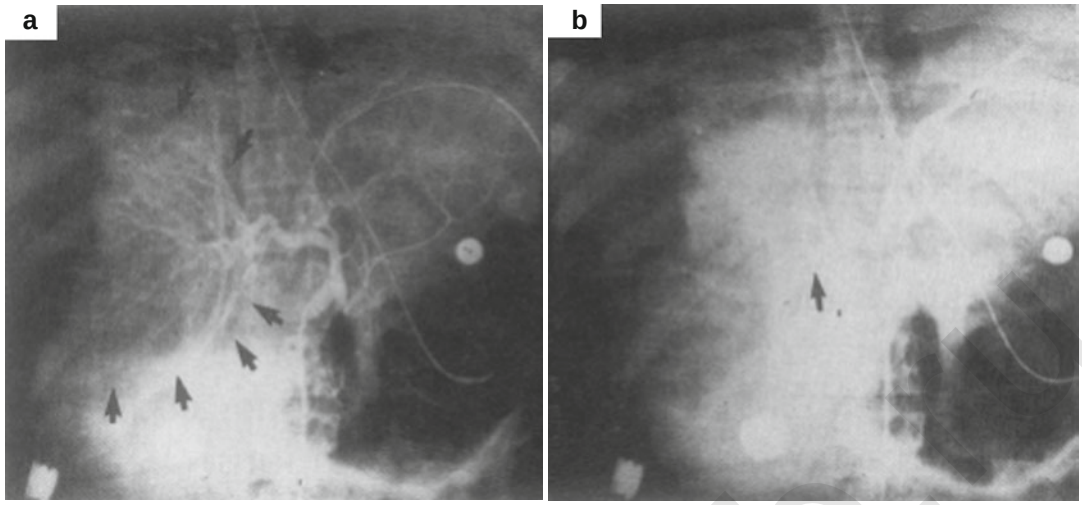

Fig. 11.4 (**a**) Hepatic arteriogram of patient with bleeding subcapsular hematoma. *Arrows* identify multiple pseudoaneurysms with bleeding. (**b**) Arteriogram after embolization of right hepatic artery (*arrow*) [117]

with Feliciano et al.'s series because their report does not provide details of the magnitude of the liver lesion or the morbidity associated with the two operations in each of their four patients. An analysis of the references cited by Smith et al. [76] in their collective review reveals that in at least six of the reports, significant numbers of the patients were not treated with perihepatic packing, but with local measures, including Surgicel (Johnson & Johnson Medical, Inc., Arlington, TX) or Gelfoam (Upjohn Company, Kalamazoo, MI) [94, 96, 119–122]. It is unclear if these patients exhibited the full spectrum of the syndrome, including rupture of the hepatic hematoma with life-threatening hemorrhage, or had contained nonbleeding hematomas. Packing should be reserved for patients in whom the diagnosis of SHHP is made at the time of Cesarean section and in whom a Pringle maneuver incompletely controls the hepatic hemorrhage. In this situation, hepatic packing may have a role as a temporizing measure en route to the angiography suite. It does require a second operative procedure for removal of the packs. However, if in the operating room the bleeding is controlled by clamping of the right, left, or common hepatic artery, hepatic arterial ligation is preferable as a definitive treatment. Figure 11.5 presents the algorithm for the treatment of spontaneous hepatic rupture in pregnancy proposed by Stein et al.

Obstetric Management

If a rupture occurs during pregnancy, delivery of the fetus is one of the first steps. A classical Pfannenstiel incision is, however, not suitable because the full abdomen cannot be visualized unless a second upper abdominal incision is made. A median laparotomy is therefore the recommended approach because it has the great advantage of visualizing the entire abdomen, speed of execution, and less blood loss [106].

11.3.8 Prognosis

Up to 1943, there were 29 cases (the case of Vesalius included) of true spontaneous rupture of the liver, and only two of these complicated pregnancy (Abercrombie 1844, the patient died, and Rademaker 1943, the patient recovered but the fetus died) [80]. In general, five of these came to operation, and four recovered making maternal mortality after surgical therapy 80 %. In that time if liver rupture was evident, the Porro procedure (excision of the Fallopian tubes, the ovaries, and the uterus at supravaginal level) was recommended after incision of the uterus and deliverance of the fetus.

In 1976, Bis and Waxman, in a collective review, reported 62 % fetal and 59 % maternal

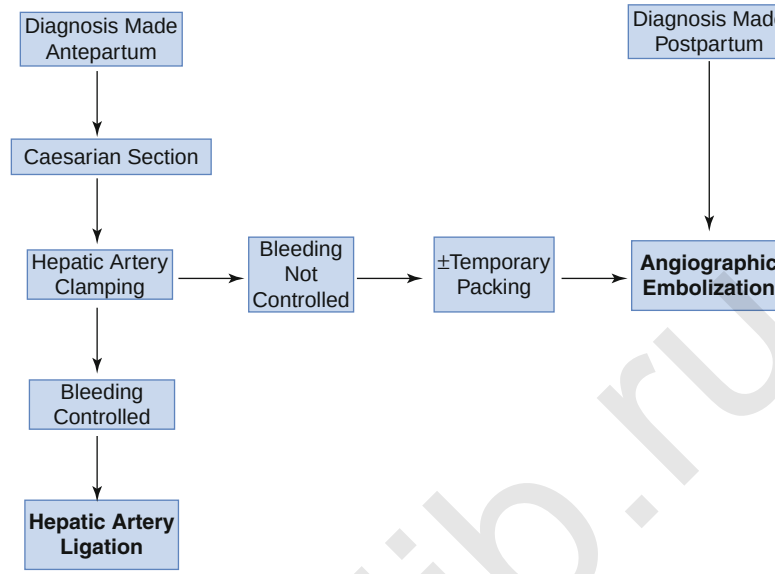

Fig. 11.5 Algorithm for the treatment of *spontaneous* hepatic rupture in pregnancy (see text for details) [117]

mortality rates of liver rupture during pregnancy [89]. In the collected reports of 15 patients treated with hepatic artery ligation/occlusion (radiologically or surgically), the mortality was 29–37 % [54, 110, 111, 117, 119, 123, 124].

11.4 Peptic Ulcer Bleeding

11.4.1 Introduction

Pregnancy seems to have a beneficial effect on peptic ulcer (see Chap. 4). Clark in 1953 investigated dyspeptic symptoms during 313 pregnancies in 118 women with the diagnosis of peptic ulcer before pregnancy [125]. He found that there was a remission of ulcer symptoms in 88 % (276/313) of the pregnancies. More than 50 % of these women claimed to have been completely symptom-free during the whole pregnancy; the remainder had minor symptoms which they regarded as unconnected with the ulcer. In the remaining 12 % (37/313), symptoms persisted which were indistinguishable from those of ulcer, and 14 women were admitted to hospital for treatment of the "indigestion." In no case did hemorrhage or perforation occur during the pregnancy.

11.4.2 Incidence

Small hemorrhages from the upper part of the alimentary tract do not appear to be very rare in pregnancy, although Avery Jones in 1947, investigating for ulcer activity a series of 10,000 women attending an antenatal clinic, found only one case of mild hematemesis, and no ulcer could be demonstrated [126]. In a series of 587 cases of hematemesis and melena admitted to Dr Norris's unit at Whittington Hospital during the 4-year period 1957–1960, there were four pregnant women (MacCaig JN, 1962, personal communication). These data show that only 0.7 % of bleeding peptic ulcers occur during pregnancy. It may be that the small number of proven cases is due to a reluctance to carry out radiological investigations during pregnancy before the era of endoscopy. If investigations were done after the birth of the child, the ulcer would probably have healed. Up to 1971, 31 perforations and 32 cases of hemorrhage from proved peptic ulcer during pregnancy have been reported [127]. The ratio of gastric and duodenal ulcers in pregnancy and also bleeding peptic ulcers during pregnancy is not known.

Peptic ulcer bleeding occurs in the late third trimester or during the first days postpartum [128].

There are only several case reports of operated bleeding peptic ulcers [129–132].

11.4.3 Risk Factors

In 1948, Bernstine and Friedman reported four cases of hemorrhage from peptic ulcer in pregnant women [133]. All of these women had been treated with *progesterone* before the onset of the gastrointestinal hemorrhage.

11.4.4 Diagnosis

Bleeding peptic ulcer is diagnosed by esophagogastroduodenoscopy (EGD). Before the era of endoscopy, peptic ulcers were diagnosed with radiological examination. Due to the ionizing radiation, it was contraindicated during pregnancy. Therefore, for many cases of peptic ulcer hemorrhage during pregnancy, the diagnosis was never confirmed [134].

11.4.5 Treatment

11.4.5.1 Conservative Treatment

Today, with potent acid suppression medications, most of peptic ulcer bleeding can be treated without operation. During long period of occurrence during pregnancy, most of these bleedings stopped with medical management [128]. If needed EGD intervention is performed. Endoscopic interventions are not contraindicated during pregnancy (see Chap. 2). Johnston, in a period between 1939 and 1953, found two with duodenal ulcer, one complicated by hemorrhage and one by perforation [135]. Bleeding ulcer responded to conservative management.

11.4.5.2 Surgical Treatment

In general population the type and location of bleeding peptic ulcer dictates the type of surgical procedure. Due to only several cases operated during pregnancy, these surgical principles should be applied in pregnant patients. Durst and Klieger in 1955 reported a case in which hemorrhage from a gastric ulcer occurred at term and continued after delivery; late consent was given for emergency surgery, and death occurred during the operation [129]. In 1957, Vasicka reported a case of massive gastrointestinal hemorrhage from peptic ulcer. Gastric resection with gastroduodenostomy was performed in the 20th week of gestation. This was the first reported case of surgical intervention for this complication during pregnancy. Hypertension, albuminuria, and vaginal hemorrhage developed in the 28th week, and a viable infant was delivered by Cesarean section during the 33rd week [132]. In the third case, a Spanish girl, already in labor, was bleeding from a gastric ulcer. Cesarean section was performed, but the fetus was dead. The operation was continued by performing partial gastrectomy, and the patient recovered [130]. Ulcer pain in aged 23 in 28 week pregnancy occurred only during her second and fourth pregnancies. It is also remarkable that the fetus survived such a massive hemorrhage in the mother and that the pregnancy continued to term, 8 weeks after emergency partial gastrectomy [131].

There are three known cases of surgical treatment for hemorrhage from duodenal ulcer occurring during pregnancy. In one case vagotomy and pyloroplasty were performed [136], and another two cases partial gastrectomy was made [127].

11.4.6 Prognosis

Maternal mortality from 1905 to 1955 was 83 % and from 1905 to 1962 lowered to 71 % with fetal mortality 60 and 67 %, respectively (one case did not report fetal outcome) [131]. Due to the extreme rarity of the disease, maternal mortality, in studies during the first half of the twentieth century, was also evaluated in cumulative pregnancy or puerperal deaths. MacNalty found in 770 puerperal deaths in 1937 only one death from hemorrhage due to gastric ulcer [137]. Hooker studied 350,000 pregnancies over a 3-year period (1930–1932) and found only one death from perforation of a gastric ulcer [138]. Sandweiss studied 70,310 pregnancies seen in the 10-year period (1928–1937) in various Detroit hospitals and found one death due to perforated duodenal ulcer [139]. In 1943, Sandweiss, in a review of the literature on deaths due to perforation and hemorrhage from gastroduodenal ulcer during

Table 11.4 Reported cases of hemorrhage from peptic ulcers during pregnancy 1905–1962 [131]

Authors	Week of pregnancy	Lesion	Mother outcome	Fetal outcome
Le Play (1905)	7th month	Gastric ulcer	Died	Abortion
Mulsow and Brown (1936)	35th week	Duodenal ulcer	Died	Lived (twins)
Ministry of Health [137]	Puerperium	Gastric ulcer	Died	Not recorded
Le Winn (1947)	37th week	Duodenal ulcer	Lived	Died
Johnston [135]	Labor	Duodenal ulcer	Died	Died
Durst and Klieger [129]	Term	Gastric ulcer	Died	Lived
Stevenson [130]	Term	Gastric ulcer	Lived	Died

pregnancy and the puerperium, found only 14 cases. In seven cases they were gastric ulcers, and in seven duodenal. All of the 14 patients died postpartum, and premature delivery occurred in four [140].

Carangelo reported four cases of massive gastrointestinal hemorrhage in pregnancy, with three deaths [134]. Three of the four patients had an eclamptic syndrome with hypertension, edema, convulsions, oliguria, and albuminuria, and all four had a septic course with fever. The onset of labor in three of the patients occurred between 24 and 48 h after the onset of hematemesis. There were three stillbirths and one premature but viable infant.

Reports of only seven cases of hemorrhage from proved ulcers could be found in the literature (Table 11.4). Two of the mothers survived, and not more than three of the pregnancies produced live births [131].

11.5 Mesenteric Ischemia

11.5.1 Mesenteric Vein Thrombosis

> *… not everyone is aware that violent abdominal pain, ileus, and collapse may mean mesenteric vascular occlusion…*
>
> Warren and Eberhard, 1935

11.5.1.1 History

Mesenteric vein thrombosis (MVT) was first summarized as a cause of intestinal infarction in 1895 by Elliot, who treated the infarcted bowel with resection, creating two stomas and reanastomosing those 2 weeks later. Elliot stated that the patient had thrombophlebitis. He collected 14 cases of MVT from the literature [141]. In 1898, Köster

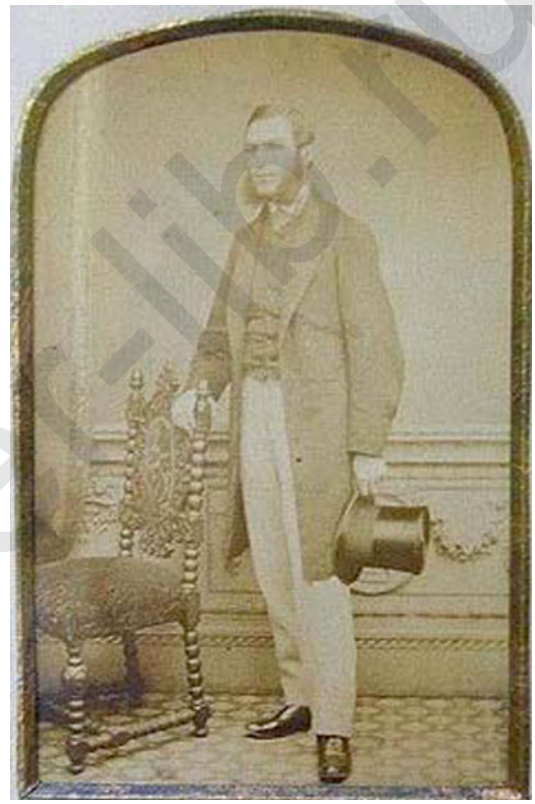

Fig. 11.6 Charles Hilton Fagge (1838–1883) (Courtesy of the Gordon Museum, King's College London)

in his inaugural address at Gothenburg reviewed the literature and described three further cases of mesenteric venous occlusion [142]. Charles Hilton Fagge (Fig. 11.6), at Guy's Hospital, London, published the first case in puerperium in 1876 [143]. A woman died a month after delivery in a few hours after the onset of severe abdominal symptoms. Autopsy showed thrombi in the superior mesenteric veins extending into the trunk of the portal vein nearly to the point where it breaks

up into its branches. The thrombosis extended into the veins beyond the territory that was congested. There was no endocarditis or any evidence of peritonitis or any cause for internal strangulation found. The report by Warren and Eberhard [144] helped to establish MVT as a distinct clinical entity. It has been classified clinically as primary (idiopathic) or secondary [145].

11.5.1.2 Incidence

MVT is an extremely rare condition in general population and accounts for 0.002–0.06 % of all inpatient admissions [146], 0.01 % of all emergency surgical admissions, and <1/1,000 laparotomies for acute abdomen [147]. Abdu et al. found in their literature review of 372 cases of MVT in general population (1911–1984) that the condition was most common in the sixth and seventh decades of life [148]. In contrast, recent series in general population found the average age to be between 45 and 65 years [149–154]. In the study by Rhee and Gloviczki [155], MVT comprised only 6.2 % of all patients treated for mesenteric ischemia in general population. In autopsy studies, MVT is found in 0.2–2 % of the population in general [144, 146]. In a study by Ottinger and Austen, MVT was found in less than 1 % of patients with mesenteric ischemia [146].

In pregnancy and puerperium, up to 1963, there were 15 cases described [156–159]. Of these, 27 % (4/15) followed abortions, 13 % (2/15) occurred during pregnancy, and 53 % (8/15) during the puerperium. One case was not proved. After 1963, similar number of patients is described [55, 160–168].

In general population, Milch and Masotti in 1936 stated that in mesenteric arterial thrombosis, the superior mesenteric artery is involved 40 times more often than the inferior mesenteric artery [169], while Jackson et al. in 1904 stated that in cases with venous mesenteric occlusion alone, 99 % occur in the superior mesenteric vein [170]. The venous collateral circulation of the inferior mesenteric vein is more elaborate than that of the superior - therefore MVT of the inferior mesenteric vein, followed by infarction of the descending colon, it is exceedingly rare.

11.5.1.3 Risk Factors

Three factors, usually referred to as Virchow's triad, are concerned in the formation of every thrombus. These are damage to vascular endothelium, changes in the velocity and character of the local bloodstream, and changes in the constituents of the blood. MVT is a very uncommon surgical pathology frequently associated with known coagulation defects [160, 162, 165, 166, 171–173]. The maternal risk of thromboembolic episodes is increased eight times in the presence of any one of the coagulopathies [174]. The incidence of the factor V Leiden mutation may be as high as 46 % in patients with a history of venous thromboembolism during pregnancy [175].

The presence of MVT is found also when there is no detectable coagulation error and is extremely rarely encountered in pregnancy [166, 176, 177]. This condition is attributed to physiological hypercoagulability which occurs during pregnancy due to multiple factors including rise in factors VII and VIII and fibrinogen and reduction in fibrinolytic activity [176]. But a rise in platelet count together with an increase in platelet stickiness maximal on the 12th day of puerperium has been demonstrated [178]. There are only four cases in the literature with no precipitating factor for the development of MVT and is called *primary* (*idiopathic*) *MVT* [166, 176, 179, 180].

Specific group of MVT has been reported in pregnancy in association with certain surgical and medical comorbidities [165] which include repeated abdominal surgery, Cesarean section, appendectomy for gangrenous appendicitis, elective laparoscopic cholecystectomy, mesenteric cyst excision, vesicoureteral reflux, and mistaken intake of oral contraceptives during pregnancy (Table 11.5) [168, 181]. MVT caused by postoperative stasis in general population was first described by Maylard in 1901 [186].

Reed and Coon reported the first case of MVT from oral contraception in 1963 [187]. Other cases have been infrequently described [181, 188–190]. Hoyle et al. discussed 21 cases, 9 had been taking 0.05 mg estrogen, and the rest had taken higher doses [188]. Twelve had been taking the agent for more than a year, and two had suffered MVT in the first cycle. The problem with

Table 11.5 Primary (idiopathic) and secondary MVT with known risk factors in pregnancy and puerperium

Hypercoagulopathies [160, 161]
Oral pills during pregnancy or puerperium [55, 56, 181]
Postoperative
Single or repeated abdominal surgery [182, 183]
Cesarean section [162]
Cytomegalovirus infection (with complications) [163]
Chronic idiopathic MVT [164]
IVF pregnancy [184, 185]
Hemoglobinopathy [165]
Primary (idiopathic) [166, 176, 179, 180]
Smoking
Obesity
β-thalassemia
Antiphospholipid syndrome
Abnormal fibrinogen
Homocystinuria
Paroxysmal nocturnal hemoglobinuria
Thrombocythemia
Abdominal trauma
Abdominal sepsis
Myeloproliferative disorders
Cancer

association of risk factors and MVT is that patients sometimes have additional risk factors like heavy smoking [181]. Even in this case by Graubard and Friedman with two risk factors, BMI of the patient was not mentioned which is also a possible additional risk factor.

The anatomic location of venous thromboembolism associated with IVF cycles has been suggested to differ from those seen in the general population. In venous thrombosis associated with IVF, the veins of the upper extremities and neck are involved in 80 % of reported cases, whereas only 11 % of deep vein thrombosis diagnosed in the general population involves the upper extremities [191]. Further, 97 % of upper extremity deep vein thrombosis reported in the literature during pregnancy was associated with assisted reproductive technology [192].

11.5.1.4 Clinical Presentation

Clinical symptoms of *acute* MVT are variable, nonspecific, and difficult to differentiate from arterial occlusion. In most cases of acute MVT, the main symptom is abdominal pain lasting from several days to more than 3 months [157], first cramp-like before becoming continuous when peritonitis supervenes. They continued to have bowel movements initially, becoming constipated later. Patients had pain out of proportion to abdominal tenderness. This was noted by Berry and Bougas, who believed it as an important differential point in diagnosis [193]. Other symptoms are nausea/vomiting, fever, and abdominal distention. The tendency toward hemoconcentration was also seen in their patients and probably reflects slow progress of the disease, allowing sequestration of extracellular fluid in the gut. Donaldson and Stout state that occult blood can always be found in the stools [194]. On rectal examination, there may be blood on the examining finger. If hematemesis in acute form is found, then splenic vein thrombosis is present. On the other hand, splenic vein thrombosis is not necessarily followed by hematemesis [195].

Subacute or *chronic* MVT is usually asymptomatic due to the development of collateral vessels, but when it is combined with portal vein thrombosis, esophageal variceal bleeding with hematemesis may occur [150, 196].

Most patients in general population using oral contraception had at least 2 weeks of symptoms such as abdominal pain, discomfort, anorexia, vomiting, and change in bowel habits [189, 197, 198].

Sometimes the leading presentation can be spontaneous abortion or stillbirth [157].

11.5.1.5 Diagnosis

Clinical diagnosis of MVT is usually difficult, and it is frequently delayed due to lack of awareness among primary physicians and absence of active signs in early stages of the disease. Furthermore the early features of the disease get masked by the effects of pregnancy. Early diagnosis is possible only if high degree of suspicion is exercised in cases of severe abdominal pain with the absence of positive physical signs. In general population, in 1914, in only 4 % of patients the condition was diagnosed preoperatively [199].

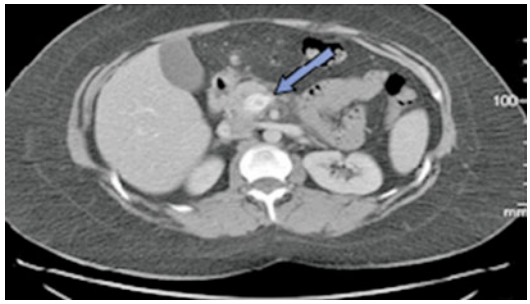

Fig. 11.7 CT scan with superior mesenteric vein thrombosis (*blue arrow*) in a patient on IVF program [185]

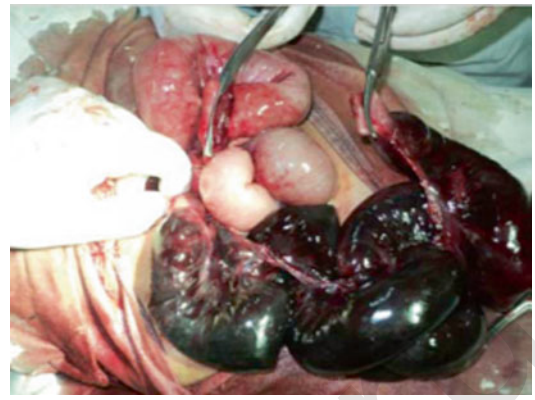

Fig. 11.8 Gangrenous ileal segment due to mesenteric vein thrombosis [177]

Almost all patients present with leukocytosis with elevated hematocrit, but these are not helpful for diagnosis [200]. Grieshop et al. reported an 80 % incidence of elevated white cell count in cases of MVT in general population [201].

The diagnosis can be confirmed with color Doppler ultrasound [173] which is widely available, cheaper, feasible for emergency imaging, and applicable in pregnancy due to lack of need for X-rays or potentially harmful intravenous contrast, but this modality requires expert hands, and some studies have shown this modality to have only 70 % sensitivity [149].

Contrast-enhanced abdominal CT in general population currently holds a sensitivity of >90 % and is the most common diagnostic test of choice (Fig. 11.7). Magnetic resonance imaging offers no distinctive advantage over CT [150].

Some authors claim that angiography findings in general population of veno-occlusive disease are less sensitive. In recent studies, angiography showed only 55 % sensitivity and has not been suggested as a primary diagnostic modality [150, 202].

Often, definitive diagnosis is made during surgical exploration mostly due to acute abdomen. If there is no strangulation, volvulus, mesenteric thromboembolism, or cocaine abuse should be excluded [53].

11.5.1.6 Treatment

Management involves multiple disciplines including surgery, clinical hematology, obstetrics, and neonatology and depending on the presentation of a particular case. Most importantly, the treatment depends on the stage of the disease [150].

Surgery

Explorative laparotomy is indicated for patients with symptoms and signs of acute abdomen or suspected or confirmed intestinal infarction (Fig. 11.8) by diagnostic modalities. Pielliet is reported by Elliot as being the first to perform a successful resection for venous occlusion in general population and published his findings in 1895 [141]. During operation, fresh and organized thrombi are found extruding from the veins, while arteries are constricted but patent [182]. Consideration should be given to the use of intra-arterial papaverine to reverse (arterial) spasm [202] and thrombolytic agents via operatively placed catheters [203, 204] which, together with continued heparin, may prevent extension of infarction (see further paragraphs for pregnant population).

If there are segmental gangrenous segments, minimal resections should be performed to minimize the possibility of short bowel syndrome. Multiple resections with anastomoses with or without proximal stoma are recommended. Another option after multiple segmental resections is to close (potentially) viable bowel segments by stapling and abdomen left open with vacuum-assisted closure (VAC) with 125 mmHg continuous negative pressure (Fig. 11.9) in the aim of assessing the viability of remaining bowel after 24 and 48 h [168].

At the second and third surgical looks, some intestinal segments could require subsequent additional resections. Eventually, after 48 h of

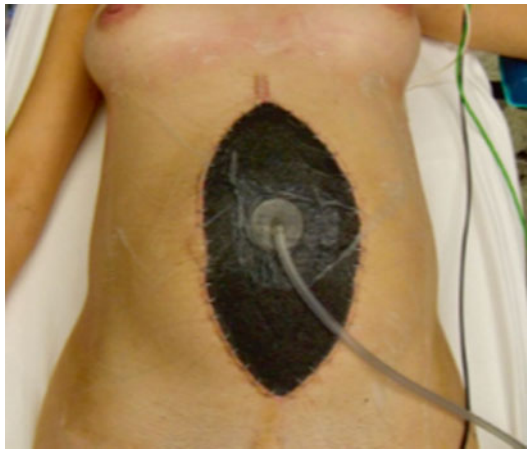

Fig. 11.9 Open abdomen with vacuum dressing [168]

open abdomen management, the intestinal continuity should be restored. Abdominal wall should be primarily closed without aponeurotic defect.

The rare cases of laparostomy use in pregnant women previously reported have not been successful in terms of fetus or mother issue [205]. There are two case reports of favorable outcome after laparostomy as a treatment of wound dehiscence in pregnant women [206] and second- and third-look operations due to mesenteric ischemia [168]. In both cases VAC was included as a part of treatment process. Among many techniques developed for open abdomen management, VAC allows currently the best results in terms of primary abdominal wall closure [207]. In some series of nonpregnant patients, using VAC protocols, complete fascial closure rate was achieved in 100 % [208]. In abdomen with constantly growing gravid uterus and low intra-abdominal pressure requirements, primary closure appears to be a particularly challenging task. It is nevertheless a key endpoint in a pregnant woman, in order to protect the fetus and to assure a vaginal delivery.

As the enlargement of the spleen in protein C deficiency and its gastric pressure could become prominent together with anemia and leukopenia in addition to mild-severe thrombocytopenia, splenectomy seems to be an appropriate choice together with the periodic use of protein C concentrate [209].

Thrombectomy

Other treatments such as peripheral or regional thrombolysis with or without surgical thrombectomy and a combination of surgical thrombectomy and regional heparinization have been reported in general population [210–213]. There are anecdotal reports of venous thrombectomy, but this has not shown improved outcome and is generally not recommended [214, 215]. In pregnancy, treatment with thrombolytics is not advocated [176].

Anticoagulation

In the patients without bowel infarction or peritonitis, anticoagulation with heparin followed by warfarin after delivery is the mainstream therapy [150]. Two of the first proponents of anticoagulation therapy in general population were Murray in 1940 [216] and Strohl and Lasner in 1948 [217]. Anticoagulation for MVT has been shown to be associated with improved outcome by Naitove and Weisman in 1965 when mortality was 50 % for those who did not receive anticoagulants compared with 0 % for those who received postoperative anticoagulation [218]. Heparin has been shown to prevent recurrence of thrombosis after intestinal resection (14 % vs. 26 % [148] and 0 % vs. 19 % [219]) and to be associated with lower mortality when recurrence does occur (22 % vs. 59 % [148]). In anticoagulated patients not undergoing surgery, most thrombosed veins will partially or completely recanalize over time. In one study, 80 % of anticoagulated patients with mesenteric and/or portal vein thrombosis showed vascular recanalization over a mean follow-up time of 5 months compared with <10 % of non-anticoagulated patients [220]. During pregnancy LMWH is recommended in order to avoid the possible side effects of warfarin on the fetus, especially its teratogenic and bleeding effects. There are no defined guidelines for the duration of anticoagulation after pregnancy, and decisions on a case-by-case basis need to be taken by expert clinical hematologists [176]. In patients with inherited hypercoagulable disorders (i.e., protein S, protein C, antithrombin III deficiencies, and factor V Leiden mutation), lifelong anticoagulation is warranted. For patients with

reversible predisposing causes, at least 6 months of anticoagulation is recommended [221].

A review in *Thrombosis Research* published guidelines for anticoagulation management strategies for various clinical situations before and after controlled ovarian stimulation [222]. Patients with a history of prior MVT should be placed in the clinical classification of "previous episode(s) of venous thromboembolism receiving long-term anticoagulation." It is recommended switching from oral anticoagulants to LMWH therapy (e.g., enoxaparin 1 mg/kg every 12 h) before controlled ovarian stimulation and continuing this regimen throughout pregnancy [222]. These authors recommend refraining from the administration of LMWH for 24 h before egg retrieval and restarting therapeutic anticoagulation 3 h after egg retrieval [222]. In the setting of IVF, associated MVT, and the absence of large studies, lifelong oral anticoagulation in patients at low risk for bleeding and full anticoagulation with LMWH per the above protocol during repeat IVF cycles is considered prudent.

However, controversy in management for the prevention of venous thrombosis still exists after delivery. Though the induction of oral anticoagulation in protein C deficiency has been widely used, it carries significant risks in a patient with esophageal varices and thrombocytopenia [209].

Obstetric Management

Continuation of Pregnancy

The decision on continuation or termination of pregnancy is taken as per the case and available facilities. While workers like Engelhardt et al. [166] and Fouad et al. [176] successfully continued the pregnancy, Lin et al. and Foo et al. terminated the pregnancy [179, 223]. In one recent case report with several operations due to gangrenous bowel and open abdomen, the pregnancy was uneventfully carried to full-term vaginal delivery [168].

Mode of Delivery

If the pregnant woman has proven PVT, every effort should be made to prevent further complications during and after delivery. The straining and bearing down that take place during vaginal delivery have also been reported to result in a marked but transient portal vein pressure in all pregnant women. Thus, the avoidance of vaginal delivery and the use of Cesarean section should minimize the portal vein pressure increase and reduce the possibility of variceal bleeding [209, 224].

11.5.1.7 Prognosis

The prognosis of MVT does not appear as ominous as that associated with arterial thrombosis in general population [150], but mortality in general population was 60 % in the beginning of the twentieth century, lowered to 34 % in 1935 [144]. Currently, the mortality in general population is in the range of 13–50 % [203, 225–227]. In general population, the subgroup with oral contraception as the cause had high rates of the mortality and morbidity in the review from 1977 – 50 % of the patients died and 50 % required at least two operations. Arterial thrombosis carried twice the mortality of venous thrombosis but was half as common [190].

In pregnancy, up to 1963, out of 15 described cases mortality was 87 % (13/15), and the two patients that survived were from the last year (1963) of the analyzed period [156, 157].

11.5.2 Portal Vein Thrombosis

11.5.2.1 Introduction

Portal vein thrombosis (PVT) shares the same or similar characteristics as MVT inclusion localization, risk factors, diagnosis, and therapy.

11.5.2.2 Incidence

PVT is even rarer in pregnancy than MVT with only few cases published [209, 228–230]. One case was in the first trimester [229], two in the second trimester [228, 230], and one in the third trimester [209].

11.5.2.3 Risk Factors

Risk factors are the same as for MVT (Table 11.5) which are the same as for MVT during pregnancy. Concurrence of several disorders seems to be relatively common in PVT in adults, and extensive investigation should be considered in

these patients [231]. Probably the only risk factor more influential on the development of PVT than MVT is cirrhosis, but due to extremely low incidence of both conditions in this age group, the conclusions cannot be made.

11.5.2.4 Clinical Presentation

Clinical presentation is different from MVT. Mostly patients present with short history of acute right hypochondrial pain that lasts from hours to several days and fever of around 38 °C [229]. The signs include tachycardia, fever, and tenderness in the upper right abdominal quadrant without peritoneal irritation.

11.5.2.5 Diagnosis

Abdominal Ultrasound/Doppler

Diagnosis is made by ultrasound or more specifically by Doppler. Unlike contrast CT and helical CT associated with CT angiography, color Doppler does not involve potentially harmful intravenous injection of contrast [232, 233]. Also, unlike MRI and 3D magnetic resonance portography with contrast, color Doppler is more widely available, cheaper, and feasible on emergency basis [234, 235].

Urgent abdominal ultrasound is sometimes performed to rule out acute cholecystitis but can demonstrate well-defined homogenous hyperechoic oval-shaped formation in the splenomesenteric confluence and/or branches of the portal vein. Color Doppler study confirms these findings by showing margination of the colored flow in the residual lumen. Splenic and mesenteric veins should be visualized because their thrombosis could lead to bowel ischemia. The hepatic artery shows increased compensatory flow. Collateral venous circulation should be verified or excluded because it helps establishing definitive diagnosis. The color Doppler sonographic features of acute thrombosis in portal vein or superior mesenteric vein are as follows:

1. The thrombosed vein usually displays an echogenic appearance (70 % of the cases in general population) [236]. Ultrasound study shows a dilated vein with loss of respiratory motions and venous distension upstream of the thrombosis. Transient ascites may be seen denoting an acute portal hypertension. Color Doppler confirms the diagnosis by demonstrating either the absence of intraluminal colored flow in case of complete thrombosis or eccentric or marginated colored flow in case of partial thrombosis. Also Doppler study demonstrates an increased compensatory flow in hepatic artery as well as periportal collateral venous circulation that may develop after 1 week [236].
2. Alternatively the thrombosed vein displays an anechoic appearance (20–30 %). Ultrasound may miss the thrombus, and color Doppler constitutes the modality of choice as it enables demonstration of the colored filling defect within the venous lumen [236].

When PVT is confirmed by Doppler, complete coagulation profile should be obtained.

11.5.2.6 Treatment

Anticoagulation

Prompt treatment of PVT is essential in order to prevent extension to superior mesenteric vein, splenic vein, and hepatic vein which could lead to the development of hepatic or mesenteric infarction [232, 237]. Prompt treatment could also prevent progression to portal hypertension with risk of variceal hemorrhage [209, 238, 239]. Furthermore, early treatment could result in complete lysis of the clot, and the resolution of the clot could be as early as 4 days, but could take up to 1 month.

Interventional Techniques

Some authors have reported the use of fibrinolytic infusion by the systemic route, transhepatically, or via the superior mesenteric artery with controversial results [240–242].

Percutaneous interventional techniques such as balloon dilatation and stenting have been effective in some cases with acute, recent PVT; however, these treatment modalities do not prevent rethrombosis [241]. Therefore, patients at risk should be kept on prophylactic anticoagulants for life in order to prevent rethrombosis.

Response to Therapy

Response to therapy in pregnant patients cannot be estimated due to extremely small number of patients, but color Doppler provided reliable means of monitoring response to therapy of the PVT [229].

11.6 Inferior Epigastric Artery Bleeding

11.6.1 Anatomy

The inferior epigastric artery (IEA) arises from the external iliac artery deep to the inguinal ligament. It both serves as a surgical landmark and constitutes a potential target for injury during inguinal hernia repair. The IEA divides deep to the rectus sheath into two branches: an ascending branch that anastomoses at the umbilicus, medial to the rectus sheath, with the abdominal branch (or superior epigastric artery) of the internal thoracic artery, and a descending branch that gives off obturator branches that course along the ischium and anastomose with the obturator artery and pubic branches, which in turn course along the pubic rami and reach the pubic symphysis [243].

11.6.2 Mechanisms of Injury

11.6.2.1 Direct Trauma

Direct injuries of the IEA include *blunt trauma* [244] or *penetrating abdominal wall trauma*. Direct blunt injuries as well as indirect injuries can cause damage to the artery probably by stretching of the artery over its elastic properties causing avulsion with subsequent bleeding [245]. Penetrating abdominal wall trauma during interventions including Cesarean section, paracentesis [246], and insertion of trocars during laparoscopy [247] causes direct injury to the IEA. Injuries to the ascending branch are well documented and usually occur after direct trauma to the abdominal wall, for instance, during laparoscopic surgery, subcutaneous injections, insertion of lumboperitoneal shunts, or ascites fluid aspiration [248–250]. In one of the Indian studies, 95.5 % of patients with injury of IEA had intrapartum Cesarean delivery, while 4.5 % had an elective operation. Therefore, emergency Cesarean section is a risk factor for IEA bleeding [251]. During Cesarean section, care during transverse cutting and suturing of lateral extension of rectus sheath is advised [252].

11.6.2.2 Spontaneous

Rarely, the ascending branch may rupture spontaneously, most notably in patients taking anticoagulant medications, after lifting heavy weights, coughing, or straining. Thus, tearing of the branches of the epigastric vessels is a well-known cause of rectus sheath hematoma (see Sect. 11.6.8) [253–255].

11.6.2.3 Blunt Pelvic Trauma/Fracture

In contrast, there have been only five reports in nonpregnant population of massive bleeding from the pubic branch of the IEA in patients with pubic rami fractures caused by blunt pelvic trauma [256–259].

11.6.3 Incidence

Early reoperation rate after Cesarean section in India is 0.45–0.6 % [251, 252]. In two Indian studies with early relaparotomy after Cesarean section, rectus sheath hematoma was found in 21–27 % of cases [251, 252]. In Western countries this is an extremely rare condition during pregnancy with only several case reports after Cesarean section [244, 260, 261]. Incidence of spontaneous IEA bleeding is lower due to several reasons:

- Pregnant women are more cautious and are not exposed to blunt or penetrating abdominal/pelvic trauma as general female population (more at home, less car driving).
- Avoidance of heavy lifting.
- Avoidance of closed spaces and people with infectious diseases mostly respiratory conditions.
- Lower incidence of surgical or other invasive interventions during surgery.

11.6.4 Clinical Presentation

Clinical presentation depends on the severity of the injury and the timing of the incident. If observed intraoperatively and IEA itself is injured/transected, then significant bleeding is present. If the peritoneum is intact, then

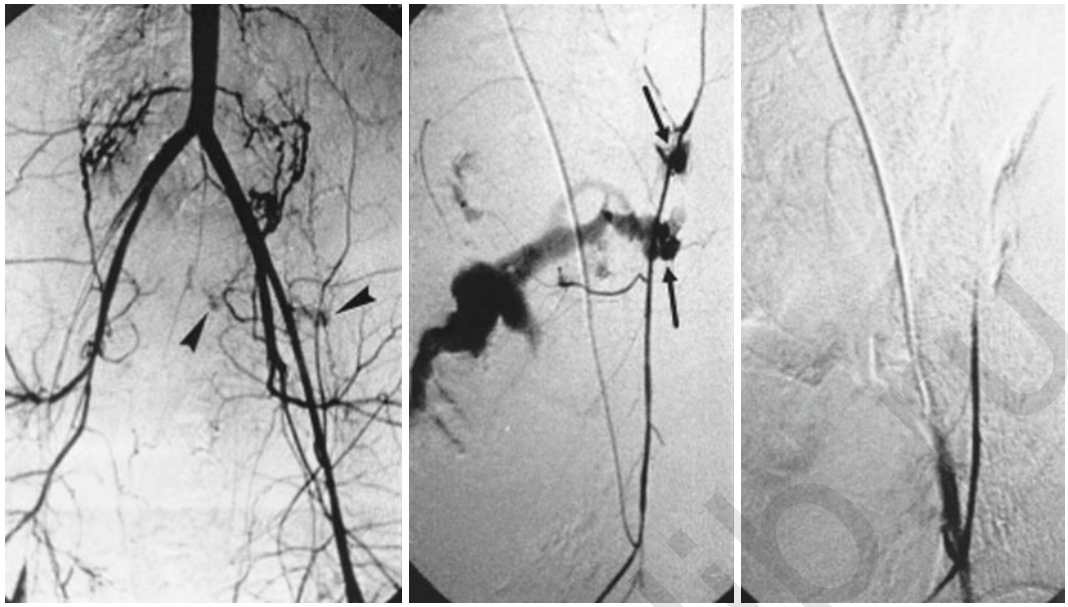

Fig. 11.10 *Left*, aortoiliac arteriogram showing suspicious abnormal stains (*arrowheads*) in the left side of the pelvis. *Middle*, selective left inferior epigastric arteriogram showing massive bleeding from two injured portions (*arrows*). *Right*, complete occlusion of bleeding points after embolization [260]

large subperitoneal hematoma is found. If the peritoneum is damaged, significant bleeding into the abdominal cavity from the abdominal wall is found. If the bleeding is not observed intraoperatively, then the severity of the clinical presentation depends on the caliber of the artery that is injured. If IEA is damaged, then immediately after the operation there will be symptoms and signs of significant blood loss and hemorrhagic shock: tachycardia, lowered blood pressure, increased pulse rate, pallor, and cold sweat. Additionally the patient will have distended and painful abdomen. On inspection hematoma over the IEA is found.

11.6.5 Differential Diagnosis

Spontaneous rupture presents significant diagnostic problem because skin changes in smaller hematomas could be absent, and the patient presents with acute significant pain with peritoneal irritation which mimics intra-abdominal conditions such as appendicitis, diverticulitis, cholecystitis, tumors, and visceral injuries [255].

11.6.6 Diagnosis

The IEA represents a potentially overlooked source of pelvic arterial hemorrhage. The IEA should be considered as a possible source of arterial hemorrhage if arteriography of internal iliac artery branches does not yield a bleeding source [244].

11.6.7 Treatment

11.6.7.1 Transarterial Embolization

Almost all cases of bleeding IEA after Cesarean section are treated by transarterial embolization (Fig. 11.10) [244, 260, 262]. In only one case by Randall et al., the patient was treated conservatively (abdominal CT was used for the diagnosis) [261].

11.6.7.2 Analgesia

Most patients are treated with peroral NSAIDs and/or opioids for pain relief. There is one case of transversus abdominis plane block for severe pain eliminating large dosage of peroral pain killers [261].

11.6.8 Spontaneous Rectus Hematoma

11.6.8.1 History

Rectus sheath hematoma (RSH) is an ancient disorder first being accurately described by Hippocrates and mentioned by Galen. The first reported case in the United States was by Richardson in 1857 [263]. In 1882, Karl Maydl, of Vienna, wrote a most valuable series of articles on the subcutaneous tearing of muscles and tendons [264]. He devoted much attention to the tearing of the rectus abdominis muscle and tabulated his cases. In 1918, Emerson recorded a case of rupture of the deep epigastric artery due to muscle strain. Perman was the first to write a comprehensive article on hematoma in the sheath of the rectus abdominis muscle. In 1925, Carey Culbertson reported two cases of *hematoma occurring spontaneously in the sheath of the rectus abdominis muscle, with consideration of its gynecological and obstetrical significance* [265]. First Thomas Stephen Cullen (Fig. 11.11) in 1918 described bluish periumbilical discoloration due to ruptured ectopic pregnancy and then with Brödel in 1937, at Johns Hopkins Hospital, reported two cases of spontaneous hematoma of the rectus abdominis during pregnancy [266, 267]. Both were black patients. Resolution was uneventful in one with a 7-month pregnancy, but operative exploration was carried out on the other with success.

11.6.8.2 Incidence

Maxwell in 1929 found 11 cases [268]. Of these, 73 % (8/11) were during pregnancy and 27 % (3/11) during labor. Torpin in 1943 analyzed 27 reported cases in pregnancy [269]. In 1946, Teske reported a case and analyzed 100 cases from the literature in general population. He showed that 60 % are on the right side and more than 80 % in the lower quadrants [270]. Aird stated that only about 150 cases have been reported up to 1949 [271]. Riera et al. in 2009 claim that there are 52 cases of the condition during pregnancy described [272]. There are numerous case reports during the last several decades [273–283].

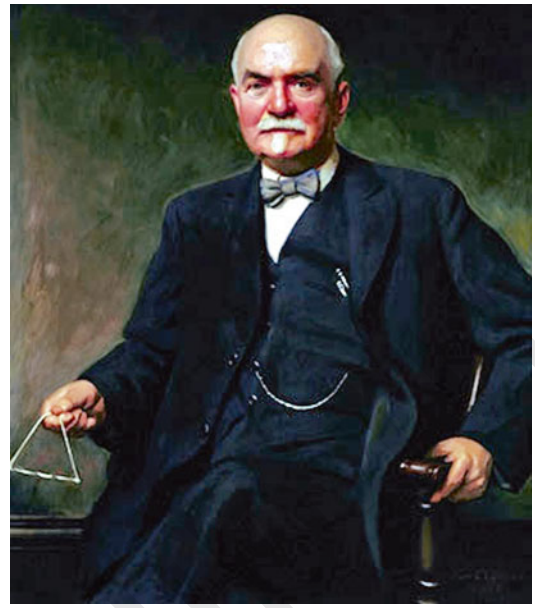

Fig. 11.11 Thomas Stephen Cullen (1868–1953); painting by Thomas C. Corner; oil on canvas, 48 by 40 in., 1907 (Courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions)

11.6.8.3 Mechanism

The condition occurs mainly in multipara and late in pregnancy. It has also been described in the puerperium and even within half an hour of delivery and expulsion of the placenta. In almost all cases in pregnancy, there was some evidence of trauma from labor, from coughing, or from a fall. Muscle degeneration from influenza or typhoid is a possible cause. The precipitating factor in most spontaneous cases seems to be inelasticity of the wall of an artery or vein which prevents the vessel from accommodating itself in a movement, a cough, or a sneeze or, in or after labor, to the remarkable variations in length which the rectus muscle undergoes between extreme contraction and extreme relaxation. According to Brodel, there is only one major vessel to take care of this long stretch of muscle, and in order to avoid damage to itself, it must keep away from the muscle so far as possible and send its branches into the muscle substance in such a manner that the muscle action does not interfere with vascular freedom. The larger intramuscular arteries branch freely and form numerous anastomoses. They run

at an angle varying from 60° to 90° to the axes of the muscle bundles. If an occasional artery runs parallel to the muscle bundle, it shows greater tortuosity. The arteries are less apt to tear than the veins, because they are far more resistant. They lie and so loosely embedded in the intramuscular connective tissue that they can be pulled out quite far without injury, but not so with the veins. They are frail, of smaller caliber, and have a much thinner wall. Tears may be partial or complete. In a partial tear only branches of the main vessels rupture beyond their point of entrance into the muscle body, but a complete tear is apt to rupture the main trunk also.

Right-sided hematomas in general population are presumably more common because more people are right handed and, thus, are more prone to right-sided strain of the rectus muscle during strenuous activity. The lower quadrants are more frequently involved because of the long vascular branches that are present and because muscle excursion during contraction with the absence of the tendinous inscriptions is greater [270].

11.6.8.4 Classification

Three types of RSH in general population can be distinguished by computed tomography appearances. *Type I* is unilateral and contained within the muscle; *type II* is uni- or bilateral and has blood between the muscle and transversalis fascia; *type III* invades the prevesical space or peritoneum and may or may not affect the muscle [284]. Until a classification in pregnancy is defined, the best option for the treatment algorithm is to adhere to the aforementioned classification.

11.6.8.5 Clinical Presentation

A history of trauma, anticoagulant therapy, and trivialities such as coughing, straining, or twisting to one side may remind the clinicians of this diagnosis [285]. Awareness of RSH during pregnancy is important because the abdominal wall is easily overlooked as a cause of acute abdominal pain [286, 287], given the higher prevalence of other pregnancy-associated pain.

Among the clinical findings, premonitory vague discomfort at the site of bleeding is common with the lesser degrees of hemorrhage. Probably a great number of the hematomas are small, unnoticed, and consequently unreported. In most recorded cases the hematoma was limited to the rectus sheath, and pain and tenderness were felt over the bleeding area. Muscle rigidity is often marked in the involved rectus, but in small hemorrhages there is little more than a local tenseness in the muscle. Swelling and palpable firm, nonpulsatile mass is usually confined to the affected muscle sheath. Swelling of the hematoma is limited to the rectus abdominis muscle, with its sheath not extending beyond the abdominal midline or the lateral borders of the muscle (*Romanzew's sign*). However, below the arcuate line, the posterior sheath may communicate, and the mass may project across the midline or extend inferiorly and posteriorly toward the bladder. In some cases the hemorrhage escaped the limits of the muscle sheath and extended into the broad ligament or ruptured into the peritoneal cavity. In two cases in the literature, death occurred before help arrived [288].

The hemorrhage lies initially between the transversalis fascia and the posterior surface of the rectus muscle, spreading later to surround the muscle and ascend over the linea semilunaris between the rectus muscle and its posterior sheath and sometimes downward behind the rectus. If the patient lifts her head off the pillow so as to contract the rectus, the mass can be felt confined to the rectus sheath and immovable. The mass is equally palpable with the patient lying in a supine position or partially sitting up (*Fothergill's sign*). Swollen and palpable mass is usually confined to the affected muscle sheath and severe, usually unilateral, abdominal pain that is aggravated by movement [289–292]. *Carnett's sign* is performed by first localizing the area of maximal tenderness while the patient is relaxed. While this area is being pressed, the patient is asked to raise her upper back effectively tensing the abdominal wall. Worsening of the pain is considered a positive test [285]. In 1926, Carnett recognized that abdominal pain could be caused by neuralgia affecting one or more of the lower six intercostal nerves and developed a simple test to help localize the origin of symptoms to the abdominal wall [293]. For this part of the abdominal examination, the patient

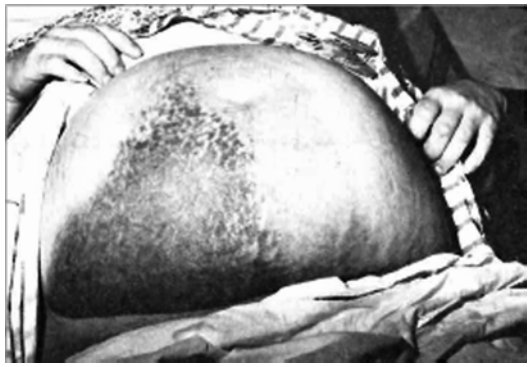

Fig. 11.12 Staining of the skin and ecchymosis are very common over the palpable mass (*Cullen's sign*) not extending over the midline [296]

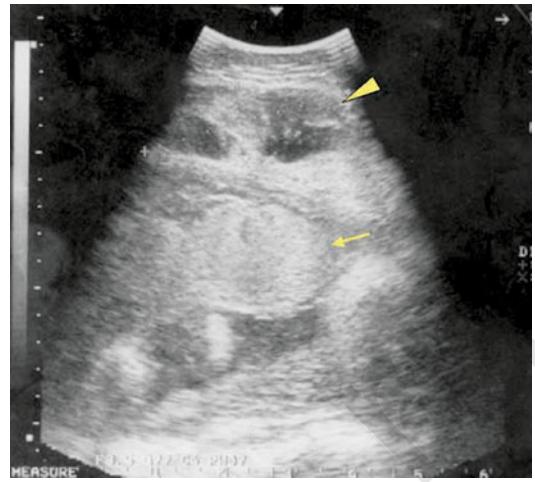

Fig. 11.13 Abdominal ultrasonography shows a heterogeneous hypoechoic mass (*arrowhead*) adjoining the placenta (*arrow*) [298]

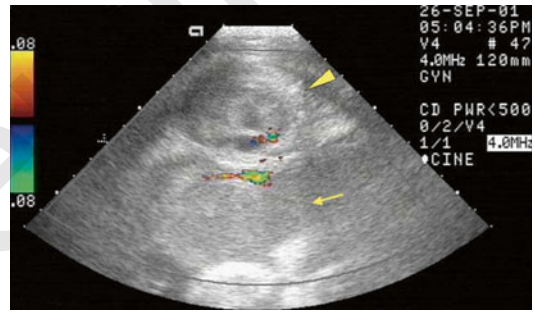

Fig. 11.14 Doppler sonography shows vascularity with blood flowing around the mass (*arrowhead*) and between the mass and the placenta (*arrow*) [298]

can be asked to lift the head and shoulders from the examination table to tense the abdominal muscles. An alternative is to ask the patient to raise both legs with straight knees. Staining of the skin and ecchymosis are very common over the palpable mass (*Cullen's sign*) [294], first described by Guthrie and Stamfey, who also found *Grey-Turner's sign* with rectus sheath hematoma [295]. They occur over the center of the hematoma, as a semicircle around the umbilicus, above the pubis, or along the linea alba (Fig. 11.12). The extravasated blood can pass more easily superficially around the medial border of the rectus. The pigments that produce this phenomenon may reach their destination by following the ordinary fascial planes but not by the lymphatics as was previously believed. In rectus sheath hematoma, ecchymosis appears after 2–5 days.

11.6.8.6 Diagnosis

The diagnosis of RSH should be suspected on clinical grounds and supported by additional imaging evidence. Abdominal ultrasonography, computed tomography (CT), radionucleotide imaging, and magnetic resonance imaging (MRI) have all been used to establish the diagnosis. Ultrasonography often shows a heterogeneous hypoechoic mass in the abdominal wall and is most useful for detecting RSH [287, 297]. Type III hematomas are large and could mimic intraperitoneal emergency such as torsion of the adnexa or placenta percreta with bleeding into the extrauterine compartment (Fig. 11.13) [298]. In unequivocal cases Doppler can aid the diagnosis showing nonvascularized structure (Fig. 11.14). During pregnancy, exposure of the fetus to radiation has limited the use of CT and radionucleotide imaging [287, 297, 299]. On the other hand, MRI appears to be a safe option (Fig. 11.15) [297].

11.6.8.7 Treatment

Conservative Treatment

Management is guided by the size of the hematoma and hemodynamic stability of the patient. Where the hematoma was small, it usually spontaneously resolves uneventfully within 1–2 weeks, although complete resolution of the hematoma

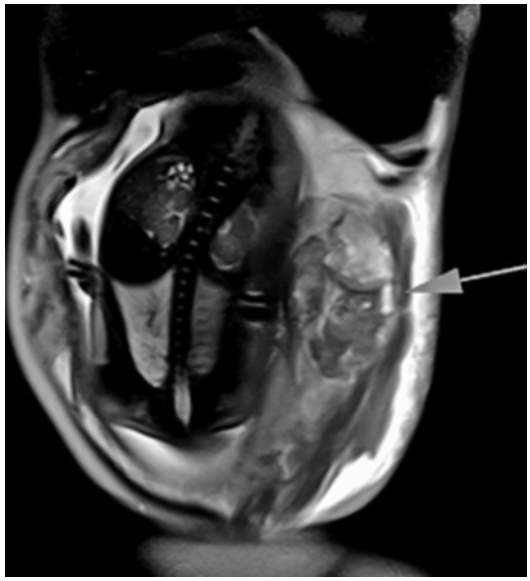

Fig. 11.15 A coronal T2-weighted magnetic resonance image showing a large left-sided rectus sheath hematoma measuring 160 × 70 × 55 mm (*arrow*). Note the subcutaneous fat stranding and a small hemoperitoneum coexisting with a fetus of 33 weeks of gestation [272]

may take as long as 2–3 months. Treatment generally consists of rest, peroral analgesia, and discontinuation of anticoagulation (if present). After resolution, RSHs usually do not recur and typically do not cause long-term sequels.

Embolization

Identification of a bleeding point is useful in guiding management; a massive hematoma that extends into the retroperitoneum may originate from a bleeding inferior epigastric vessel or may be coming from a retroperitoneal structure such as a leaking iliac or abdominal aortic aneurysm [300]. Selective percutaneous transcatheter arterial embolization is considered an effective hemostatic in the treatment of a patient with a large hematoma [272]. With regard to the safety of embolization during pregnancy, the general late onset of this pathology reduces the risks associated with fetal irradiation. The large hematoma displaces the uterus and the fetus to contralateral side reducing the dose of X-rays delivered to the fetus [272]. Selective epigastric embolization in severe RSH during the third trimester of pregnancy should be considered as the potential primary and alternative management path to classical laparotomy. However, this technique is time consuming, expensive, and not always available. This procedure is also associated with complications such as contrast-induced nephropathy [301] or bleeding from the puncture site [302]. Another disadvantage is that the bleeding vessel cannot always be identified. Further studies are required to confirm that the maternal and fetal benefits outweigh the fetal risks associated with embolization.

Surgical Treatment

In cases with rupture into the peritoneum, infection, or active bleeding with unstable hemodynamics, prompt surgical intervention is indicated. If the hematoma is very extensive and when shock is controlled, a paramedian incision with section of the rectus sheath and retraction of the muscle laterally will facilitate visualization of the bleeding vessel. Suture of the ruptured vessel or muscle should be performed. If the rupture is intraperitoneally, laparotomy is indicated to evacuate blood and clots and to control bleeding. If infection is present, evacuation of purulent material is mandatory with bacterial swabs and drains left in place.

11.6.8.8 Prognosis

In Maxwell series of 11 patients, eight were during pregnancy with 0 % maternal mortality and 37.5 % fetal mortality (additional two of eight cases do not mention fetal outcome). Three spontaneous RSHs during labor resulted in 0 % maternal and fetal mortality. In Torpin's series there was a 15 % maternal mortality and a 50 % fetal mortality [269]. Reports from the 1950s show a maternal mortality of 12 % and a fetal mortality of 25 %. In 1997, maternal mortality rate of 11 % and a perinatal morbidity rate of 34 % were reported [286].

11.7 Omental Infarction

11.7.1 Incidence

Omental infarction is a rare clinical event that affects predominantly young and middle-aged women [303]. Omental infarction was first

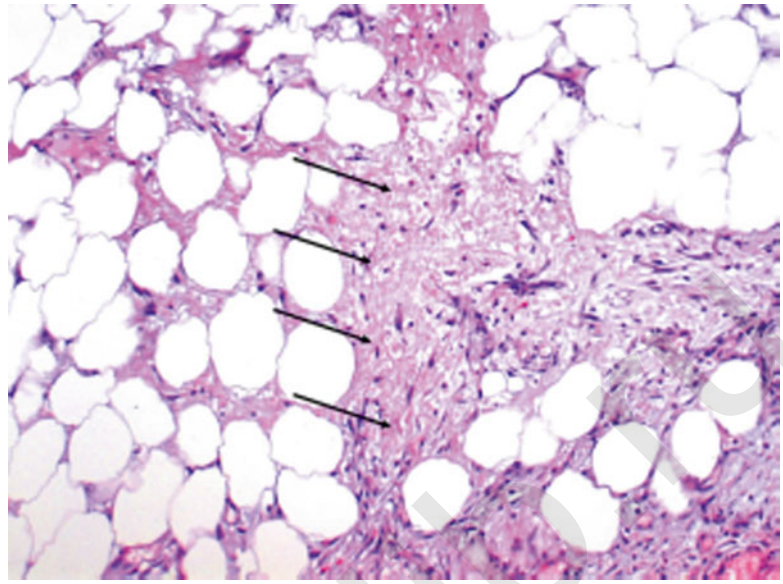

Fig. 11.16 Histological findings of major omentum show fresh hemorrhagic circulation disorders (*arrows*), partial necrosis of fatty tissue with acute inflammatory cell infiltrate (hematoxylin, 100×) [307]

reported in 1882 by Oberst [304], and, since then, only a few hundred cases have been published in the English literature [305].

There are three published cases describing omental infarction in the postpartum period – one after Cesarean section and two after vaginal deliveries [306–308].

11.7.2 Etiology

Torsion of the omentum in general population is the main reason for infarction, and two different forms have been described: primary torsions (without other pathologic intra-abdominal findings) and secondary torsions (tumors, cysts, inflammatory changes, adhesions, hernias). Predisposing factors for torsion are anomalies of the omentum, such as a small root, irregular vascular anatomy, abdominal trauma, cough, and physical strain [304].

The etiology of omental infarction without torsion remains uncertain, but several mechanisms have been proposed, such as an anomaly of the venous vessels [309]. Other possible causes for primary infarctions could be disorders of hemostasis or vascular diseases. It is known that hematological changes occur during pregnancy and the puerperium and that hypercoagulability leads to an increased risk of thromboembolic events [310]. Depending on the duration and the degree of torsion, omental necrosis ensues (Fig. 11.16).

The exact mechanism leading to infarction in puerperium remains unclear. Possible changes during the return of the mother's body to the prepregnancy physiological condition may have provoked the infarction.

11.7.3 Clinical Presentation

Usually the clinical symptoms of an omental infarction are localized peritoneal irritation on the right side of the abdomen, sometimes associated with low-grade fever.

11.7.4 Differential Diagnosis

The clinical picture often misleads physicians to assume an incorrect preoperative diagnosis such as [304, 311, 312]:

- Acute cholecystitis
- Acute appendicitis
- Diverticulitis
- Appendagitis epiploica
- Umbilical hernia

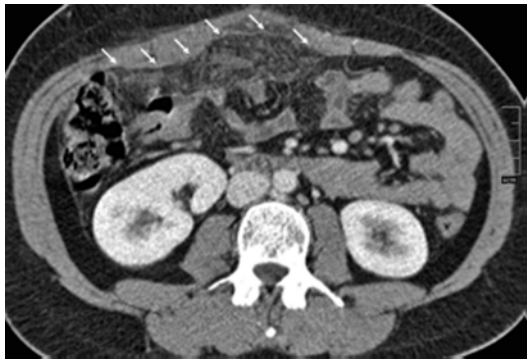

Fig. 11.17 Computed tomography scan of the abdomen showing a hypoperfused mass in the anterior portion of the median epigastrium with fatty density (*white arrows*) and a thin layer of free fluid surrounding the liver [308]

11.7.5 Diagnosis

11.7.5.1 Laboratory Findings

The C-reactive protein and white blood count may be elevated.

11.7.5.2 Abdominal CT Scan

As most patients show symptoms of an acute abdomen, CT of the abdomen and pelvis should be the diagnostic imaging of choice [313]. If omental infarction is caused by torsion, characteristic CT findings might be detectable. The torsion leads to the presence of concentric linear strands in the fatty mass, a so-called fat spiral pattern (Fig. 11.17) [314].

Differentiating the omental infarction from other abdominal or omental diseases was challenging, and the radiological findings could be misinterpreted as a small incarcerated umbilical hernia as in case by Tachezy et al. [308].

11.7.5.3 Diagnostic Laparoscopy/ Laparotomy

Diagnosis of an omental infarction has traditionally been made intraoperatively during an exploratory laparotomy or laparoscopy, and the treatment has been partial or total omentectomy. If there is other underlying pathology, it should be treated during the exploration.

11.7.6 Therapy

11.7.6.1 Conservative Therapy

Recent reports highlight cases of patients with CT-diagnosed omental torsions who have been successfully treated conservatively without any other complications (such as bacterial superinfections) [315–318]. Whenever conservative treatment fails or the clinical status of the patient worsens, a surgical intervention should be quickly implemented.

11.7.6.2 Surgical Therapy

Patients present symptoms of an acute abdomen. The clinical findings are very unspecific, and, therefore, in most cases surgical exploration leads to the diagnosis. All parts of the omentum that are macroscopically changed should be resected to eliminate the possibility of recurrent torsion and infection that can supervene omental necrosis.

11.8 Gastrointestinal: Genital Communications

11.8.1 Introduction

The high mortality rate associated with these cases indicates the seriousness of perforation of the vascular gravid genital system into the intestinal tract, the need for suspicion of the condition, and the knowledge of the principles essential for successful management.

11.8.2 Incidence

Communication of the gastrointestinal tract with the genital system from any cause is an unusual occurrence. Franco and Clough, reporting a review of the world's literature to 1956, found only 75 cases of entero-uterine fistula [319]. In a review of over 1,000 consecutive cases of ectopic pregnancy at the Cook County Hospital (1940–1956), Webster and Kerr found only one associated with bowel invasion [320]. Documentation of entero-amniotic fistulas resulting from complications of ectopic pregnancy is even more unusual, only

Table 11.6 Obscure intestinal hemorrhage (up to 1964) [321]

Author	Year	Site of ectopic pregnancy	Site of perforation	Symptoms	Treatment	Outcome
Edgar [322]	1901	Unknown	Sigmoid colon	Rectal hemorrhage, abdominal pain	Posterior colpotomy	Expired
Webster and Kerr [320]	1956	Right interstitial	Terminal ileum and appendix	Rectal hemorrhage, abdominal pain	Resection of ileum, ileoileostomy, appendectomy, right salpingectomy, wedge resection of the right cornu of the uterus	Expired
Engel [323]	1961	Left interstitial	Mid-ileum	Rectal hemorrhage, hypotension	None	Expired
Shirkey et al. [321]	1963	Left interstitial	Terminal ileum	Rectal hemorrhage, abdominal pain	Suture ileum, total abdominal hysterectomy, left salpingectomy, right salpingo-oophorectomy	Recovered

occasional cases being found in the literature. Only four cases presenting with rectal hemorrhage from an unknown source, ultimately proved to have arisen from rupture of an ectopic pregnancy into the bowel, have been reported (Table 11.6). The first known case is by Armstrong, in 1835, of a woman in her sixth month of pregnancy who suddenly passed bloody stools containing fetal bones and died of hemorrhage [324].

11.8.3 Etiology

Le Jemtel, in 1909, presented an etiological classification of entero-uterine fistulas which with addition by Hawkes [325, 326]. There are four major etiological categories:

- Cancer – by infiltration and invasion arising in either the bowel or uterus
- Peritonitis – from trauma, puerperal infections, appendicitis, or diverticulitis, and fistulas following abscess formation involving the inflamed adjacent walls of both the uterus and intestine
- Traumatic or spontaneous rupture of the gravid uterus with strangulation of a loop of bowel caught in the defect
- Perforation of the uterus and bowel at the time of curettage

Danforth and Case, reviewing the relative incidence of the various causes of 58 cases of communication between the bowel and uterus dating from the 200 years previous to 1933, found 64 % due to injury, 24 % due to inflammatory or congenital processes, and 12 % due to carcinoma [327]. Diverticulitis has been reported as the underlying cause for a small number of fistulas between the uterus and large bowel [328–330]. In 1929, Noecker was the first to report a colouterine fistula secondary to diverticulitis in general female population [329]. Chronic salpingitis [326], criminal abortion [331, 332], retained pregnancy [333], and curettage of a bicornuate uterus [334] have been reported as specific causes for fistulas between the intestinal and genital tracts. An additional cause for fistula formation between the intestinal and genital tracts is rupture of an ectopic pregnancy into the bowel, causing an entero-amniotic fistula.

11.8.4 Pathogenesis

Infection is of paramount importance in the pathogenesis of entero-amniotic fistulas resulting from complications of pregnancy. Stock has previously described the role of infection in a case of secondary abdominal pregnancy complicated by fistula formation and rupture through the umbilicus [335]. The approximation of a vascular placenta, with the potential of villous invasion of adjacent structures, to intestine creates a precarious set of

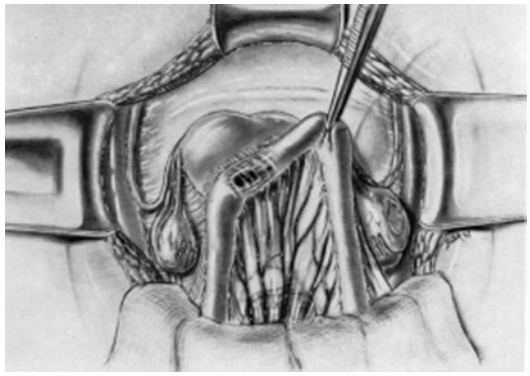

Fig. 11.18 Drawing and illustrating terminal ileum firmly attached to the left cornu of uterus with fistula between ectopic gestation and lumen of the bowel as seen diagrammatically through the bowel wall [321]

circumstances. Following villous invasion of the bowel wall, on approximation of the gestational sac to the intestine, inflammatory reaction and infection may create fistula formation. The source of infection may vary according to the location of the ectopic sac. Intraperitoneal ectopic sacs are most commonly infected from the adjacent bowel, whereas intraligamentary sacs are most often contaminated by bacteria from the vagina or uterus [335]. The vascular gestational structures aggravated by infection and villous invasion of adjacent vascular structures provide a dangerous source of massive hemorrhage (Fig. 11.18).

11.8.5 Prevention

The importance of meticulous surgical technique in reperitonealization of the pelvic floor, uterus, and Fallopian tubes and in manipulation of the bowel is exemplified in the case reported by Engel [323]. This case, documented by careful postmortem examination of involved structures, illustrates how inadequate reperitonealization of the uterus during a previous ipsilateral salpingo-oophorectomy allowed a loop of ileum to become adherent to the uterus. This set of circumstances made perforation of the adjacent ileum by a subsequent interstitial pregnancy a more likely possibility, ultimately costing the patient her life due to profuse hemorrhage into the bowel from an intrauterine vessel.

11.8.6 Management

Knowledge of the possibility of fistula formation between an ectopic gestational sac and bowel and suspicion of its presence are essential in successful management. Intestinal hemorrhage in any potentially pregnant woman should stimulate consideration of this dangerous condition. Consideration of the role played by an inevitable presence of infection in these cases makes necessary complete excision of all involved structures when possible. The patient reported by Masterson and Baum that died of sepsis and peritonitis resulting from infected placental tissue left in situ after removal of only the fetus demonstrates this concept [336]. When technically feasible, all structures, including the uterus, should be excised when involved in the infected fistula and inflammatory process. One exception is the abdominal pregnancy, where extensive intimate invasion of the surrounding structures by the placenta makes removal dangerous and usually impossible. Even in this situation, consideration should be given to resection of as much involved tissue as possible with drainage in an attempt to prevent intra-abdominal abscess formation. In simple fistula formation with only a small opening into the intestine and absence of marked inflammatory reaction, simple closure of the bowel is acceptable. Otherwise, segmental resection with end-to-end anastomosis in the case of the small bowel and colon, or diverting procedure in involvement of the rectum, is indicated.

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Part II

Gynecology

Adnexal Torsion

12

12.1 General Considerations

if a woman with child be bled, she will have an abortion, and this will be the more likely to happen, the larger the fetus
when a pregnant woman has a violent diarrhea, there is danger of her miscarrying
in a pregnant woman, if the breasts suddenly lose their fullness, she has a miscarriage
if, in a woman pregnant with twins, either of her breasts lose its fullness, she will part with one of her children; and if it be the right breast which becomes slender, it will be the male child, or if the left, the female
when women, in a moderate condition of body, miscarry in the second or third month, without any obvious cause, their cotyledons are filled with mucosity, and cannot support the weight of the fetus, but are broken asunder
in women that are about to miscarry, the breasts become slender; but if again they become hard, there will be pain, either in the breasts, or in the hip-joints, or in the eyes, or in the knees, and they will not miscarry
women with child who are seized with fevers, and who are greatly emaciated, without any (other?) obvious cause, have difficult and dangerous labors, and if they miscarry, they are in danger

Hippocrates, 400 B.C.E

12.1.1 Introduction

Evaluation of a female patient in general and/or during pregnancy who presents with an acute abdominal pain must always include surgical and gynecologic disorders. Parsons in 1958 stated that 40 % of women in general population who present with symptoms of pain in the lower abdomen and pelvis do not have gynecologic disease [1].

The two general considerations in the surgical evaluation of these conditions are laparoscopic approach versus the traditional laparotomy and preservation of reproductive capability. Preservation of reproductive capability (childbearing, hormonal function and sexual health) has a major impact on the wellness of a woman. These important issues should be considered in surgical management of acute gynecologic problems.

12.2 Incidence

Depending on the method and definition of a clinically significant adnexal mass, the prevalence of pregnancies complicated by an adnexal mass varies, but has been reported to be between 1 and 4 % [2, 3]. A small percentage of these, approximately 5 %, will represent malignant tumors, making ovarian cancer the fifth most common cancer diagnosed during pregnancy [4].

Torsion of the adnexa accounted for 2.7 % of all surgical emergencies in one series of acute gynecologic complaints [5], and in pregnancy, adnexal masses have been noted to occur in up to 1 % [6]. The rate of torsion decreases as the gestational age increases. However, maternal ovarian torsion (OT) during pregnancy is a rare event, with a reported incidence of 1–10/10,000 spontaneous pregnancies [7, 8]. Adnexal torsion has been reported to occur in 7–28 % of all pregnancies complicated by adnexal masses [5, 9–13].

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In one study of 12 years experience, 98 % of cases were elective with only one emergent operation for adnexal torsion preformed [14].

Although it is a relatively rare phenomenon, adnexal torsion should always be considered as part of the differential diagnosis of acute pelvic/abdominal pain in women, especially those with pelvic masses diagnosed by examination or ultrasonography. Early diagnosis is important because prompt surgical intervention can result in ovarian preservation by saving the ovary and adnexa from infarction.

The majority of adnexal torsions occur in the first or second trimester of pregnancy with only 10 % in the third trimester [15–17]. If cysts are found in pregnant women on sonography, these very rarely (3.8 %) result in torsion [18]. Bilateral torsion, either simultaneously or sequentially, is infrequent, with few cases reported in the literature [19, 20].

Eighty percent of torsions were found on the right side [17].

12.3 Risk Factors

12.3.1 Assisted Reproductive Technologies

The increased use of assisted reproductive technologies such as controlled ovarian hyperstimulation (COH), in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI) has led to an increase in the risk of adnexal torsion, particularly in pregnant women or women with ovarian hyperstimulation syndrome (OHSS). Mashiach et al. studied adnexal torsion in 201 women with OHSS over a period of 10 years and reported an incidence of 2.3 % in nonpregnant women and an incidence of 16 % in pregnant women [15]. However, 12–25 % of all adnexal torsions occur in pregnant women, often in combination with assisted reproduction and its complications (OHSS). The reported incidence is low for oocyte donation cycles (0–0.2 %) and IVF cycles (0–0.13 %); however, the incidence increased to 6 % under stimulation for ART and to 16 % with OHSS [15, 18, 21–23]. But even when adnexal torsion occurs simultaneously with OHSS, the reported incidence varies between 1 and 33 % [19]. Seventy percent of torsions occur in multiple pregnancies [24]. The incidence in study by Spitzer et al. with 1,411 fresh embryo transfers in 1,007 patients was 0.35 % [17].

12.3.2 Pregnancy

Some authors found that pregnancy itself is a risk factor for recurrent torsion despite the method of conception, and gestational age at time of torsion but recurrent torsion is more frequent in multicystic ovaries [7, 25].

12.3.3 Ovarian Tumors

In an 80-year review of the world literature, Jubb [26] collected only 34 cases of ovarian cancer associated with pregnancy. In 1973, Munnell [27] also emphasized the infrequent association of ovarian cancer and pregnancy at 1/18,000 pregnancies. A more recent comprehensive report summarized the incidence of 0.179–1.1/10,000 pregnancies [28]. In the Dobashi et al. series, ovarian malignancies during pregnancy were estimated to occur in 0.8–2.8/10,000 pregnancies, which is slightly higher than the incidence discussed previously [29]. It is uncertain whether incidence of ovarian cancer associated with pregnancy is rising. However, since the age of childbearing among older women increases, the incidence of cancer is also likely to rise in pregnancy. In Dobashi et al. series, six cases of epithelial ovarian cancer with the median age of 32.5 years were presented [29], while it was 30 years in Jubb's report [26] in 1963, suggesting the aging trend of this minor subset of patients.

The effect of pregnancy on mature cystic teratomas has also been evaluated, and one study noted increased complications. Torsion occurred in 19 % and rupture in 17 % of these cysts in pregnancy [30]. Because of the high incidence of

adverse pregnancy outcomes in association with emergency surgery previously reported, some authors recommend elective removal of all masses that persist until 16 weeks and are 6 cm or greater regardless of appearance on imaging studies, unless it is suspected to be a leiomyoma [31]. Conversely, torsion occurred in only 1/139 conservatively managed patients in the study by Grimes et al. from 1954 [32].

12.3.4 Anatomic Variations of Adnexa

There are even cases of torsion of normal ovaries. The causes of torsion may be hypermobile ovarian ligaments, long ovarian ligaments, or other inherent ovarian mobility. Other factors may operate to cause torsion of normal adnexa during the second trimester of pregnancy [33]. The relative situation of the adnexa and the uterus (i.e., the ovaries emerging from the pelvis by the increasing size of the uterus) may predispose the ovaries to twist by allowing them a greater mobility [34].

The main histopathologic findings in both groups were cysts of the follicular or corpora lutea [35]. Although cysts and neoplasms account for over 90 % of all cases, torsion can occur in the normal-appearing ovary as well [36].

12.4 Clinical Presentation

The presenting complaint of adnexal torsion is pain that is often abrupt in nature, very severe, lateralized to the right or left lower quadrant of the abdomen, and usually causing nausea and vomiting. It is often described as sharp and "knifelike," although it can be colicky in nature. The pain is proportional to the degree of circulatory obstruction; that is, complete obstruction interrupting venous return results in sudden severe pain with nausea and vomiting developing rapidly. The pain may radiate to back, flank, or groin. There may be a history of waxing and waning pain if the adnexa has been twisting and untwisting or has undergone partial torsion, causing vascular slowdown but not thrombosis [15, 37–39]. The infundibulopelvic ligament may twist and untwist by itself, reducing and increasing the pain. There may also be a history of some sort of jarring or movement that has caused the torsion, such as exercise prior to the onset of the pain or even just turning over in bed. Acute abdominal pain occurs in more than 80 % of cases, often starting suddenly at night and persisting for more than 24 h [15, 16, 40, 41]. Signs of peritoneal irritation, which are considered fundamental for the diagnosis, were present in 43 % of the pregnant women and 19 % of the nonpregnant women [7, 19, 42]. Low-grade temperature elevations may occur, but significant fevers are unlikely and, if present, may point to another cause of the pain.

Pelvic examination usually reveals a tender mass on the affected side. If the patient had normal adnexa prior to the torsion, she may not have a mass present until later in the course of the torsion when edema and swelling of the adnexa have set in. Therefore, serial examinations may be necessary in a patient suspected of torsion. Only rarely will patients have evidence of abdominal guarding or rebound tenderness on physical examination.

12.5 Diagnosis and Differential Diagnosis

12.5.1 Differential Diagnosis

The differential diagnosis, particularly for right-sided adnexal torsion, includes [41, 43]:

- Acute appendicitis
- Renal colic
- Renal or urethral calculi/obstruction
- Obstructive bowel disease
- Ectopic/heterotopic pregnancy
- Hemorrhagic cysts
- Corpus luteum cysts
- Ovarian hyperstimulation syndrome

The differential diagnosis of adnexal torsion is particularly difficult in combination with OHSS or pregnancy, as abdominal pain, nausea, and vomiting can be presenting symptoms of hyperstimulation or pregnancy itself because the

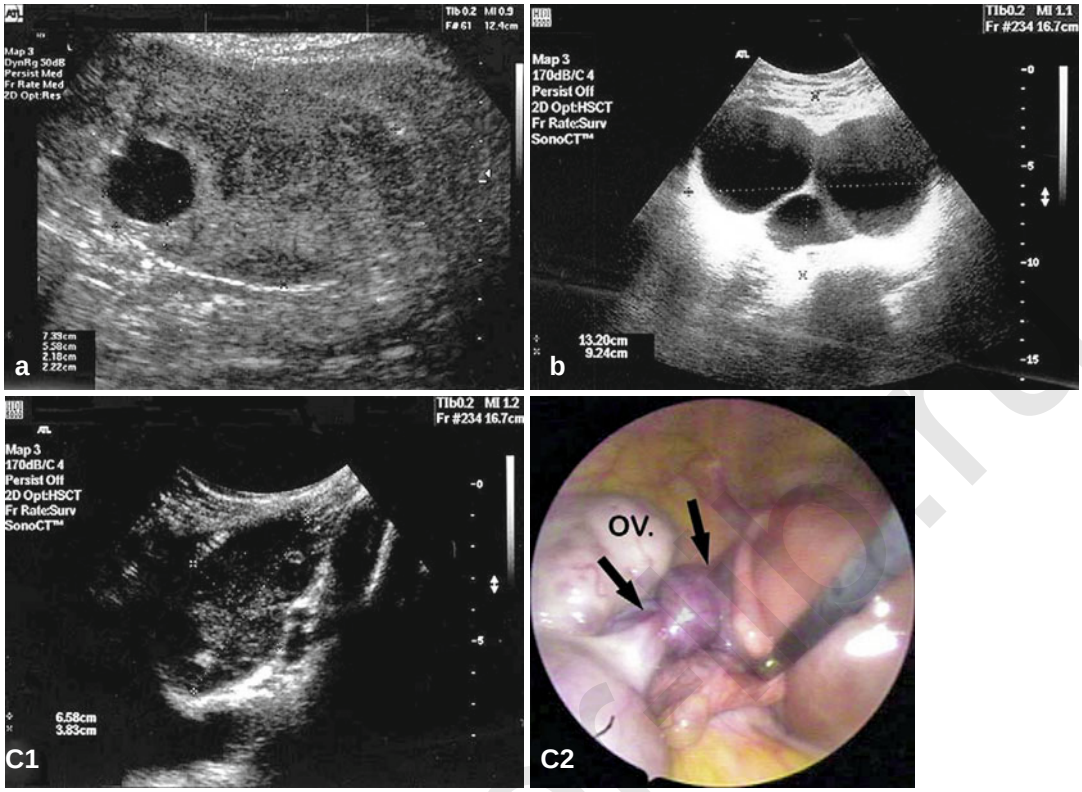

Fig. 12.1 Three different ultrasound images of twisted ovaries in pregnancy. (**a**) Transabdominal scan of an enlarged ovary with a 20 mm simple unilocular cyst. The ovarian parenchyma appears edematous; (**b**) transabdominal scan of an enlarged 130 × 92 mm ovary with multicystic components; (**c**1) transabdominal scan of an enlarged 65 mm ovary without cystic components. Again, the ovarian parenchyma appears edematous; (**c**2) laparoscopy of the same patient as in (c1). *Arrowheads* point to the twisted ovarian pedicle [34]

abdomen is already distended and tender because of the enlarged cystic ovaries [38].

12.5.2 Diagnosis

12.5.2.1 Laboratory Findings

An elevation of the white blood cell (WBC) count may be present but is also not very predictive. Several authors have reported that patients had mild leukocytosis; however, while levels may be increased in nonpregnant women, levels may be within normal ranges for pregnant women [19, 40, 41]. Leukocytosis is also one of the laboratory indicators which may change with OHSS. If necrosis and infection of the twisted organ occur, then higher fever and leukocytosis may be present.

12.5.2.2 Transvaginal Ultrasound

When adnexal torsion is suspected, abdominal ultrasound is indicated. Transvaginal ultrasound may often show enlargement of the ovaries and polycystic changes without this being evidence of torsion. It is extremely rare for adnexal torsion to occur with a mass less than 5 cm in diameter [17, 44], and ultrasound almost always demonstrates an adnexal mass of this size. Nonetheless, sometimes a large mass might be missed in third trimester presentations, when the adnexa can be hidden by a large uterus. Because of varying degrees of ovarian arterial, venous, and lymphatic occlusion with torsion, the ovarian parenchyma is initially congested (Fig. 12.1), and hemorrhagic infarction occurs later [10, 45]. Sonographic findings associated with the diagnosis of adnexal torsion include a predominantly solid-appearing

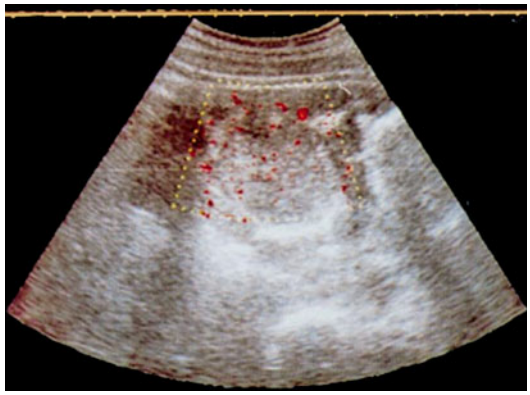

Fig. 12.2 Doppler mapping of the left adnexa showing absence of vascular flow [51]

ovary, unilateral ovarian enlargement, ovarian peripheral cystic structures, and marked stromal edema and pelvic fluid [39, 45–49].

OHSS presents significant differential diagnostic problem. Twisted adnexa are usually characterized by a solid-appearing ovary on ultrasound, enlargement of the organ, ovarian peripheral cystic structures, and marked stromal edema and pelvic fluid. These characteristics are routinely present in a hyperstimulated ovary, and usually both adnexa are enlarged. Mild OHSS could be suspected in these patients, delaying the correct diagnosis and treatment. There is an overlap in the gray-scale appearance of ovaries in mild OHSS and OT. Ovaries in mild OHSS are enlarged, with prominent, heterogeneous stroma, and contain multiple 1–2 cm follicles, many containing hemorrhage. Torsed ovaries are also enlarged, with prominent, heterogeneous central stroma and with multiple, small, peripheral follicles [50]. In addition, in OHSS, both ovaries could be enlarged, and symmetry among them may be present contrary to the situation with adnexal torsion [41]. Although the absence of Doppler flow indicates venous and arterial occlusion and thus adnexal torsion (Fig. 12.2), the presence of flow should not exclude the diagnosis of torsion [46–49, 51, 52].

With OHSS, ovaries often show an increase in diastolic blood flow; thus, decreased blood flow may indicate adnexal torsion in a patient with OHSS [52, 53]. Furthermore, the reduction in diastolic flow is diagnostic of OT in patients with OHSS. In the hyperstimulated ovary, the diastolic flow is usually increased [54]. However, a torsed ovary may demonstrate normal venous and arterial flow completely symmetric to the normal side [50]. Recent review of all surgically diagnosed OT cases showed that normal Doppler flow was found in 60 % of surgically diagnosed OT [7, 52]. Hasson et al. therefore recommended not to base the decision for surgical evaluation only on the results of Doppler flow investigation (as proposed by Arena et al.) but also to take past medical history, clinical appearance, and laboratory assessment into account [7, 41]. If there is a strong clinical suspicion for adnexal torsion, consultation with an obstetrician/gynecologist is mandatory.

12.5.2.3 Abdominal MRI

If the diagnosis cannot be established, especially in cases with OHSS, emergent MRI of the abdomen and pelvis can define the adnexal torsion. The MRI appearance of OT is well described [55]. Solid ovarian tissue appears enlarged and edematous (Fig. 12.3).

Currently, the diagnosis of maternal adnexal torsion is missed in 15–35 % because of nonspecific clinical features and uncommon objective findings [5, 35, 56]. Probably more frequent use of MRI in doubtful cases could increase the preoperative diagnostic accuracy.

12.6 Treatment

12.6.1 Time Between Hospital Admission and Surgery

In the literature, the time between admission to hospital and surgery is in range of 6–15.5 h and may be even significantly shorter in the first trimester of pregnancy. However, several days may pass between the start of symptoms and surgery [15, 17, 34]. In the laparoscopic era, acute symptoms or persistence of complaint meant early surgery (less than 24 h in all cases), and treatment was still in time to preserve fertility [17]. Patients in the second and third trimesters were operated

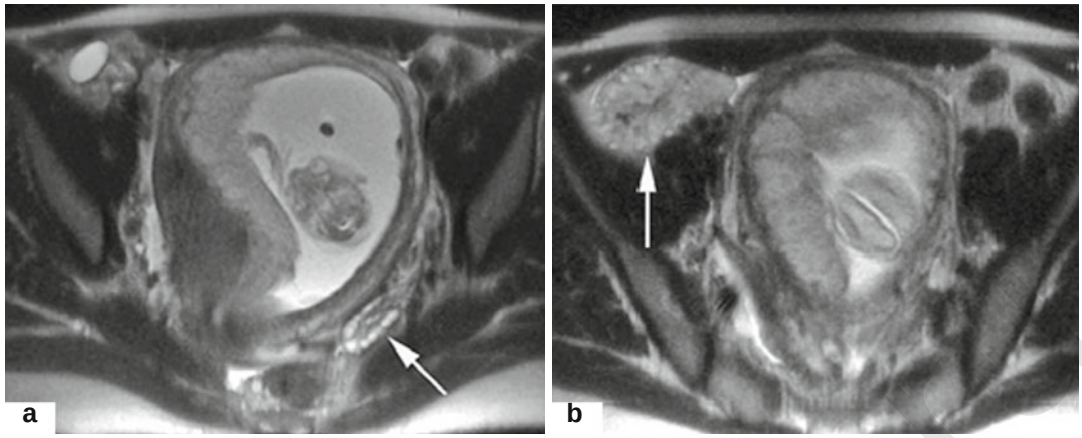

Fig. 12.3 A 30-year-old woman at 15 weeks' gestation with sharp intermittent right lower quadrant pain. (**a**) Transverse image shows the normal left ovary with normal follicles and stroma (*arrow*); (**b**) transverse image shows enlarged and edematous right ovary (*arrow*), which is consistent with torsion [80]

significantly later than those in the first trimester. This difference may be either due to a difficulty in assessing the ovaries on palpation and on ultrasound examination or because patients with suspected OT are more readily operated in early pregnancy when the risk from the (laparoscopic) surgery itself is minimal [34]. In one large study, 50 % of patients had surgery within 24 h, and 85 % received surgery within 72 h [56].

12.6.2 Procedures

Sometimes adnexal torsion produces no classic symptoms, and there are no definitive diagnostic tests or studies; surgical exploration of the pelvis is required for definitive diagnosis (Fig. 12.4). Traditionally, this was done by means of laparotomy; however, laparoscopy has become the preferred surgical approach for both diagnosis and management of adnexal torsion [57].

Traditionally, adnexal torsion was treated aggressively with salpingo-oophorectomy of the involved side; unwinding the torsion was condemned for fear of releasing a potentially fatal embolus [58, 59]. This was not confirmed and current conservative management involves unwinding the adnexa and assessing its viability. No emboli in general population have been noted in several series using this approach [12, 60]. An

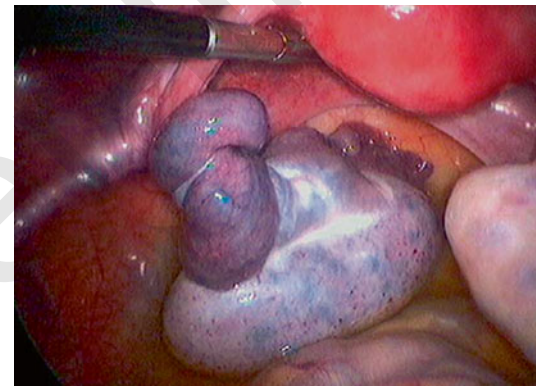

Fig. 12.4 Laparoscopic view of torsion of the enlarged left adnexa [17]

embolic complication could have been encountered when adnexal torsion was not treated promptly and twisted organs were found to be obviously gangrenous at laparotomy.

Once torsion is unwound, the adnexa show one of the following:

- No evidence of ischemia or mild ischemia with immediate and complete recovery
- Severe ischemia with a dark red or black tube and ovary and partial recovery after the pedicle is untwisted
- Gangrenous adnexa without recovery

Only the gangrenous adnexa needs complete removal of the adnexa; the first two situations can

be conservatively treated with detorsion and preservation of the ovary, even after severe ischemia has occurred [12]. When an ovarian cyst is present, a complete ovarian cystectomy should be performed to obtain a histological diagnosis [60]. Infarction may make accurate diagnosis difficult; therefore, the cyst should be completely removed. This may also prevent recurrence. Routine ovariopexy after detorsion does not seem warranted because the risk of retorsion is very low when a cause is found and treated [60].

Despite the necrotic, hemorrhagic, or bluish-black appearance of a torsed ovary, detorsion saves over 90 % of these ovaries, and ovarian function recovers [10, 12, 13, 48, 61]. Taskin et al. [62] showed that even with complete ischemia gross appearance does not correlate with outcome and that detorsion within 24 h did not show an increase in free radical reperfusion injury. The importance of early diagnosis and surgical intervention in the case of adnexal torsion is highlighted by a report showing that the delay of intervention for 36 h resulted in significant congestion and necrosis [62]. Assessment of ovarian viability such as ultrasound visualization of follicular development, inspection during a subsequent procedure, observed response to stimulation during IVF, and documentation of fertilization of oocytes from the ovary has consistently shown that the ovary does recoup function after torsion and detorsion [10, 12, 13, 15, 61]. Furthermore, because an increased risk of thromboembolism has not been associated with detorsion procedures [10, 13], conservative management with detorsion is encouraged. In a study of 94 women with adnexal torsion, Zweizig et al. [63] showed an overall morbidity of 12 % in the group with salpingo-oophorectomy versus 3 % in the conservatively treated control group. In a study by Spitzer et al. adnexectomy was avoided in all cases, and therefore fertility was preserved [17]. After unwinding, aspiration of ovarian cysts, if present, is recommended [51].

Since the successful conservative management of adnexal torsion in general female population was described by Mage et al. in 1989 (laparoscopically) [60] and Bider et al. in pregnant population in 1991 [35], this technique has been extended for the management of such conditions during pregnancy. Laparoscopic detorsion of adnexal torsion is recommended as the first-line treatment and has been successfully performed during pregnancy mostly up to 20 weeks of gestation, first performed laparoscopically by Levy et al. in 1995 [64]. One large study shows 60 % of patients treated with laparoscopy with most of the women in the first trimester (75 %) [56]. The patients in that study who underwent laparoscopy had a significantly smaller ovarian mass and a shorter hospital stay than those undergoing laparotomy. Compared with laparotomy, laparoscopic procedures are associated with shorter hospitalizations, a lower rate of febrile morbidity, reduced consumption of narcotics, and greater patient comfort [10, 13]. After laparoscopic detorsion, 24 h of postoperative observation is recommended [65, 66]. Even a case of laparoscopic detorsion in the early third trimester of pregnancy has been published [51].

The operative procedures in one large study were as follows: detorsion followed by cystectomy in 80 %, oophorectomy in 10 % for masses larger than 12 cm, and simple detorsion in 10 % [56]. Smorgick et al. [34] performed detorsion in all their cases in their series of 33 pregnant women with OT, followed by cystectomy 12 % (4/33) and oophorectomy in one case with a 10 cm cystic teratoma. Of 20 patients who had OT in pregnancy in Bider et al.'s series [35], 85 % received detorsion, followed by biopsy, aspiration, and cystectomy in 45 % patients. In Hasson et al.'s study [7], all patients received detorsion and 55 % also undergoing an additional procedure(s).

12.6.3 Operative Technique

12.6.3.1 Laparoscopic Detorsion in the Third Trimester

A small incision of 2 cm is made in the left upper abdominal quadrant (Fig. 12.5) and a 10 mm trocar is introduced as open (Hasson) technique on the left side of the epigastrium. Pneumoperitoneum is induced with an insufflation volume of CO_2 of 1 L/min and an intra-abdominal pressure of

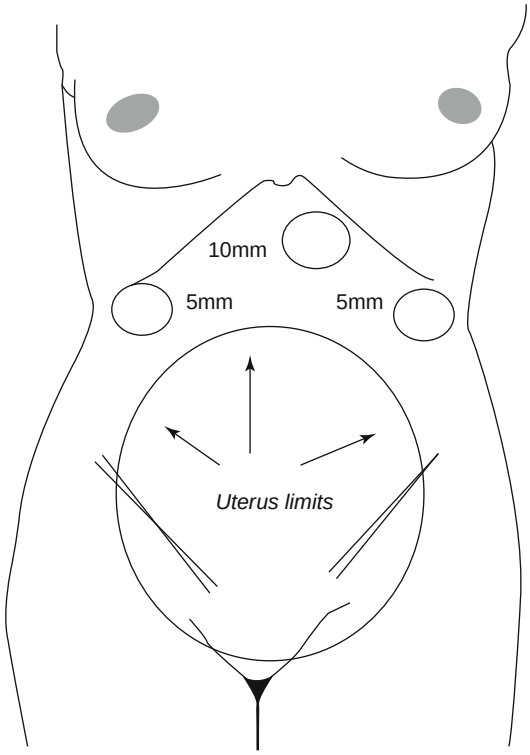

Fig. 12.5 Sites of trocar insertion in the third trimester of pregnancy for laparoscopic detorsion of adnexal torsion (*circle* marking upper limits of the uterus) [51]

10 mmHg. The patient is kept in a horizontal position. Secondary trocars are inserted at opposite sites, one in the right upper abdominal quadrant and the other on the extreme left of the middle abdominal quadrant. These secondary trocars are inserted under direct laparoscopic control. Two atraumatic probes are introduced into these trocars: one on the left side, allowing washing and gentle pressure on the uterus in a brief lateral Trendelenburg position, and with the other probe elevating the twisted adnexa, pushing it contralaterally to the direction of rotation. Serial manipulations achieve the unwinding of the adnexa. The lateral Trendelenburg position is then abandoned, and after abundant washing, the procedure is stopped for 10 min, with desufflation of the abdominal cavity. Once the procedure resumed, the pedicle of the ovary and the tube are carefully examined and an improvement in color and a decrease in edema should be noted. These signs establish the beginning of recovery of the adnexa, which should turn pink shortly after the procedure. Monitoring of the uterine contractions and fetal heartbeat should be carried out during the entire procedure [51].

12.6.3.2 Technique of Adnexal Unwinding

Unwinding of the affected adnexa is usually carried out by simply pushing the ovary contralaterally to the direction of the torsion. This can be performed with the aid of two probes without grasping the tissue, to avoid bleeding. The release of pressure ensures the normal positioning of the adnexa. After unwinding, aspiration of ovarian cysts, if present, is recommended. However, this is not always possible since cysts are often filled with clotted blood.

12.6.3.3 Ovariopexy

Surgical management to prevent recurrence has included "triplication" of utero-ovarian ligament by Germain et al. [67], where the ligament is plicated and shortened with a running stitch; ovariopexy, where the ovary is sutured to the posterior aspect of the uterus or to the lateral pelvic wall; and oophoropexy, where the utero-ovarian ligament is sutured either to the posterior aspect of the uterus or to the lateral pelvic wall (Fig. 12.6). Oophoropexy, although not evaluated in randomized trials, has been done in women of all ages as well as during pregnancy. Although not commonly done, oophoropexy has been performed laparoscopically with good results and has been recommended for childhood torsion and in women who have previously undergone an oophorectomy for prior OT [67–71].

Weitzman et al. described a unique form of treatment for the prevention of recurrent adnexal torsion. Although oophoropexy has been performed successfully in pregnant women, it was felt that the increased vascularity of the area precluded performing this procedure. Owing to the concern of yet another recurrence, and the length of the utero-ovarian ligament, the ligament is shortened. In this approach, a grasping forceps is passed through an Endoloop and then used to tent up the utero-ovarian ligament in the midsection. The pretied endoscopic knot (e.g., Endoloop

Ligature, Ethicon, Johnson & Johnson) is then tightened, pulling the ovary close to the uterus and shortening the utero-ovarian ligament [20].

12.6.3.4 Laparotomy

In the presence of an ovarian cyst, a simple cystectomy can be performed in the absence of overt malignancy. When possible, the entire ovary is delivered from the abdominal cavity and surrounded by moist laparotomy pads to avoid intra-abdominal spillage of cyst contents if rupture occurs. The thin ovarian capsule is carefully incised, usually with a scalpel. Blunt dissection is used to separate the cyst from the ovarian tissue. Electrosurgery can be used on the internal ovarian surfaces for hemostasis but should not be used near the cyst wall to minimize the risk of cyst rupture [72].

Rupture is inevitable in some ovarian cysts, particularly in endometriomas and functional cysts, such as luteomas. If a dermoid is accidentally ruptured, every effort should be made to avoid spilling the very irritating sebaceous contents into the peritoneal cavity. If this occurs, prolonged peritoneal irrigation with warmed saline will prevent peritonitis. Likewise, if the "chocolate" contents of an endometrioma or the fluid content of a potentially malignant cyst spills within the peritoneal cavity, prolonged irrigation with warmed saline is judicious. It remains to be determined if these precautions avoid the detrimental effect of intraoperative rupture on stage I ovarian cancer [73].

Regardless of rupture, all cysts should be completely opened after removal and the internal surface of the cyst wall examined for excrescences. When present, microscopic examination of frozen sections can help determine if intraoperative staging is required. In all cases, definitive

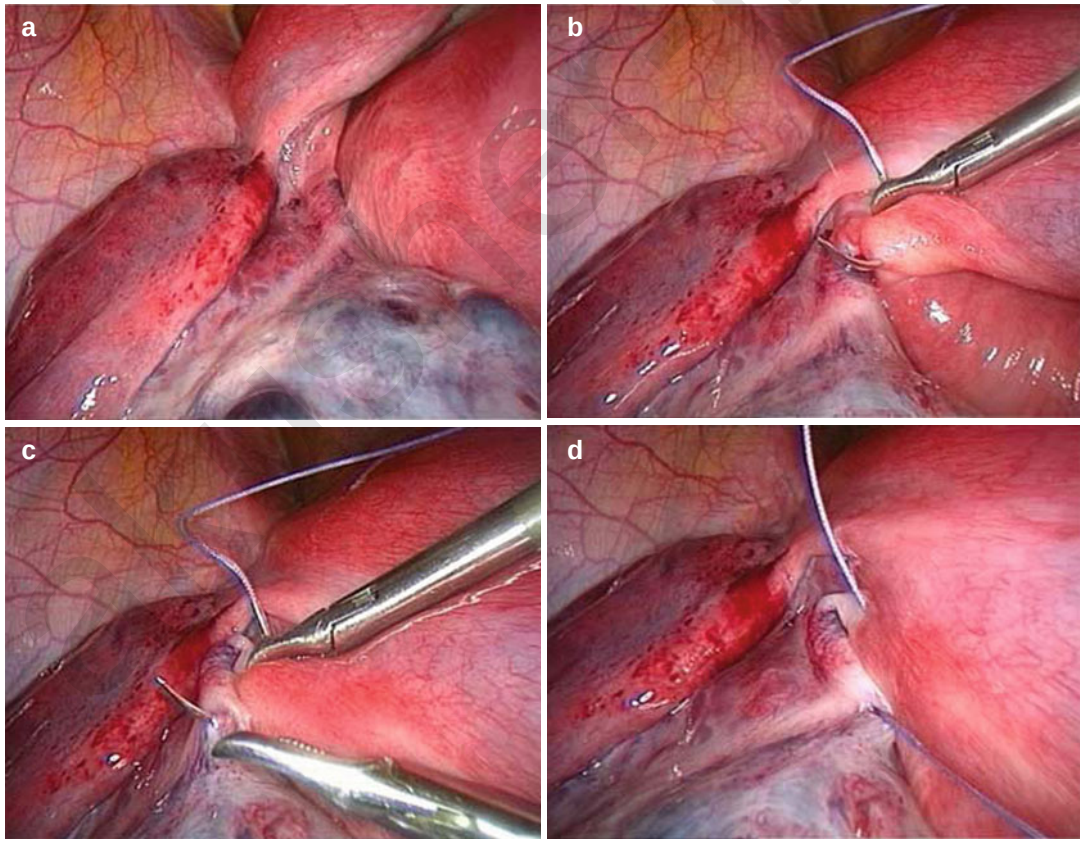

Fig. 12.6 Oophoropexy of the left ovary. (**a**) Intraoperative finding after ovarian detorsion. (**b**–**e**) Shortening of the proper ovarian ligament by suturing the distal and proximal end of the ligament for prevention of recurrent ovarian torsion in pregnancy. (**f**–**h**) Ovarian fixation for the remaining proper ovarian ligament [71]

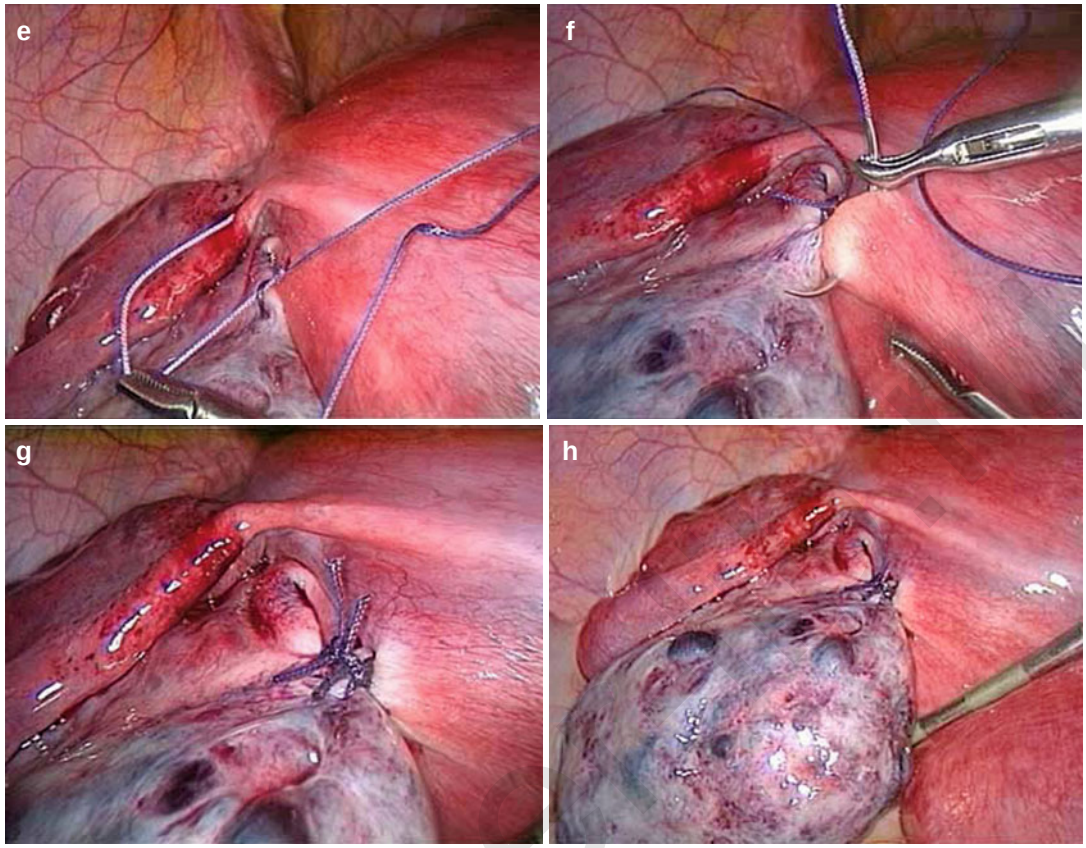

Fig. 12.6 (continued)

diagnosis must await careful examination of permanent sections.

The ovary does not require precise reconstruction as was thought in the past. Reapproximation with internal sutures may help subsequent reformation of the normal ovarian profile, but sutures on the external ovarian surface should be avoided to minimize the subsequent risk of adhesion formation [74].

12.6.4 Pathology

It is important to define the pathologic cause of the adnexal torsion. Table 12.1 shows pathology of adnexal masses causing torsion in pregnancy. If the mass is benign, there is no need for additional surgical or oncologic therapy.

Table 12.1 Pathological findings of ovarian torsion in pregnant women [56]

Pathological finding[a]	(%)
Teratoma	30
Corpus luteum cyst	20
Follicular cyst	15
Serous cystadenoma	15
Endometrioma	10
Mucinous cystadenoma	5

[a]Two cases undergoing detorsion were without pathological results

12.6.5 Special Considerations

There are several cases of adnexal torsion and concomitant contralateral tubal ectopic pregnancy (Fig. 12.7) [75, 76]. In such cases, it is especially important to make early diagnosis and

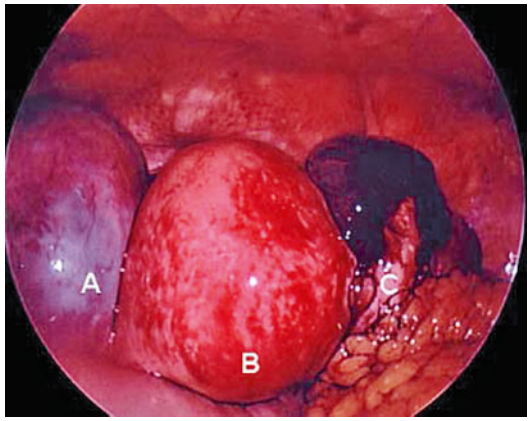

Fig. 12.7 Intraoperative photograph of (*A*) adnexal torsion and concomitant contralateral ectopic pregnancy (*C*). (*B*) Uterus [76]

laparoscopic exploration to save the detorsed adnexa because salpingectomy or adnexectomy is indicated in the contralateral adnexa due to ectopic pregnancy. Such procedure preserves fertility.

12.6.6 Perioperative Management

12.6.6.1 Tocolysis

Prophylactic tocolysis are not routinely given, only administered if the patient experienced uterine contraction after surgery. The tocolytic protocol included oral or intramuscular administration of progesterone in the first trimester and oral or intravenous administration of ritodrine in the second and third trimesters [56].

12.7 Prognosis

Smith et al. reported a reduced fertilization rate (FR) of 40 % for oocytes aspirated from a detorsed ovary, while the FR for the unaffected ovary was 93 %. Seventy-five percent of oocytes from the unaffected side and 64 % of oocytes from the affected side developed into blastocysts. A reduced FR had been previously described in earlier reports in connection with reduced flow in the ovarian artery [77]. In a repeat IVF procedure, Oelsner et al. retrieved oocytes from laparoscopically detorsed ovaries in six patients, and these oocytes could be subsequently fertilized and therefore recommended detorsion as the procedure of choice for ischemic ovaries [13]. The subsequent course of a pregnancy after treatment for adnexal torsion is generally favorable; abortion rates of 8.3–16.6 % do not appear to be increased [7, 15]. In a study by Spitzer et al. 60 % (3/5) of pregnancies continued to term with the vaginal delivery of healthy children. One pregnancy was terminated in the 19th gestational week for medical reasons as ultrasound showed sirenomelia (mermaid syndrome). There was one case of missed abortion in a 40-year-old patient; however, 11 months later, this patient gave birth to a healthy child [17]. In one large study, there were 60 % term deliveries, 15 % preterm deliveries (at 31, 32, and 34 gestational weeks, respectively), 5 % missed abortion, and 20 % elective abortions in the first trimester, with patients citing fear of surgical and anesthetic risk inflicted on the fetus. There was no significant difference in pregnancy results between laparoscopy and laparotomy. Twenty-seven percent delivered by Cesarean section for common obstetric indications, and 73 % underwent vaginal deliveries [56]. Bider et al. [35] reported that 61 % patients delivered at term and one delivered prematurely at 26 gestational weeks; similarly, 83 % of pregnant women in Hasson et al.'s study [7] delivered healthy babies at term, and 8 % had preterm delivery. Pregnancy outcome in Smorgick et al.'s study [34] was also favorable, with 70 % term deliveries and 26 % preterm births.

12.7.1 Risk of Recurrence

Laparoscopic fixation of the adnexa (ovariopexy) or shortening of the utero-ovarian ligament can be done to avoid recurrence of adnexal torsion, but this should be the exception rather than the rule [19, 20, 69, 71]. In their retrospective case control study, Hasson et al. reported a recurrence rate of 19.5 % for pregnant women and 9.1 % for non-pregnant women; however, 73.2 % of pregnant

women and 20.8 % of nonpregnant women had been treated with ART prior to torsion [7, 78]. There was no recurrence in a study by Spitzer et al. with five patients during the subsequent course of the pregnancy [17]. Torsion recurrence is higher in patients with OHSS [19, 79].

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(Isolated) Torsion of the Fallopian Tube

13

13.1 Incidence

Isolated twisting of a Fallopian tube is an uncommon event. The incidence from previous reports is 1/1,500,000 women [1]. The diagnosis of isolated twisted Fallopian tube in pregnancy is also very rare; only 12 % of cases are found during this time [2]. Phupong and Intharasakda found incidence of 1/120,000 pregnancies from a 10-year period (1991–2000) in their institution [3]. The English language literature concerning twisting or torsion of the Fallopian tube and pregnancy available from Cumulative Index Medicus from 1962 to 1965 and Medline from the year 1966 to 2009 were reviewed. There have been nine publications reporting 15 cases [3–5]. All cases occurred in reproductive age (range 20–41 years). The condition occurred in the first trimester in 13.3 % of cases, in the second trimester in 20 %, in the third trimester in 60 %, and intrapartum in 6.7 % of cases.

13.2 Pathophysiology and Risk Factors

13.2.1 Pathophysiology

Collectively, the existing reports indicate that the mechanism underlying tubal torsion is apparently a sequential mechanical event. The process begins with the mechanical blockage of the adnexal veins and lymphatic vessels by ovarian tumor, pregnancy, hydrosalpinx, or pelvic adhesions after tubal infection or pelvic operation. This obstruction causes pelvic congestion and local edema with subsequent enlargement of the adnexa, which in turn induces partial or complete torsion [6].

13.2.2 Risk Factors

Torsion of the Fallopian tube can occur at any age, and most of the patients are under 30 years of age. Youssef et al. noted factors that could possibly influence the occurrence of Fallopian tube torsion and divided them into two categories: *intrinsic factors* such as congenital anomalies of the Fallopian tube and acquired pathology of the Fallopian tube, for example, hydrosalpinx, hematosalpinx, neoplasm, surgery, autonomic dysfunction, and abnormal peristalsis, and e*xtrinsic factors*, for example, changes in the neighboring organs such as neoplasm, adhesions, pregnancy, mechanical factors, movement or trauma to the pelvic organs, or pelvic congestion [7]. More detailed theories for tubal torsion can be classified as [3, 8–16]:

- *Anatomic abnormalities*: long mesosalpinx, tubal abnormalities, hematosalpinx, hydrosalpinx, hydatid of Morgagni, tubal ectopic pregnancy, paratubal cyst
- *Physiological abnormalities*: abnormal peristalsis or hypermotility of tube, tubal spasm, and intestinal peristalsis
- *Hemodynamic abnormalities*: venous congestion in the mesosalpinx (progesterone effects of edema and increased vascularity of tissues)

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- *Sellheim theory*: sudden body position changes
- *Trauma, previous surgery, or disease* (tubal ligation, PID)
- *Gravid uterus* (direct mechanical cause and progesterone effects of edema and increased vascularity of tissues)

Many reports indicate that twisted Fallopian tube is more common on the right [8–18] than the left [3, 5]. This may be due to the presence of the sigmoid colon on the left [8, 9, 12, 14, 16] or to slow venous flow on the right side, which may result in congestion [16]. The other reason is that more cases of right-sided pain are operated because of the suspicion of appendicitis [9, 13], whereas left-sided cases may be missed and resolve spontaneously.

13.3 Clinical Presentation

The most common presenting symptom is pain, which begins in the affected lower abdomen or pelvis but may radiate to the flank or thigh [8–14, 16]. The onset of pain is sudden and cramp like and may be intermittent [9, 12, 14]. Other associated symptoms include nausea, vomiting, bowel and bladder complaints, and scant uterine bleeding [9, 11–14, 16]. Pelvic examination may reveal a tender, tense adnexal mass associated with cervical tenderness [19]. The case by Phupong and Intharasakda presented with only left lower abdominal pain and nausea and vomiting [3]. Because these signs, symptoms, and physical findings are associated with other common diseases, the diagnosis is never established before operation [8–18].

13.4 Diagnosis and Differential Diagnosis

13.4.1 Differential Diagnosis

The differential diagnosis includes [8, 9, 12–14, 16]:

- Acute appendicitis
- Ectopic pregnancy
- Pelvic inflammatory disease
- Twisted ovarian cyst
- Ruptured follicular cyst
- Degenerative leiomyoma
- Placental abruption
- Urinary tract disease
- Renal colic

13.4.2 Diagnosis

13.4.2.1 Laboratory Findings

The body temperature, white blood cell count, and erythrocyte sedimentation rate may be normal or slightly elevated [9, 11, 12, 14, 16].

13.4.2.2 Abdominal Ultrasound

There have been reports of using ultrasound in the diagnosis of twisted Fallopian tube [20]. The ultrasonographic appearance includes an elongated, convoluted cystic mass, tapering as it nears the uterine cornu and demonstration of the ipsilateral ovary [20] or normal ipsilateral ovary, free fluid, a dilated tube with thickened echogenic walls, and internal debris or a convoluted echogenic mass [21, 22]. High impedance, reversal, or absence of vascular flow in the tube has also been reported although, in practice, confident spectral Doppler analysis of the tubal wall may be difficult [23].

13.4.2.3 Abdominal CT

Reported CT findings of isolated tubal torsion include an adnexal mass, a twisted appearance to the Fallopian tube, dilated tube greater than 15 mm, a thickened and enhancing tubal wall, and luminal CT attenuation greater than 50 Hounsfield units consistent with hemorrhage. Secondary signs include free intrapelvic fluid, peritubular fat stranding, enhancement and thickening of the broad ligament, and regional ileus [21, 24].

The English language literature concerning twisting or torsion of the Fallopian tube and pregnancy available described 9 publications reporting 15 cases [3–5]. All of the cases were not able to be diagnosed as twisted Fallopian tube before surgery.

13.5 Treatment and Prognosis

13.5.1 Treatment

The management of this condition is early operation [9, 14, 18].

13.5.1.1 Types of Operation

If the tube is beyond recovery (gangrenous, suspected malignancy), then salpingectomy is necessary.

Indications for untwisting (detorsion) are:

- Twisting is incomplete or recent [8–10, 12, 14–16].
- Ischemic damage appears to be reversible [8–10, 12, 14–16].
- No malignancy and ruptured/unruptured ectopic pregnancy suspected [4].

13.5.1.2 Laparotomy/Laparoscopy

Laparotomy is often performed [8–12, 14–16, 18], but laparoscopic surgery has recently been described in the management of twisted Fallopian tube [3, 13] and is currently recommended as access of choice in general population [25]. A recent report confirmed that laparoscopic surgery is safe for use in the first trimester of pregnancy [26]. Recovery is much faster after laparoscopy than laparotomy. Laparoscopy also causes fewer pelvic adhesions which are particularly important for women of reproductive age who wish to preserve their fertility. If the patient is in her third trimester, most surgeons prefer laparotomy, because laparoscopy is technically very difficult [25].

13.5.2 Prognosis

The English language literature concerning twisting or torsion of the Fallopian tube and pregnancy consists of 9 publications reporting 15 cases [3–5]. There were no associated findings during operation in 26.7 % of cases, while reported associated findings were paratubal cyst in 20 %, ovarian cyst in 13.3 %, and 6.7 % of cyst of the mesosalpinx, cyst in the broad ligament, sactosalpinx, hydrosalpinx, hematosalpinx, and unruptured tubal ectopic pregnancy. Most of the cases were treated with salpingectomy of the affected tube. In all of the cases, the pregnancies ended with a favorable outcome (except tubal ectopic pregnancy).

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Ruptured/Bleeding Ovarian Cysts/Tumors

14

14.1 Incidence

14.1.1 Ovarian Cysts

Follicular and corpus luteum cysts of the ovary are functional cysts and benign growths of the ovary. A follicular cyst arises from a normal follicle that fails to undergo ovulation or does not undergo the normal atretic process. It is usually clear and fluid filled. Corpus luteum cysts are less common than follicular cysts but are more associated with clinical symptoms. Ovarian cysts are not commonly found in pregnancy. Eiss, in 1930, reports a case of bilateral tumors, each of which ruptured in pregnancy. Their frequency varies with reports of different series. In Sloane Hospital (1931), the incidence was 1/500 pregnancies; in the University of California Hospital, 1/1,500, and in McKerron's compilations (1903), it was 1/2,500 pregnancies [1]. The tumors are thought to occur more often in nonpregnant women of the same relative age for which reason some believe they interfere with conception. Most of the cysts are small; they may or may not grow rapidly during pregnancy.

In the first trimester of pregnancy, ovarian cysts are often functional and generally resolve without complications, and therefore these were assumed to be physiological in nature [3, 4]. These resolving cysts were classified as cystic or hemorrhagic corpus lutea based on their appearance on gray-scale ultrasound [5]. After 16 weeks' gestation, the prevalence of ovarian cysts is 0.5–3.0 % [3, 5]. Interestingly, of the ovarian cysts that persisted at 20 weeks' gestation, 78.6 % were present at the 6-week postnatal scan, and all of these were pathological [5]. Zanetta et al. in a recent cross-sectional study assessed the prevalence of ovarian cysts at various stages of pregnancy, i.e., in the first, second, and third trimesters [4].

Only 1.2 % (79/6,636) of the women had an ovarian cyst with a maximum diameter of >30 mm. This figure is significantly lower than 5.4 % published by Condous et al. which is probably a reflection of different population groups. The earlier in gestation a scan is performed, the more ovarian cysts, and in particular functional corpora lutea, will be detected. Borgfeldt and Andolf investigated the rate of occurrence of adnexal pathology in premenopausal women aged 25–40 years. They defined an adnexal lesion as either a simple cyst with the largest diameter of at least 25 mm or a complex cyst of any size. Adnexal lesions were found in 7.8 % of the women [6]. Being a thin-walled vascular structure, such cysts are predisposed toward rupture; hemorrhage can be the primary event, but also a previous torsion can cause the cyst to rupture [7]. Rupture of adnexal torsion during pregnancy may also occur secondary to softening of the lesion following stromal decidualization [8]. Hemorrhage in the corpus luteum is a rare complication that occurs more frequently in younger women [9], especially when associated with pregnancy [10].

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14.1.2 Ovarian Teratoma

The frequency of ovarian tumors is about 1/1,000 pregnancies [2], and those which are malignant are found in about 1/15,000–1/32,000 pregnancies [3]. Mature cystic teratoma (dermoid cyst) is one of the most common benign ovarian neoplasms discovered during pregnancy (24–40 %) [35, 36]. The word teratoma is derived from the Greek word *teraton*, meaning monster, and was used initially by Virchow in the first edition of his book on tumors, which was published in 1863 [35]. Since mature cystic teratomas are composed of all three germ cell layers, the term "dermoid" is a misnomer. The majority of these tumors occur during the reproductive years providing further support for the germ cell theory [35]. Benign cystic teratoma (BCT) is the most common benign ovarian neoplasm comprising 10–15 % of all ovarian tumors. It occurs at all stages of life, the majority of cases being diagnosed between 20 and 30 years of age [37]. This fact makes it the most common tumor during pregnancy (22–40 % of all ovarian tumors) [37]. In pregnancy, the risk of complications increases significantly including rupture, torsion, infection, and malignant degeneration. As BCT has a tendency to remain in the confines of the true pelvis, it could lead to dystocia and obstructed labor [37].

The age shift of childbearing women could cause the changing of the histological distribution pattern. Jubb [38] reported 34 cases of primary ovarian carcinoma associated with pregnancy, with only 54 % being of epithelial type [39]. Further review of 22 additional cases reported between 1963 and 1988 revealed 27 % to be of epithelial type [40, 41]. In contrast to those previous reports, Dobashi et al. showed that the most common histological types were 80 % epithelial, 60 % invasive, and 20 % borderline tumors. Of note were the two clear cell carcinomas (20 %), which is a relatively high incidence compared to other studies outside Japan; the incidence of ovarian clear cell carcinoma in Japan is the most frequent in the world [43]. Incidence of malignancy in ovarian tumors complicating pregnancy was 2–5 %, and Jubb found only 24 authentic case reports between 1882 and 1963. The characteristic age group was 30–35 with a high incidence of nulliparity [38]. The age range in the study by Creasman et al. was 18–34, and around 50 % were primigravidas [42].

14.2 Clinical Presentation

Functional cysts of the ovary commonly do not cause pain unless the cyst is accompanied by rupture, torsion, or hemorrhage. Around 37 % of Caverly's 73 cases never gave symptoms. If the tumor is large, it may cause pressure symptoms, varying from discomfort dyspnea, bladder irritability, etc., to actual pain. Corpus luteum cysts arise from the mature corpus luteum. They more frequently attain a larger size than the follicular cyst. Corpus luteum cysts often produce a delay in the onset of the menstrual period, and when it occurs, it may be heavy in nature (*Halban's syndrome*). Because the cysts are usually larger than follicular cysts and associated with intraluminal bleeding, pain may be a common complaint. The cysts usually regress spontaneously and resolve in 4–8 weeks. Rupture of a follicular cyst may cause an acute onset of pain that is usually short-lived. Corpus luteum cysts are very vascular, and severe life-threatening hemorrhage may occur when they rupture. The combination of a delayed menstrual period, acute pain, pelvic mass, and evidence of hemoperitoneum is strongly suggestive of a ruptured corpus luteum cyst. The acute pain associated with rupture of a blood-filled corpus luteum cyst is indistinguishable from that of a ruptured ectopic pregnancy. A serum beta-human chorionic gonadotropin (βHCG) level may be helpful in distinguishing these two entities.

Jubb found that common symptoms of malignant ovarian tumors during pregnancy are excessive generalized enlargement of the abdomen and lower abdominal pain which were the common presenting symptoms. Five of Jubb's 24 patients (21 %) presented with an acute abdomen due to complications of the carcinoma such as rupture, torsion, or strangulation [38].

McKerron collected 1,290 cases in 1903 and said that 80 % of small tumors occupying the

pelvis are found only upon pelvic examinations in labor [1]. On the contrary, the diagnosis was made during pregnancy in 77 % of Caverly's 83 cases. The absence of symptoms in one-fourth of cases shows the necessity of most careful antepartum routine examinations. The physical findings are often misleading. Hard semisolid dermoids or cystic tumors made tense by pressure may be mistaken for fibroids or vice versa. The abdominal distention with large flaccid cysts and fat abdomen may be most confusing. Ascites is common with cysts, but rarely occurs with fibroids.

Pelvic examination usually reveals diffuse pelvic tenderness, often lateralized to the side of the cyst, and a mass may be palpated. If hemorrhage is severe, it may produce abdominal distention and shock.

14.3 Diagnosis

14.3.1 Laboratory Findings

Diagnosis between hemorrhagic ovarian cyst and ectopic pregnancy is sometimes difficult. The distinction between these entities largely depends on the serum βHCG level. Assuming no intrauterine pregnancy is seen in an elevated serum βHCG level makes these findings strongly suggestive of the adnexal ring heralding an ectopic gestation, whereas a negative serum βHCG level makes a hemorrhagic ovarian cyst more likely [14].

14.3.2 Abdominal Ultrasound

If the patient is hemodynamically stable, pelvic and abdominal sonography is valuable. The diagnosis is easy if the cyst is in the pelvis, but it is often missed if the tumor is small and behind the uterus, when its presence may not be revealed until after labor. The hemorrhagic ovarian cyst exhibits a myriad of sonographic appearances. Most commonly it is depicted as a rounded hypoechoic mass containing low-level echoes, fine strands, or septations; however, other patterns are seen so frequently that the hemorrhagic ovarian cyst has been termed "the great imitator" [12, 13]. Occasionally, a hemorrhagic ovarian cyst presents as a thick echogenic wall surrounding a central rounded echolucent area – a pattern remarkably similar to that of the adnexal ring sign of an ectopic pregnancy. The identification of an intrauterine gestational sac essentially excludes the diagnosis of ectopic pregnancy and may permit expectant management even when intraperitoneal bleeding has occurred [11].

14.4 Treatment

14.4.1 Introduction

Because complications of abdominal surgery are increased in pregnancy, surgical management of ovarian cysts in pregnancy has been reconsidered [15]. Historically, pregnant women with persistent adnexal masses underwent elective removal of the masses in the second trimester [16]; this is no longer an acceptable practice in asymptomatic women, as surgical intervention, as either an emergency or after 24 weeks' gestation, is associated with a poorer obstetric outcome [17]. Complications include spontaneous miscarriage or preterm premature rupture of membranes [15].

Growing understanding of the natural history of *borderline ovarian tumors* has allowed us to be more conservative in their surgical management, preserving fertility in many young women [18]. However, the natural history of such tumors is still unclear. In one study, three women were thought to have borderline lesions. This was based on the sonographic appearance and the presence of papillary projections that were nonvascular on color Doppler. Only one of these was confirmed histologically; the others were a benign cystic teratoma and a benign hemorrhagic ovarian cyst that had undergone torsion [18].

This highlights the difficulty in classifying some ovarian masses, and it is well accepted that 10 % of adnexal masses are extremely difficult to classify [19]. Despite the fact that the borderline lesions in the study by Crispens were managed surgically, there is evidence to suggest

that expectant management of such ovarian cysts is an option [18]. In recent studies, this approach to such lesions was shown to be safe. After the pregnancy, these patients underwent surgery [5, 19].

14.4.2 Conservative Treatment

14.4.2.1 Observation

As only 0.13 % of women with an ovarian cyst required acute intervention during pregnancy, conclusion is that examining the ovaries at the time of a first trimester scan is of limited value. Those women requiring intervention will present with pain, while prior knowledge of the presence of a cyst may only increase anxiety even though the risk of complication is very low. If an apparently nonmalignant ovarian cyst is noted at the time of a first trimester ultrasound examination, the woman should be offered a follow-up scan 6 weeks after the pregnancy has concluded. Although there are no randomized clinical trials to determine the optimal management of an adnexal mass in pregnancy, experience suggests that expectant management is safe and without serious adverse outcome for both mother and fetus [4, 5].

In emergent settings, if a provisional diagnosis of hemorrhagic corpus luteum cyst with minimal hemoperitoneum can be made, most such cases may be best served by expectant management with serial clinical examination and hemoglobin measurements [9].

14.4.2.2 Aspiration

Aspiration of simple ovarian cysts during pregnancy is safe and may prevent the need for surgical intervention; in some cases, this will be the definitive treatment [20]. Neither anesthesia nor analgesia is required for such intervention. Ultrasound-guided aspiration for the relief of pain generated by simple ovarian cysts in nonpregnant women can be performed either transvaginally or transabdominally depending on the location of the cyst [21]. After 14 weeks' gestation, the uterus is an abdominal organ, and as a result the ovaries are more easily targeted transabdominally. If the pain persists after the procedure without other symptoms or complications, a laparoscopic ovarian cystectomy after delivery is indicated [5]. Fine-needle aspiration is not appropriate if the cyst has any suspicious morphological features. It is not a common diagnostic problem because the frequency of ovarian cancer in pregnancy is reported to be 1/15,000–1/32,000 pregnancies [3].

14.4.3 Operative Treatment

If the patient is hemodynamically unstable or the diagnosis is in question, exploratory surgery is required. In hemodynamically unstable patient, emergency laparotomy, not laparoscopy, is indicated because definitive surgery is mandatory in the shortest possible time period. If rupture and bleeding do occur, diagnostic and therapeutic laparoscopy is appropriate.

If a provisional diagnosis of hemorrhagic corpus luteum cyst with minimal hemoperitoneum can be made, most such cases may be best served by expectant management [9]. However, once massive hemorrhage from ruptured corpus luteum cysts occurs, it can be a life-threatening condition that requires emergent surgical intervention [10]. With advances in laparoscopic surgical procedures and the development of surgical equipment, laparoscopic treatment of a ruptured corpus luteum cyst with hemoperitoneum is highly desirable [22–25]. Further, utilizing intraoperative autologous blood transfusion, transfusion of bank blood can be avoided even in cases of massive hemoperitoneum due to ruptured corpus luteum cyst in patients with ectopic pregnancy [23, 25].

14.4.3.1 Laparoscopy

Introduction

Laparoscopic cystectomy in pregnancy was first reported in 1991 by Nezhat et al. [26] and then a second case in 1994 by Howard and Vill [27]. Since then, for various reasons, laparoscopic surgery in pregnancy has rapidly increased as

surgeons realized the safety of the technique in general as well as in pregnancy. Pregnancy is no longer considered as an absolute contraindication for laparoscopic procedures. There is evidence to suggest that laparoscopy and laparotomy do not differ with regard to fetal outcome, that is, fetal weight, gestational age, growth restriction, infant survival, and fetal malformations [31]. However, the major advantages of laparoscopy are magnification and panoramic view of the pelvis resulting in reduced intraoperative uterine manipulation which may lead to decreased postoperative uterine irritability, miscarriage rate, and preterm labor which is seen in 50 % of third trimester cases with an open approach. In addition, the cosmetic results are much better, and the discomfort of stretching and distension of the laparotomy scar due to the rapidly growing uterus is avoided. Very few case series provide long-term follow-up. Only one series with 11 cases of 1–8 years of follow-up has reported no evidence of developmental or physical abnormalities in the resultant children after acute non-obstetrical surgery during pregnancy [32].

With increasing gestational age, the uterus rises out of the pelvis, and there is an increasing chance of injury while inserting the Veress needle. Generally, open cannulation laparoscopy or Palmer's point entry is recommended for laparoscopy during pregnancy. This avoids the risk of penetrating injury to the pregnant uterus by either the Veress needle or the trocar cannula [28].

Cystectomy

After confirmation that the bleeding is secondary to a cyst, conservative therapy consisting of removing the cyst and coagulating its base is standard therapy. If it is necessary to remove a corpus luteum of early pregnancy (prior to 12 weeks), progesterone replacement is advisable following surgery.

Large cystic masses may require decompression to fit though a small incision. By decompressing a cyst into a laparoscopic bag, spillage can be minimal or nonexistent. Copious irrigation also helps to keep the residual content to a minimum [29]. After cystectomy, the ovarian incision can be left open or approximated by three techniques:

- Fine monofilament suture of the edges
- Tissue glue
- Coagulation of the ovarian cortex adjacent to the surface, which will in some instances evert the edges

Stitching is necessary to avoid adhesions between the raw ovarian surface and the raw peritoneal surface left after bowel adhesiolysis in the left adnexa [29].

Furthermore, the risk of obstruction of labor by ovarian cyst or tumor is calculated to be 17–21 % [30]. Antenatal operative procedures ranging from aspiration of the cyst to oophorectomy are described in the literature to prevent the risk of obstruction of labor.

14.4.3.2 Bilateral Ovariectomy/ Adnexectomy

There are many reported cases where both ovaries have been removed and the pregnancy has normally continued. It is usually stated that the corpus luteum is indispensable to pregnancy for the first two months and removal during that time precipitates abortion. Waldstein, however, recently removed bilateral dermoids at the second month without interrupting the pregnancy. Caverly reports two abortions following eight single ovariotomies before the third month of pregnancy. Another two patients continued early pregnancy to term after bilateral ovariectomy. Both women, however, had many children [33].

14.4.3.3 Ovarian Teratoma

Elective

Treatment of suspected ovarian teratoma is surgical removal as soon as possible after diagnosis to avoid complications. They may be responsible for torsion, rupture, and obstruction during labor. Rupture is rare, but once it has occurred, it can cause complications such as chemical or granulomatous peritonitis mimicking advanced ovarian malignancy [37, 44, 45].

All efforts should be made to avoid rupture or leakage of cyst fluid during the operation. If it happens before or during the operation, copious

saline washing should be performed to minimize chemical peritonitis and its sequel [44, 46, 47]. When BCT is found incidentally in the first trimester of pregnancy, surgical removal should be performed at 14–16 weeks of gestation to avoid the risk of damage to the corpus luteum. If diagnosis of BCT occurs at 16–22 weeks, surgery should be performed as soon as possible. If it is first discovered after 22 weeks of pregnancy, the treatment may be deferred until delivery [37]. Over 200 cases of BCT in pregnancy have been reported in the literature, and many of them ruptured spontaneously or iatrogenically. In a review of 47 cases, Kocak et al. reported that during cyst extraction, minimal spillage occurred in 42.5 % of cases and none developed chemical peritonitis [48]. Clement et al. [46] and Achtari et al. [47] reported chemical peritonitis following cystic fluid spillage. The patients needed further surgeries to treat the complications. Two other case reports by Suprasert et al. [37] and Phupong et al. [45] reported a diffuse peritoneal reaction mimicking advanced ovarian malignancy where full surgical staging was performed. Postoperative histological examination revealed BCT and chronic granulomatous peritonitis. A conservative approach was adopted, and patients were free of symptoms without further treatment at 12 months [36, 45]. The incidence of chemical peritonitis after rupture and leakage of cystic fluid in the peritoneum is less than 0.5 % [35]. The incidence of chronic granulomatous peritonitis after rupture or leakage of cystic fluid is also extremely rare. In granulomatous peritonitis after ruptured ovarian teratomas, numerous nodules of mature glial tissue implant on a widespread area of the peritoneum [49].

Emergent

Ruptured BCT of the ovary mimicking gynecological malignancy is uncommon and could be misdiagnosed [45]. Intra-abdominal peritoneal seedlings, adhesions, and/or masses are frequent sequel. In most such cases, abdominal seedlings are essentially of mature neuroglial elements, and long-term survival rate is good. Recognition of a dermoid tumor associated with glial seedling is important to avoid unnecessary debulking surgery. Following postoperative adhesions, fibrous bands, or obstructions, conservative management seems to have a good prognosis.

14.5 Prognosis

14.5.1 Maternal Outcome

14.5.1.1 Continuation of Pregnancy

There are several possible pathophysiologic mechanisms that can interfere with normal continuation of pregnancy. First is hormonal influence. The problem could arise if bilateral adnexectomy/ovariectomy is performed. Fortunately, there are cases with normal further pregnancy after that procedure (see Sect. 14.4). Second is obstruction of labor or pregnancy with the tumor or uterus incarcerated in the pelvis. The third is secondary infection of primary ovarian pathology. Graefe stated that ovarian cysts produce abortions or premature labor in 14–20 % of cases.

14.5.1.2 Malignant Tumors

In 21 of the reviewed cases by Jubb, the diagnosis was followed by immediate laparotomy and unilateral oophorectomy. Fourteen of these patients had no further treatment. In the 33 % (7/21) of reexplored patients, no residual carcinoma was found. Unfortunately, there is no record of grading of the carcinoma, and follow-up was inadequate. Because of this, the figure for the 5-year survival rate of nearly 60 % is unreliable [38]. All of Creasman et al.'s more radically treated patients with stage IA ovarian carcinoma were well at 5 years, and they claimed that this demonstrated the value of a more radical approach to treatment. It would seem equally likely that the good survival rates reflected early diagnosis at routine antenatal examinations of patients. It is obvious that sacrifice of the pregnancy does not improve the maternal prognosis and that unilateral oophorectomy can be employed [42].

14.5.2 Fetal Outcome

Even with therapeutic interventions, fetal mortality remains high at 31 % for significant nontraumatic intraperitoneal bleeding [34].

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Ruptured Ectopic Pregnancy 15

15.1 Ectopic Pregnancy in General

If one is confronted with a pelvic condition that follows no rules and conforms to no standards, he should think of ectopic pregnancy and pelvic tuberculosis.

Howard A. Kelly

15.1.1 Incidence

Although the total number of pregnancies has declined over the past two decades, the rate of ectopic pregnancy has increased dramatically. It is defined as implantation of a fertilized egg outside the uterine endometrium. The *Centers for Disease Control and Prevention* (*CDC*) reported that the number of ectopic pregnancies quadrupled from 17,800 in 1970 to 88,000 in 1989 [1]. This is an increase in rate from 4.5 to 16.8/1,000. In 1992, CDC estimated the US ectopic pregnancy rate at 1.97 % of all pregnancies [2] and appears to be rising [3]. Ectopic pregnancy caused an estimated 876 US deaths between 1980 and 2007 [4]. The prevalence of ectopic pregnancy among women who go to an emergency department with first trimester bleeding, pain, or both ranges from 6 to 16 % [5]. Ectopic pregnancy occurs with some seasonal variation and is most common in June and December [6]. The reason is unclear; the authors postulated that reproduction is seasonal, depends on photoperiod and temperature, and varies with different latitudes.

15.1.2 Risk Factors

The overall risk is approximately 1/200 pregnancies but may be increased 20- to 100-fold in certain subsets of women. These risk factors include [3, 7]:

- Previous laparoscopically proven pelvic inflammatory disease (PID)
- Previous tubal (ectopic) pregnancy
- Current intrauterine device use
- Previous tubal surgery, including tubal sterilization
- Previous infertility treatments

As many as 50 % of uterine tubes removed because of an ectopic pregnancy show prior inflammatory disease. The increased incidence of PID is thought to be a major factor in the increased numbers of ectopic pregnancies [8]. Although the risk of pregnancy is very low with a tubal ligation, if a pregnancy does occur, there is a significantly higher risk of the gestation being an ectopic one. Of those pregnancies occurring after tubal ligation, 10–50 % are ectopic, which represents a 20- to 100-fold increased risk [9].

15.1.3 Classification

15.1.3.1 Tubal Pregnancy

The vast majority of ectopic pregnancies implant in the Fallopian tube. Pregnancies can grow in the fimbrial end (11 %), the ampullary section (70 %), the isthmus (12 %), and the cornual and interstitial part of the tube (2 %) [10].

G. Augustin, *Acute Abdomen During Pregnancy*,
DOI 10.1007/978-3-319-05422-3_15,

A review published in 2010 supports the hypothesis that tubal ectopic pregnancy is caused by a combination of retention of the embryo within the Fallopian tube due to impaired embryo-tubal transport and alterations in the tubal environment allowing early implantation to occur [11].

15.1.3.2 Non-tubal Ectopic Pregnancy

Two percent of ectopic pregnancies occur in the ovary, cervix, or intra-abdominally [10]. Transvaginal ultrasound examination is usually able to detect a cervical pregnancy. An ovarian pregnancy is differentiated from a tubal pregnancy by the *Spiegelberg criteria* [12].

- Gestational sac is located in the region of the ovary.
- Ectopic pregnancy is attached to the uterus by the ovarian ligament.
- Ovarian tissue in the wall of the gestational sac is proved histologically.
- Fallopian tube of the involved side is intact.

While a fetus of ectopic pregnancy is typically not viable, very rarely, a live baby has been delivered from an abdominal pregnancy. In such a situation, the placenta sits on the intra-abdominal organs or the peritoneum and has found sufficient blood supply. This is generally bowel or mesentery, but other sites, such as the renal (kidney), liver, or hepatic (liver) artery or even aorta have been described. Support to near viability has occasionally been described, but even in third-world countries, the diagnosis is most commonly made at 16–20 weeks gestation. Such a fetus would have to be delivered by laparotomy.

Maternal morbidity and mortality from extrauterine pregnancy are high as attempts to remove the placenta from the organs to which it is attached usually lead to uncontrollable bleeding from the attachment site. If the organ to which the placenta is attached is removable, such as a section of bowel, then the placenta should be removed together with that organ.

This is such a rare occurrence that true data are unavailable and reliance must be made on anecdotal reports [13]. However, the vast majority of abdominal pregnancies require intervention well before fetal viability because of the risk of hemorrhage.

15.1.3.3 Heterotopic Pregnancy

In rare cases of ectopic pregnancy, there may be two fertilized eggs, one outside the uterus and the other inside. This is called a heterotopic pregnancy. Often the intrauterine pregnancy (IUP) is discovered later than the ectopic, mainly because of the painful emergency nature of ectopic pregnancies. Although rare, heterotopic pregnancies are becoming more common, likely due to increased use of IVF. The survival rate of the uterine fetus of an ectopic pregnancy is around 70 %. Successful pregnancies have been reported from ruptured tubal pregnancy continuing by the placenta implanting on abdominal organs or on the outside of the uterus.

15.1.3.4 Persistent Ectopic Pregnancy

A persistent ectopic pregnancy refers to the continuation of trophoblastic growth after a surgical intervention to remove an ectopic pregnancy. After a conservative procedure that attempts to preserve the affected Fallopian tube such as a salpingotomy, in 15–20 % the major portion of the ectopic growth may have been removed, but some trophoblastic tissue, perhaps deeply embedded, has escaped removal and continues to grow, generating a new rise in βHCG levels [14]. After weeks, this may lead to new clinical symptoms including bleeding. A decline of less than 55 % at day 3 predicts persistent ectopic pregnancy and may select early cases for second-line methotrexate therapy [15]. βHCG dynamics in the week before salpingotomy and bleeding activity at surgery may identify patients who are the most likely candidates for persistent ectopic pregnancy after laparoscopic linear salpingotomy [14].

15.1.4 Clinical Presentation

15.1.4.1 History of Physical Examination

Toward the end of the nineteenth century, the first diagnostic strategies for ectopic pregnancy were

reported, occasionally with successful outcome for the women [16]. The diagnosis of ectopic pregnancy based on clinical criteria (of gastric and mammary symptoms of pregnancy, cessation of the menstrual cycle, palpation of a tumor next to an enlarged uterus, ballottement in the tumor, and purple discoloration of the vagina) had false preoperative diagnosis of a ruptured ectopic pregnancy of 20 %, while the diagnosis of an unruptured ectopic pregnancy was virtually impossible [17].

15.1.4.2 Symptoms

Few of the conditions which come under the notice of the gynecologist are of greater interest in diagnosis than extrauterine gestation. Occasionally, cases occur which present features so striking and so characteristic that their nature is readily recognized. But this is not always the case, for the clinical features may be so complex as to puzzle the most experienced observers. And not only are the clinical features complex, they are also subject to extraordinary variation in character and severity, and it may be difficult to believe that the same pathologic condition has given rise to them all. A quote from Howard A. Kelly seems timely, that "if one is confronted with a pelvic condition that follows no rules and conforms to no standards, he should think of ectopic pregnancy and pelvic tuberculosis" [18]. The explanation of these difficulties lies in the fact that the symptoms associated with extrauterine gestation arise, not directly from the presence of the growing ovum in the Fallopian tube, but from certain secondary lesions, either traumatic or inflammatory, which supervene. These *secondary lesions* may be briefly enumerated as [19]:

- Intraperitoneal flooding from tubal abortion or rupture
- Intratubal bleeding leading to acute distension of the tube, the abdominal ostium being sealed
- Slowly progressive or recurrent hemorrhage leading to the formation of encysted collections of blood (pelvic hematoma, in the broad ligament, pelvic hematocele, in the pouch of Douglas, peritubal hematocele, around the abdominal end of the tube)
- Infection of the gravid tube or of an encysted collection of blood leading to suppuration

Until one or the other of these secondary lesions is produced, extrauterine pregnancy gives raise to no more local or general disturbance than does an early pregnancy in the uterus. An important symptom associated with this phase, a brief period of amenorrhea, is the most useful aid in diagnosis, but it is not always present. When a healthy adult woman, who is usually regular, goes for 2 or 3 weeks over the expected date of her period, there is a "strong presumption of pregnancy," but at this time, there is nothing to indicate whether pregnancy is uterine or extrauterine. In the latter case, however, amenorrhea is of very brief duration, seldom more than 7 or 8 weeks, and then gives place to hemorrhage. In something like 30 % of the cases, there is no amenorrhea at all. As it is quite unusual, for an extrauterine gestation to continue undisturbed beyond the end of the second month, there is consequently no time for the appearance of other general symptoms of pregnancy. But occasionally, morning sickness and early breast changes may be present. When the course of the gestation becomes interrupted by any of the occurrences mentioned above, the clinical features undergo rapid transformation, and symptoms appear which we are accustomed to regard as those of extrauterine pregnancy – those which result from the interruption of the pregnancy by injury to the developing ovum or to its containing sac.

These symptoms, which are regarded as *secondary symptoms*, are subject to great variation in their character and intensity in correspondence with the nature of the lesion which has given rise to them. The occurrence which is the simplest and the most easily recognized is *intraperitoneal flooding*; the symptoms which attend it are uniform and characteristic, and when a clinical history of amenorrhea can be obtained and a careful pelvic examination made, mistakes are hardly possible. Perforation of a hollow viscus, such as the stomach, duodenum, or gall bladder, is the only condition for which it is at all likely to be mistaken, even under circumstances unfavorable for diagnosis.

Hemorrhage from the uterus is a secondary symptom of extrauterine gestation which is constantly present. If no period of amenorrhea has occurred, it forms the initial symptom, and if

there has been amenorrhea, it succeeds it. In the great majority of cases, it is the earliest indication of anything wrong, but as the same thing frequently occurs from disturbance of a uterine pregnancy, little importance is usually attached to its appearance by either the patient or her doctor. The hemorrhage is slight or moderate in degree, sometimes continuous, sometimes irregular; it is usually dark, thick, and syrupy in appearance. It may continue for several weeks if the patient is not relieved by operation. The bleeding is no doubt due to separation and discharge of the uterine decidua, sometimes complete, more often in fragments; but in the majority of cases, the pieces of membrane do not attract attention.

This attempt on the part of the uterus to throw off its decidua when the tubal ovum has been damaged is the most interesting phenomenon. Some reflex mechanism is initiated which excites uterine contraction insufficiently powerful to detach portions of the membrane from the uterine wall and so gives rise to hemorrhage, which continues until the whole of the decidua has been expelled. It is possible that at the commencement some of the blood which escapes from the uterus may have made its way there from the gravid tube through the interstitial portion. In cases submitted to operation, the hemorrhage always ceases in a few days after the removal of the tube, and if portions of decidua have been retained, these give rise to persistent bleeding, as is so often the case in uterine abortion.

It is interesting to note that the effects produced by the rapid effusion of a large quantity of blood into the peritoneal cavity are, in the order of their occurrence [19]:

1. Acute abdominal pain
2. Fainting and the constitutional signs of hemorrhage
3. Shock, attended by vomiting, and lasting for several hours

No matter what may be the nature of the secondary lesions occurring in a case of tubal pregnancy, these two symptoms are common to them all – uterine hemorrhage and pain. The pain has certain characteristics. It is almost always sudden in onset, and usually spontaneous, although muscular effort, such as lifting something heavy or the act of defecation, may appear to excite it; it is always severe, and often of the most intense character; it affects at first the whole abdomen, but later may become localized; it is frequently attended with vomiting and other signs of shock, sometimes with faintness or actual syncope; after lasting acutely for several hours, it subsides and thereafter may recur at varying intervals of a few days or a week, until several attacks have been sustained; sometimes continuous pain without exacerbation follows the first attack. The initial attack of pain is almost always due to hemorrhage; the subsequent attacks have a more complex origin. But pain bearing the broad characteristics described above is a constant symptom of extrauterine gestation. In cases not immediately submitted to operation, recurrent attacks of intense pain may occur from repeated intraperitoneal hemorrhages. The classic signs of hemoperitoneum except abdominal pain include shoulder pain caused by irritation of the phrenic nerve which courses along the undersurface of the diaphragm, an urge to defecate, and syncope even in the absence of hypovolemia.

Subjective symptoms of pregnancy may also be present, such as breast tenderness and emesis gravidarum.

15.1.4.3 Signs

Cullen's Sign

Cullen's sign (Fig. 15.1) is the bluish-black appearance around the umbilicus, unassociated with any history of injury, together with a definite uterine history usually typical of the slow tubal abortion type of bleeding. Although Cullen first described the sign in 1918 and labeled it a new sign in ruptured extrauterine pregnancy [21], discoloration of the umbilicus due to the presence of peritoneal extravasations had been previously reported by Ransohoff in 1906. This author described jaundice of the umbilicus in a patient with a ruptured common bile duct, and in 1909, Hofstatter observed a blue discoloration of an umbilical hernia (*Hofstatter's sign*) in a patient with a ruptured tubal gestation. However, the discoloration in Hofstatter's case was not due to ecchymosis but rather to transmission of the color of the blood through the thinned-out semitransparent hernia.

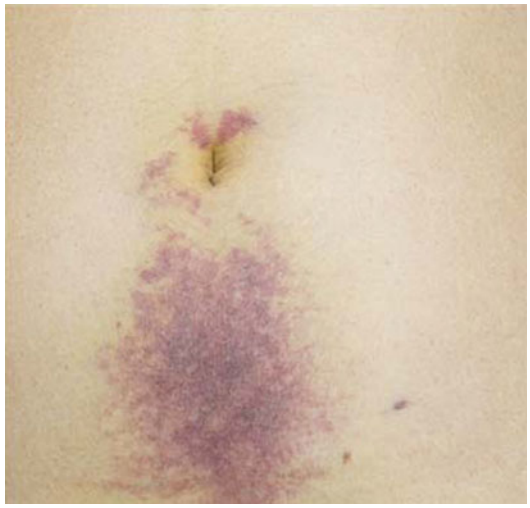

Fig. 15.1 *Cullen's sign* is a bluish-black appearance around the umbilicus; extension depends on the extension and etiology of the primary process [20]

The notion that the presence of blood in the abdominal wall might be responsible for these signs was first explored by Meyers et al., who used computed tomography [22]. They defined the anatomy of various retroperitoneal spaces and compartments, revealing that there is direct extension of hemorrhagic fluid from the posterior pararenal space to the lateral edge of the quadratus lumborum muscle, where a defect in the transversalis fascia permits access to the abdominal wall musculature. The intramuscular hemorrhagic fluid then presumably reaches the subcutaneous tissues via interruptions in muscular continuity. Cullen's sign results from the tracking of blood along the round ligament to the umbilicus. The portal of entry to the round ligament complex from the retroperitoneum is via the gastrohepatic ligament to the falciform ligament at the inferior-posterior liver edge [23]. In turn, the falciform ligament contributes to the connective tissue tube covering the round ligament (obliterated left umbilical vein) as it passes to the umbilicus.

The appearance of periumbilical ecchymosis (Fig. 15.1) is a rare observation, and when present, it is a late manifestation of intraperitoneal hemorrhage. In Cullen's case, the discoloration began 1 week after the onset of pain. Undoubtedly, prompt surgical treatment prevents the development of the sign in a great many cases. It is possible that in some cases the sign appears after operation without being observed. One also wonders how many patients with tubal abortion, who undergo spontaneous resolution without operation, may develop the sign and never come under medical observation. The degree of discoloration, or its presence, does not seem to be related to the amount of bleeding but rather to its duration and to other as yet undetermined factors (Table 15.1).

Table 15.1 Conditions associated with Cullen's sign

Pancreatitis
Ruptured ectopic pregnancy
Ruptured aortic aneurysm
Ruptured spleen
Ruptured common bile duct
Perforated duodenal ulcer
Hepatocellular carcinoma
Hepatic lymphoma
Metastatic thyroid cancer

Physical examination is variable, and adnexal masses are often not palpable [24, 25]. Tachycardia is not always present. Atypical physical findings include a paradoxical bradycardia [26], fever [27], and uterine enlargement suggestive of an IUP [27].

15.1.5 Diagnosis

15.1.5.1 Laboratory Findings

The urine βHCG assay is sensitive to ≤25 mIU/ml, and more than 95 % of patients with ectopic pregnancies have a positive test result [28]. Transvaginal ultrasound has replaced transabdominal for ectopic pregnancy diagnosis and early screening for an IUP because it can visualize an intrauterine sac at an earlier gestational age. A gestational sac should always be seen in the patient with a viable IUP when the serum βHCG reaches 2,000 mIU/ml. In many cases, the gestational sac can be seen at a level of about 1,000 mIU/ml [29, 30]. Ultrasonography is also very helpful in diagnosing blighted ovum or threatened abortions, which may be part of the differential diagnosis. Following serum βHCG

titer (which should double every 48 h in a normal, viable pregnancy) has no role in a patient with a suspected ruptured ectopic pregnancy, as that patient needs immediate surgical attention.

Depending on the severity of hemorrhage, hemoglobin concentration might be lowered or even normal [31]. Misleading and unexpected laboratory values such as hyperglycemia might also be present [32]. Many times diagnosis of an ectopic pregnancy prior to rupture may not be practical because the patient may not even know she is pregnant. These numerous diagnostic pitfalls are the reason for the maxim that any pregnant patient has an ectopic pregnancy until proven otherwise. All women of childbearing age should have a pregnancy test performed regardless of the date of their last menstrual period. Among women with symptoms and inconclusive ultrasound assessments, the progesterone test (five studies with 1998 participants and cutoff values from 3.2 to 6 ng/ml) predicted a nonviable pregnancy with pooled sensitivity of 74.6 %, specificity of 98.4 %, positive likelihood ratio of 45 (7.1–289), and negative likelihood ratio of 0.26. The median prevalence of a nonviable pregnancy was 73.2 %, and the probability of a nonviable pregnancy was raised to 99.2 % if the progesterone was low. For women with symptoms alone, the progesterone test had a higher specificity when a threshold of 10 ng/ml was used and predicted a nonviable pregnancy with pooled sensitivity of 66.5 %, specificity of 96.3 %, positive likelihood ratio of 18 (7.2–45), and negative likelihood ratio of 0.35. The probability of a nonviable pregnancy was raised from 62.9 to 96.8 % [33].

15.1.5.2 Imaging Diagnostic Tests

Positive pregnancy tests in the presence of abdominal pain mandate bedside sonography in the emergency department to locate the position of the fetal sac. The transvaginal technique is preferred because of its increased sensitivity for detecting an IUP and its superior visualization of the adnexa [3]. Most patients with ectopic pregnancies have some abnormality on the sonographic scan [34]. These abnormal findings include a cystic or complex adnexal mass (60–90 %) and free fluid in the peritoneal cavity (25–35 %, higher in a ruptured ectopic pregnancy) and should raise the suspicion of ectopic pregnancy. However, the findings are nonspecific, and not visualizing an ectopic pregnancy on ultrasonography can never definitely exclude it as a possible diagnosis. Location of ectopic fetal heart activity points to a clear diagnosis of ectopic gestation [24]. There are pitfalls involved with overreliance on laboratory values in the evaluation of ectopic pregnancy. Serum βHCG that is above the "discriminatory" level (at which ultrasound should be able to detect an IUP) might lead to a diagnosis of ectopic pregnancy when no IUP is visualized; however, values that fall below this level do not obviate the need for emergent ultrasound. In many cases, ultrasound might nonetheless be diagnostic. Recently, a case was diagnosed with three-dimensional sonography [35].

Since ectopic pregnancies are normally discovered and removed very early in the pregnancy, an ultrasound may not find the additional pregnancy inside the uterus. When βHCG levels continue to rise after the removal of the ectopic pregnancy, there is the chance that a pregnancy inside the uterus is still viable. This is normally discovered through an ultrasound. Ectopic pregnancy commonly occurs in the Fallopian tube and presents as a ring-enhancing adnexal cystic mass surrounded by hemoperitoneum on abdominal CT [36, 37] (Fig. 15.2).

15.1.5.3 Culdocentesis

Culdocentesis may be performed to gain additional information. A needle is inserted through the vaginal wall into the posterior cul-de-sac. These findings are possible:

- A dry tap is inconclusive.
- A few cubic centimeters of clear fluid (peritoneal fluid) rules out a ruptured ectopic, but neither rules out an unruptured ectopic.
- A lightly bloody fluid (hematocrit <15) is inconclusive. This could be from a traumatic tap, or early, mild bleeding from an ectopic.
- Moderately bloody fluid (hematocrit >15) indicates hemoperitoneum consistent with ruptured ectopic, but is nonspecific, and any

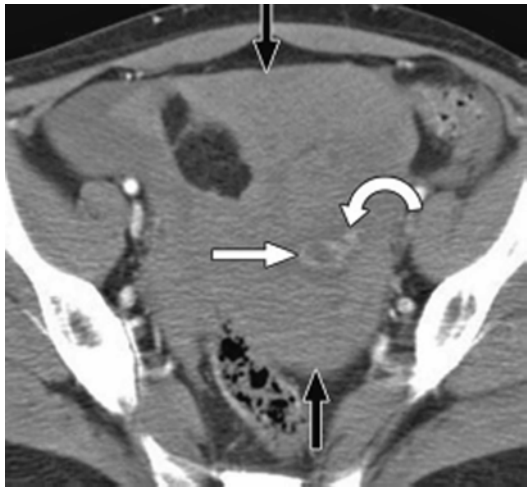

Fig. 15.2 A 42-year-old woman with increasing pelvic pain and negative urine pregnancy test. Axial contrast-enhanced CT section shows pelvic hematoma (*black arrows*) around ring-enhancing left adnexal mass (*white arrow*) and adjacent high-attenuation foci indicative of active bleeding (*curved arrow*). Rupture of ectopic pregnancy in the left Fallopian tube was confirmed at surgery. Serum βHCG test confirmed elevated levels after completion of CT scan [37]

internal bleeding (hemorrhagic ovarian cyst) can give this result.

- Bright red, clotting blood usually indicates a traumatic tap or aspiration of blood from a vessel.

Today, it is rarely done because it is not specific and is invasive, and with the use of abdominal CT scan, its lost it significance. Only about 50 % of patients with a positive culdocentesis have a ruptured Fallopian tube [38].

15.1.5.4 Diagnostic Laparoscopy/ Laparotomy

Ectopic pregnancy is commonly diagnosed during exploration (Fig. 15.3); primary ovarian pregnancy is usually diagnosed only at operation, although it may resemble a hemorrhagic corpus luteum (Fig. 15.4). The use of a laparoscope in the diagnosis of ectopic pregnancy was suggested in 1937 by Hope in the United States [41]. For example, a correct diagnosis at the time of surgery could be made in only 28 % in a series of 25 cases, because it was difficult to distinguish an ovarian pregnancy from a hemorrhagic corpus luteal cyst intraoperatively [42].

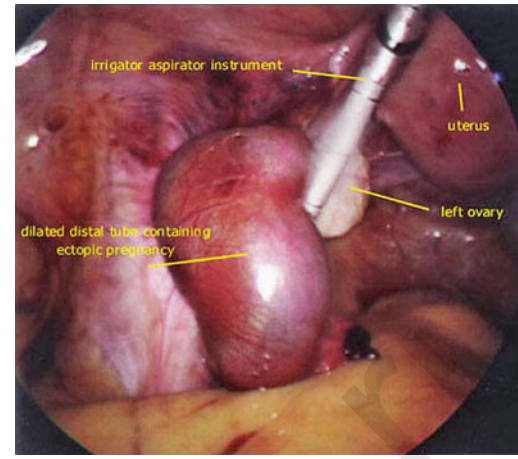

Fig. 15.3 The left Fallopian tube has been cleansed with an irrigator aspirator so that it is free of blood. The distal portion of the Fallopian tube can clearly be seen to be distended and blue [39]

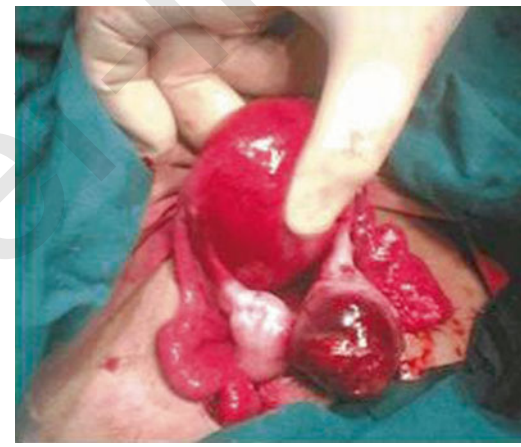

Fig. 15.4 Intraoperative view of right ovarian pregnancy. Note the yellowish-red corpus luteum on the left side of the congested ovarian pregnancy [40]

Figure 15.5 shows one of the recommended approaches to investigating first trimester pain or bleeding in the hemodynamically stable patient in the emergency department.

15.1.6 Treatment

When the diagnosis of ectopic pregnancy can be neither established nor excluded by ultrasound and laboratory evaluation, management depends

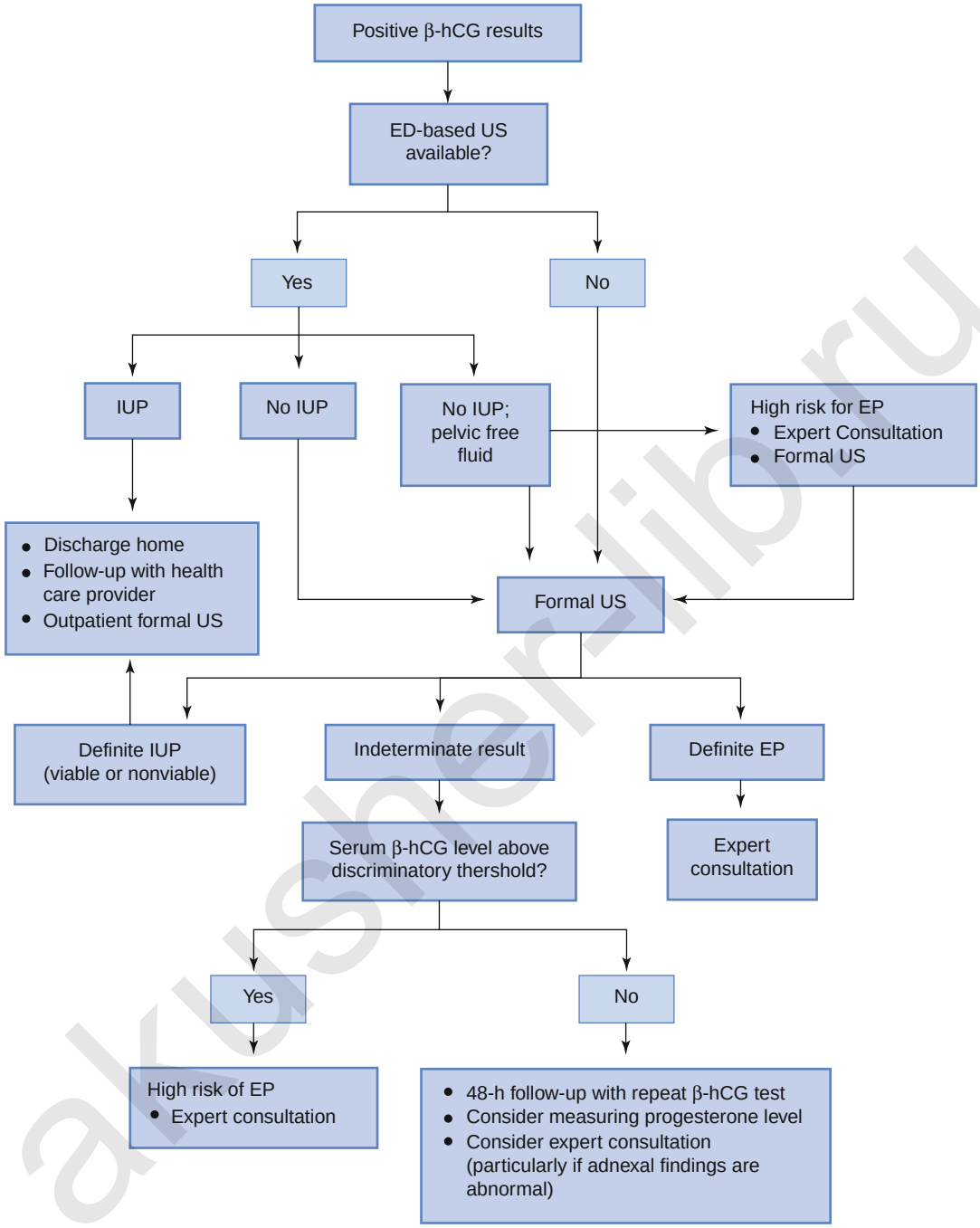

Fig. 15.5 Recommended approach to investigating first trimester pain or bleeding in the hemodynamically stable patient in the emergency department (*ED*). *βHCG* β-human chorionic gonadotropin, *US* ultrasonography, *IUP* intrauterine pregnancy, *EP* ectopic pregnancy [5]

upon many factors. The overall condition and stability of the patient, the availability of close follow-up care with an obstetrician/gynecologist, and the proximity of the patient to the hospital are important considerations if discharge is being contemplated. Decisions regarding disposition of

such patients should be made with a consulting obstetrician/gynecologist, and in some cases, admission to the hospital or surgical exploration might be preferred options.

15.1.6.1 Laparotomy

In 1849, Harbert of Louisville was the first to perform surgery early enough to stop fatal bleeding [43]. Robert Lawson Tait in London, after having performed autopsies on several women, recognized that appropriate dissection and ligation of bleeding vessels would be effective in the treatment of ectopic pregnancy. He successfully performed a laparotomy to ligate the broad ligament and removed a ruptured tube. By 1885, Tait had accumulated a relatively large number of successful cases of laparotomic salpingectomies [44, 45]. The diagnosis of an ectopic pregnancy was difficult, but if recognized, the procedure of choice was a laparotomy before rupture. In 1913, it is stated in Hartmann's textbook that: "every ectopic when diagnosed should be operated upon." Expectant management led in 86 % of women to death, but surgery saved 85 % of women [46].

In the first decades of the twentieth century, the introduction of asepsis, anesthesia, antibiotics, and blood transfusions saved the lives of many women with ectopic pregnancy. Still, the maternal mortality rate in the United States ranged from 200 to 400/10,000 cases of ectopic pregnancies [47].

Fallopian Tube-Sparing Surgery

Tube-sparing surgery is accomplished by removal of the ectopic pregnancy from the Fallopian tube via linear salpingostomy by making an incision on the antimesenteric portion of the tube over the bulge of the ectopic pregnancy, removing the pregnancy, achieving hemostasis, and allowing the tube to heal by secondary intention. There are no differences in subsequent pregnancy rates, adhesion formations, or fistula formation with or without closure of the incision site [48, 49]. Complications of salpingostomy include hemorrhage and persistent trophoblastic tissue. Trophoblastic tissue persists in approximately 5 % of patients [50]. Therefore, all patients must undergo follow-up βHCG levels. Fimbrial expression consists of "milking" the pregnancy out of the tube. This technique has been associated with complications such as persistent trophoblastic tissue and postoperative bleeding and probably should be reserved for ectopic pregnancies located at or very near the fimbria itself.

Salpingectomy

Salpingectomy is the procedure of choice if the woman has no desire for further pregnancies. It also may be necessary for hemostatic control of an attempted conservative approach with salpingostomy or with a tube that appears unable to be salvaged. Salpingectomy is the standard procedure in a patient who is hemodynamically unstable. It has also been suggested that women with a history of infertility may be better served with salpingectomy; as it has been shown in that subset of patients, treatment with salpingectomy resulted in equivalent pregnancy rates and a decrease in recurrent ectopic pregnancy [51].

Hemodynamically Unstable Patient

A patient who is hemodynamically unstable requires emergency laparotomy for surgical treatment, and laparoscopy and medical therapy (i.e., methotrexate) have no role. Patients who have a diagnosis or suspected diagnosis of ruptured ectopic pregnancy might require vigorous and immediate resuscitation with fluids and blood products before surgical intervention. Oxygen should be applied and an emergent obstetric consultation should be obtained. In a stable patient who does not have suspected rupture, nonoperative management with methotrexate therapy and close follow-up care might be considered in consultation with the obstetrician/gynecologist [3].

15.1.6.2 Laparoscopy

During the 1970s and 1980s, laparotomy was gradually replaced by operative laparoscopic options. Shapiro and Adler [52] reported laparoscopic salpingectomy using electrocoagulation followed by excision for an ectopic pregnancy in 1973. Salpingotomy by laparoscopy was first reported using multiple punctures in 1980 [53]. Linear salpingotomy with a cutting current was

described by DeCherney et al. in 1981 [54]. If clinically possible, the patient is better served with a laparoscopic approach with reduced morbidity, recovery time, costs, and equivalent future fertility rates compared with laparotomy [55–57]. Whether laparoscopic treatment should be performed conservatively (salpingotomy) or radically (salpingectomy) in women wishing to preserve their reproductive capacity has long been subject of debate. The result of a randomized controlled trial on salpingotomy versus salpingectomy in 454 women with a tubal pregnancy without contralateral tubal pathology showed that salpingotomy does not improve time to spontaneous ongoing pregnancy and leads more often to persistent trophoblast [58]. In women with desire for future pregnancy and with a tubal ectopic pregnancy in a solitary tube or in the presence of contralateral tubal pathology, salpingotomy is the treatment of choice [59, 60]. In case salpingectomy is performed due to a failed salpingotomy or other surgical difficulties, IVF is the appropriate treatment option for the loss of fertility. It should be remembered that approximately 3 % of ectopic pregnancies are not visualized by laparoscopy. Typically, these are very early gestations.

If a pregnancy has been previously determined to be nonviable by serum βHCG or if it is an undesired pregnancy, endometrial sampling by suction curettage may be performed to determine whether an IUP is present. If chorionic villi are obtained from the uterine cavity, the presence of a concurrent ectopic pregnancy along with the intrauterine one is highly unlikely. The reported incidence of coexistent pregnancies in the general population (i.e., intrauterine and extrauterine) is between 1/4,000 and 1/30,000 [55, 61]. Sampling the endometrium with biopsy instruments does not obtain an adequate sample for diagnosis and should not be used.

15.1.7 Prognosis

While the number of ectopic pregnancies has increased, the death rate from this disorder has steadily declined. It is an assumption that the decreased mortality rate is secondary to the effects of early detection and intervention. Despite this improvement, approximately 34 women die yearly of the complications of ectopic pregnancy. This accounts for 13 % of all pregnancy-related deaths [62]. With the advent of conservative surgery, the emphasis on early diagnosis and increased awareness of this condition may be an important factor in reducing the morbidity and mortality of ectopic pregnancy.

Mortality of a tubal pregnancy at the isthmus or within the uterus (interstitial pregnancy) is higher as there is increased vascularity that may result more likely in sudden major internal hemorrhage.

15.2 Ruptured Cornual Pregnancy

15.2.1 Definition

Rudimentary horn of a unicornuate uterus arises as a result of a partial development of one uterine horn and incomplete fusion of the two Müllerian ducts. In more than 75 % of cases of unicornuate uterus, a contralateral rudimentary horn is present. The majority of rudimentary horns contains functional endometrium and do not communicate with the unicornuate uterus [63–65].

15.2.2 Incidence and Pathophysiology

Pregnancy in a noncommunicating rudimentary horn has a reported incidence of 1/76,000–1/150,000 [63, 66], with less than 600 cases published. The first case was described by Mauriceau in 1669 [67], and the first case of cornual pregnancy diagnosed on ultrasound was reported in 1983 [68]. It occurs following transperitoneal migration of sperm or of fertilized ovum (zygote) [65]. Pregnancy in a rudimentary horn can result in rupture between 10 and 20 weeks of gestation with associated life-threatening hemorrhage [69] due to poorly developed musculature that cannot stretch. It is extremely uncommon for such cases to result in a viable fetus as they often result in rupture of

the horn before the third trimester [70]. Only 10 % cases reach term, and the fetal salvage rate is only 2 % [71, 72]. Rupture occurs commonly because of underdevelopment, variable thickness, and poor distensibility of myometrium and dysfunctional endometrium. Rudimentary horn pregnancy can be further complicated by placenta percreta due to the poorly developed musculature, scant decidualization, and small size of the horn, the reported incidence being 11.9 % [73].

15.2.3 Clinical Examination

As rudimentary horn pregnancies are always associated with catastrophic outcome, every effort should be made to diagnose them at an early gestation. A detailed history should be taken in every patient on her first visit including any complaints of severe dysmenorrhea. However, the rudimentary horn may be underdeveloped and its endometrium nonfunctional and dysmenorrhea may be absent [70]. A careful pelvic examination in the first trimester showing deviated uterus with a palpable adnexal mass should arouse suspicion of a Müllerian anomaly.

The unicornuate uterus with a rudimentary horn may be associated with complications such as hematometra, endometriosis, infertility, urinary tract anomalies, recurrent miscarriages, preterm labor, malpresentation, and placenta accreta [74].

15.2.4 Diagnosis

Diagnostic criteria for pregnancy in a rudimentary horn have subsequently been described such as [75]:

- Detection of a single interstitial tube in an empty uterus adjacent to the pregnancy
- Free mobility and the presence of a vascular pedicle adjoining the gestational sac and the lateral aspect of the empty uterus

Despite this, the sensitivity of ultrasound diagnosis of pregnancy in rudimentary horn is around 30 % [76, 77]. These criteria can be used with relative ease in the first trimester as pregnancy progresses it becomes more difficult to diagnose pregnancy in the rudimentary horn [78]. Furthermore, it is difficult to demonstrate the subtle anomalies that may be associated with this condition. Three-dimensional ultrasound may also play a useful role in evaluating uterine anomalies [75, 76, 78]. A high level of agreement between 3D ultrasound, hysterosalpingography, and laparoscopy in the classification of uterine morphology has been reported previously [79, 80].

The enlarging horn with thinned myometrium can obscure the adjacent anatomic structures, and the sensitivity further decreases as the gestation increases. If abdominal and/or vaginal ultrasound are equivocal and the patient stable, abdominal CT or MRI is indicated. MRI has proven to be a very useful tool for the diagnosis of pregnancy with a Müllerian anomaly and to confirm the presence of placenta percreta [81]. MRI can define a didelphys uterus with a fetus in one of the uterine bodies (Fig. 15.6).

Even with abdominal MRI, the placental invasion could remain elusive and is diagnosed only at laparotomy (Figs. 15.7 and 15.8) [70].

15.2.5 Treatment

15.2.5.1 Laparotomy/Laparoscopy

Traditionally laparotomy has been the preferred approach of choice, but with increasing expertise in laparoscopic surgery, there have been several reports of laparoscopic management of the pregnant rudimentary horn [83–87]. Laparoscopy, though the gold standard for surgical management of hemodynamically stable women with ectopic pregnancy, had long been considered a contraindication in women with hypovolemic shock. This is because of the effect of pneumoperitoneum, positioning of the patient, and the duration of surgery. There is always special

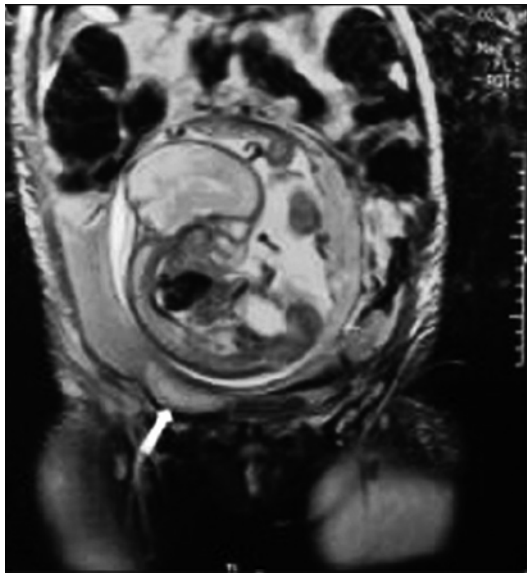

Fig. 15.6 MRI picture showing right uterine horn (*arrow*) and rudimentary horn above with fetus in situ. The placenta was left lateral, and there was no free fluid in abdomen [70]

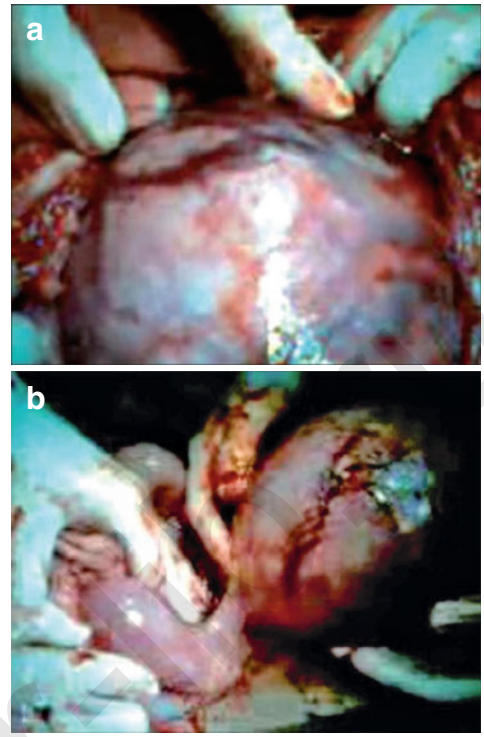

Fig. 15.7 (**a**) Placental blood vessels seen on the fundus of rudimentary horn. (**b**) Gravid left rudimentary horn seen attached to the unicornuate uterus by a fibrous band [70]

concern of pressure on the diaphragm and stomach posing significant threat of resuscitation and aspiration and pressure on the blood vessels which results in reduced cardiac output [88, 89]. Second trimester rudimentary horn pregnancies have all been managed by laparotomy [63, 65, 69, 90–92] with the exception of one 19-week unruptured rudimentary horn pregnancy which was managed by hand-assisted laparoscopy and one case of laparoscopic management in 16-week pregnancy [93].

15.2.5.2 Procedures

When diagnosed early, *excision of rudimentary horn with ipsilateral salpingectomy* is the recommended surgical treatment and provides the best prognosis. This has been recommended in the literature due to a remote possibility of ectopic pregnancy as a result of transperitoneal migration of embryo [85].

Microsurgical Fallopian tube transposition of the ipsilateral tube is recommended in the

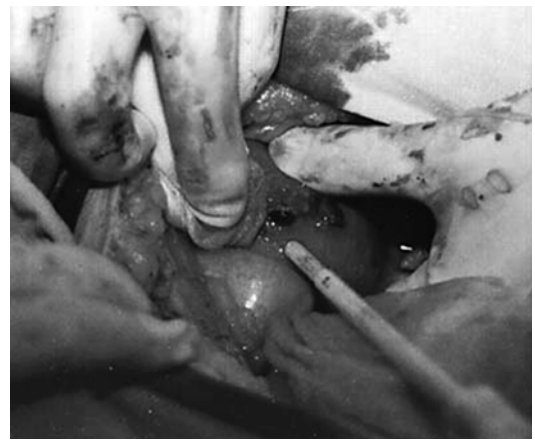

Fig. 15.8 Ruptured cornual area (0.5 cm) of the uterus with exposure of underlying intact amnion membrane [82]

presence of a damaged contralateral tube [94]. Even a case of spontaneous cornual rupture of a primigravidauterus occurring at 21 weeks' gestation was described, who underwent a direct repair followed by a continuing pregnancy until 33 weeks gestation, and finally delivered a normal fetus successfully via Cesarean section [82]. It is vital to evaluate the type of rudimentary horn and possible presence of urological anomalies before embarking on the surgical excision, in order to avoid associated complications [85]; hence, the interval excision of the rudimentary horn after complete preoperative evaluation is recommended [93, 95].

15.2.5.3 Perioperative Considerations

The use of calf length sequential pneumatic compression stockings in this group of patients not only increases venous return but also prevents the risk of venous thromboembolism [96].

15.2.6 Prognosis

The mortality rate has reduced from 23 % at the turn of the twentieth century to 0.5 % today probably due to earlier intervention. Despite this reduction in mortality, prompt intervention is necessary to remove the horn [97] and the ipsilateral Fallopian tube [83] if a diagnosis of pregnancy in rudimentary horn is made.

15.3 Abdominal Pregnancy

15.3.1 Classification

Abdominal pregnancies can be classified as *primary* when fertilization takes place outside the uterine adnexa or as *secondary* (thought to be more common) believed to result from undetected rupture of a tubal pregnancy. Primary peritoneal pregnancy can be clinically distinguished from secondary peritoneal pregnancy by *Studdiford's criteria* [98]:

- Normal tubes and ovaries with no evidence of recent or remote injury
- Absence of any evidence of a uteroperitoneal fistula
- Presence of pregnancy related exclusively to the peritoneal surface and early enough to eliminate the possibility of secondary implantation following a primary nidation in the tube

Implantation can occur anywhere in the abdomen including ligaments, liver, and spleen. Abdominal pregnancy is not strictly defined as *early* before which includes 12–28 weeks of gestation and *advanced* after that period.

15.3.2 Incidence

The incidence varies widely with geographical location, degree of antenatal attendance, level of medical care, and socioeconomic status [99]. It is believed that abdominal pregnancy is more common in developing countries probably because of the high frequency of pelvic inflammatory disease in these areas with suboptimal treatment [100, 101]. Heterotopic pregnancy is the coexistence of intrauterine and extrauterine pregnancies. Abdominal pregnancies make up a small percentage of ectopic pregnancies which are a common occurrence [102]. Moreover, 98 % of all extrauterine pregnancies are intratubal, 1 % is ovarian, and the rest are primary or secondary peritoneal implantations. Atrash et al. estimated in 1987 the incidence of abdominal pregnancy at 10.9/100,000 live births and 9.2/1,000 ectopic pregnancies in the United States [99] or between 1/3,000 and 1/8,000 deliveries in other studies [103, 104]. Ombelet et al. found an incidence of 1/402 pregnancies in developing countries and 1/10,000 pregnancies in developed countries [105]. Advanced abdominal pregnancy is rare and accounts for 1/25,000 pregnancies [106]. Recent estimated rate of occurrence of heterotopic pregnancy is 1/15,000 live births,

and the ectopic component is commonly tubal. Its incidence is increased in women undergoing assisted conception with superovulation, IVF-ET, and gamete intrafallopian transfer [107]. Incidence of heterotopic pregnancy has been reported as 1/8,000–1/30,000 in natural conception [108]. It may increase as high as 1 % with assisted reproductive techniques.

15.3.3 Risk Factors

Risk factors include a history of tubal pregnancies, pelvic inflammatory disease, tubal sterilization, and tubal infertility or tubal reconstructive surgery. Other women at risk include those who conceive despite the use of an intrauterine contraceptive device (IUCD) or progestagen-only contraceptive pills [109]. If none of the above risk factors is present, the undetected rupture of a tubal pregnancy is considered as case of heterotopic pregnancy. Cocaine abuse has been identified as a risk factor specific for abdominal pregnancy; the associated increase in risk may be up to 20-fold [110]. The first case of abdominal pregnancy after IVF was described in 1988 [111]. Mechanisms discussed for abdominal pregnancy during IVF are [112]:

- Uterine perforation during the transfer
- Spontaneous intra-abdominal fertilization
- Microfistula at the interstitial portion of the uterus

15.3.4 Clinical Presentation

Diagnosis of heterotopic pregnancy is a challenge not only for the obstetricians but also for other physicians who are following or treating the patient. Clinical findings are extremely variable, and the preoperative diagnosis is unsuspected in up to 60 % of cases [113]. Spontaneous progression of undetected IUP from the time of surgical management of acute or subacute ruptured ectopic pregnancy on postoperative follow-up is rare. On the contrary, spontaneous abortion of an IUP has followed ectopic rupture [114]. Early diagnosis depends on the clinician having a high index of suspicion. Reece et al. defined four common symptoms and findings [114]:

- Abdominal pain
- Adnexal mass
- Peritoneal irritation
- Increase in the size of the uterus

Frequent signs and symptoms include crampy abdominal pain, vaginal spotting or hemorrhage, nausea, vomiting, malaise, and painful fetal movement [103, 104, 113, 115]. The most common physical findings are abdominal tenderness, an abnormal fetal position, and displacement of the cervix. Tal et al. reported abdominal pain in 83 % and abdominal tenderness with hypovolemic shock in 13 % of the heterotopic pregnancy cases and vaginal bleeding in half of the patients. Finding of vaginal bleeding that can be concurrent in ectopic pregnancies is rarely seen in heterotopic pregnancies on account of intact endometrium of IUP [116].

15.3.5 Diagnosis

15.3.5.1 Laboratory Findings

Laboratory tests such as abnormally increasing βHCG are not sufficiently reliable on their own to make a diagnosis, as are signs and symptoms such as abdominal pain and tenderness, persistent transverse or oblique lie, and palpable fetal parts [102]. Quantitative measurements of serum βHCG levels are of no use, because the IUP will be producing normal and increasing levels of serum βHCG [117]. The absence of uterine contractions during oxytocin challenge testing is highly suggestive of abdominal pregnancy [115].

15.3.5.2 Ultrasound

Transabdominal ultrasound (Figs. 15.9 and 15.10), when coupled with clinical evaluation, has approximately 50–75 % success rate [102]. Guidelines have been provided for the use of ultrasound to diagnose abdominal pregnancy (Figs. 15.9 and 15.10) [119, 120]:

- Demonstration of a fetus in a gestational sac outside the uterus or the depiction of an abdominal or pelvic mass identifiable as the uterus separate from the fetus

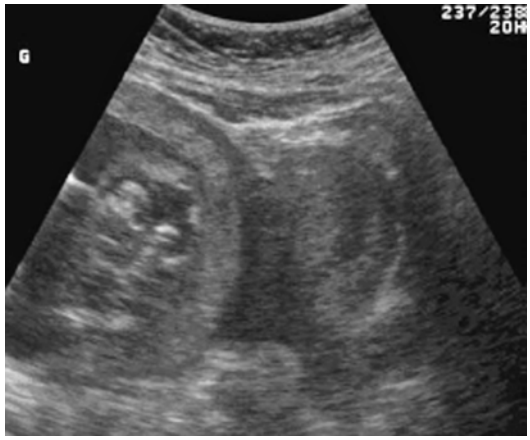

Fig 15.9 Abdominal ultrasound: pregnancy developing outside of the uterus [118]

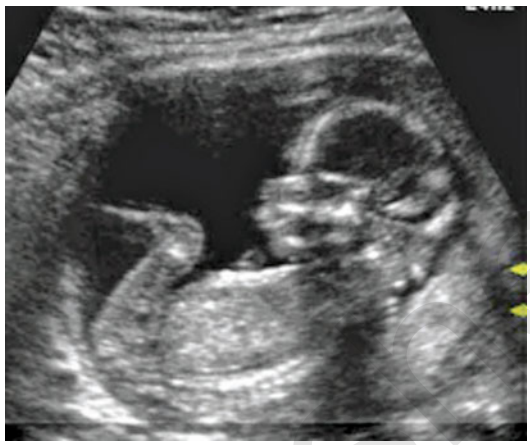

Fig. 15.10 Abdominal pregnancy: live fetus at 17 weeks with normal amniotic fluid [118]

- Failure to see a uterine wall between the fetus and urinary bladder
- Recognition of a close approximation of the fetus to the material abdominal wall
- Localization of the placenta outside the confines of the uterine cavity

The most frequent and reliable finding was separation of the uterus from the fetus (90 %). Extrauterine placenta (75 %) and oligohydramnios (45 %) were the next in frequency. Other features such as fetal parts close to the maternal abdominal wall (25 %), failure to visualize myometrium between the fetus or placenta and maternal bladder (15 %), abnormal fetal lie (25 %), poor visualization

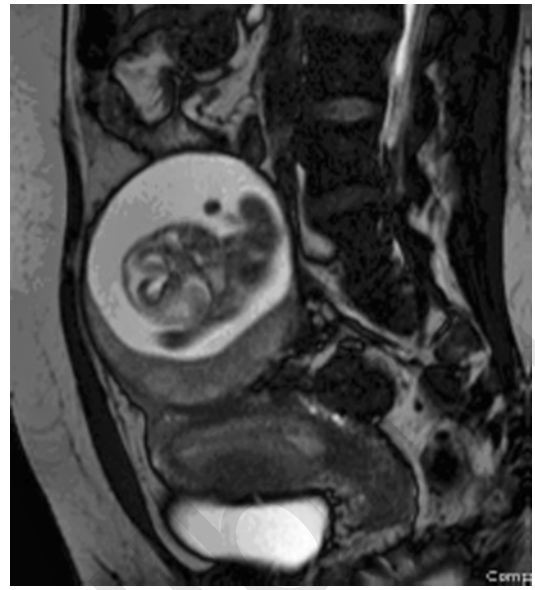

Fig. 15.11 MRI showing abdominal pregnancy: placenta is inserted on the posterior wall of the uterus [118]

of the placenta (25 %), and maternal bowel gas impeding fetal visualization (25 %) were noted [120]. To establish the diagnosis, clear identification of the empty uterus as a separate structure is important. This can be accomplished by giving close attention to the lower pelvis to ensure that there is continuity between normally appearing vaginal and endometrial echoes. Also, false-positive diagnoses must be avoided. Findings that mimic abdominal pregnancy include pregnancy in a bicornuate uterus, pedunculated uterine fibroids associated with a gravid uterus, and even an early normal pregnancy in a sharply retroflexed or anteflexed uterus.

15.3.5.3 Magnetic Resonance Imaging

An MRI scan can also be used to confirm the diagnosis of abdominal pregnancy showing the same characteristics as abdominal ultrasound (Fig. 15.11).

15.3.6 Treatment

For the management of abdominal pregnancy, factors such as maternal hemodynamic status, fetal congenital abnormality, fetal viability,

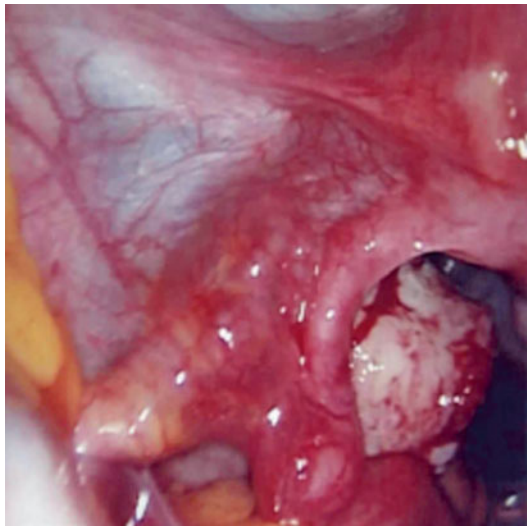

Fig. 15.12 Laparoscopic findings of a reddish and edematous mass on the left infundibulopelvic ligament of early abdominal pregnancy [122]

gestational age at presentation, and the availability of neonatal facilities should be considered. If the fetus is dead, surgical intervention is generally indicated owing to the risk of infection and disseminated intravascular coagulation. Various clinicians, however, recommend a period of observation of 3–8 weeks to allow atrophy of placental vessels [121]. If the diagnosis is uncertain and ectopic/abdominal pregnancy suspected, laparoscopy can be both diagnostic and therapeutic (Fig. 15.12).

15.3.6.1 Conservative Therapy

In the management of abdominal pregnancy with an embryo, treatment with methotrexate does not seem to be effective [123], but it could be added to surgical treatment [124]. Preoperative methotrexate treatment to minimize blood loss during surgery can facilitate maximal placental removal and has been described for abdominal pregnancy by Worley et al. [125]. Because of the risks of placental separation, most advise surgical intervention as soon as the diagnosis of abdominal pregnancy is confirmed, regardless of the fetal condition [99]. However, in some circumstances, it could be possible to await fetal maturity.

>20 Weeks' Gestation

If a conservative approach is to be considered with a diagnosis of abdominal pregnancy at >20 weeks' gestation, the following prerequisites have been proposed [126, 127]:

- Absence of fetal malformation
- Absence of maternal or fetal decompensation
- Continued surveillance of fetal well-being
- Placental implantation low in the abdomen, far away from the liver or spleen
- Adequate amniotic fluid
- Continuous hospitalization in an appropriate facility
- Informed consent from the patient

Maternal surveillance comprises physical examinations, serial ultrasound assessments, measurement of fetal growth, and daily fetal heart rate monitoring. Laparotomy can be planned for 34 weeks' gestation in the absence of complication.

<20 Weeks' Gestation

When the diagnosis is established before 20 weeks, continuing the pregnancy should be exceptional. The importance of informed consent is paramount [124].

15.3.6.2 Surgical Therapy

If the fetus is alive, laparotomy should be performed (Fig. 15.13), regardless of gestational age or fetal condition [100]. The reason is mainly based on the unpredictability of placental separation and consequential massive hemorrhage.

Perioperative Embolization

Nevertheless, removal of an abdominal pregnancy by laparoscopy after embolization has been described [128]. Embolization of the placental vascular supply can be performed before surgery to minimize blood loss, during surgery to facilitate maximal placental removal [128–130], and after surgery in case of postoperative hemorrhage

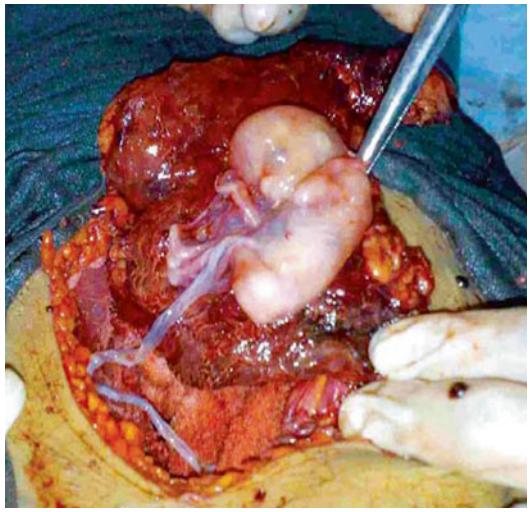

Fig. 15.13 Delivery of the fetus during abdominal pregnancy with the placenta was meticulously separated (which separation during pregnancy caused hemoperitoneum) [109]

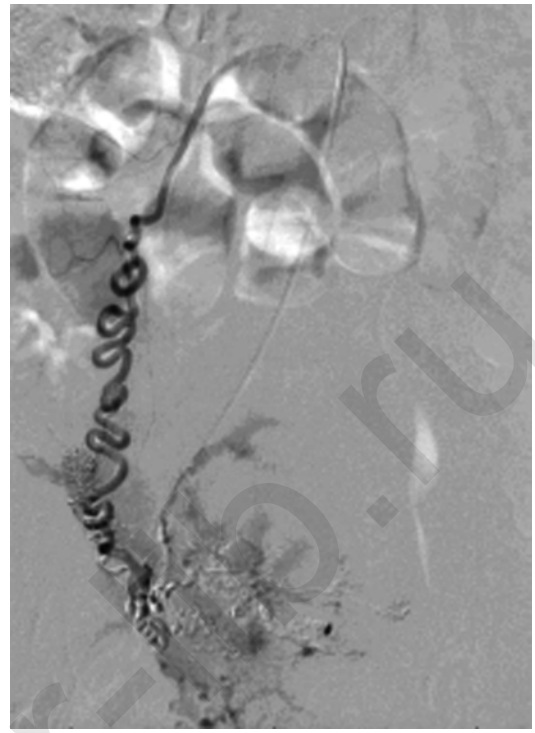

Fig. 15.14 Catheterization of the right ovarian artery, which was supplying the placenta in abdominal pregnancy [118]

[131]. Although no consensus regarding the treatment of the placenta in abdominal pregnancy has been established, most authors advocate leaving the placenta in situ unless the surgeon can be confidently assured that the entire blood supply to the placental bed can be surgically ligated without loss of excessive amounts of blood and the need for extensive blood replacement therapy. Preoperatively, the primary task of the angiographer is to identify all sources of blood supply to the placenta (Fig. 15.14) and to embolize vessels that could be difficult to ligate, such as the hypogastric artery.

Routine angiographic evaluation should include abdominal aortography with renal evaluation, selective celiac and superior mesenteric arteriography, and selective internal iliac arteriography. If embolization is not performed preoperatively, it can be performed postoperatively with the same technique in the presence of persistent bleeding.

Surgical Procedure

Laparotomy should be performed through a midline incision [102]. It is advisable to make the incision in the amniotic sac as far as possible from the placental attachment and large enough to extricate the fetus without trauma and to permit the subsequent drainage of amniotic fluid [127]. Because of the high risk of hemorrhage, it is preferable to leave the placenta in place by ligating the umbilical cord at its base. There is no effective method of controlling bleeding in the placental bed by clamping or cautery. Prolonged pressure, hot packs, and topical thrombin-containing compresses have been used with variable success. Use of temporary aortic compression or an abdominal balloon pressure pack in the pelvis can be lifesaving [127]. All efforts should be made to avoid leaving a drainage tube in place, as this increases the risk of abscess formation and septicemia [132]. Nevertheless, it may be advisable to remove the placenta if its blood supply can be secured, if the diagnosis is made early in pregnancy, or in cases with fetal demise of more than 4 weeks' duration [133]. In these

circumstances, removing the placenta has been followed by fewer complications, less need for repeat surgery, and fewer repeat hospitalizations [134, 135]. In fact, placental removal has been associated with low morbidity but high mortality [136]. In cases where placental implantation has occurred in vascular areas such as the mesentery and vital organs, it has been recommended that the placenta should be left in situ, because surgical excision can result in uncontrollable and life-threatening hemorrhage [137]. If discovery is not made until attempted Cesarean delivery, even then a safer alternative would be to defer delivery if possible, close the abdominal incision, and transfer the woman to an appropriate hospital. This could be done even after the delivery of the fetus or neonate with the placenta left in situ if there was no bleeding [125].

Postoperative Management

Patients should remain in intensive care for 24–72 h postoperatively. Complications may continue to occur for several weeks. A retained placenta can persist in situ for a number of weeks and has remained detectable for as long as 5 years [127].

Methotrexate can be used in the postoperative period to expedite absorption of the placenta. However, its use is controversial. It might increase infectious complications because of rapid tissue necrosis, but some authors argue for complete regression of the placenta. Methotrexate as a folate antagonist causes acute intracellular deficiency of these folate coenzymes, thus affecting synthesis of DNA especially in rapidly multiplying cells. Methotrexate acts on rapidly dividing cells, and it is likely to have limited effects on the mature placenta with its limited proliferative activity. With or without its utilization, the retained placenta will frequently undergo suppuration and require surgical removal [128, 138]. Risks of secondary hemorrhage could be diminished while keeping the infection risk low. A case of placental infusion with methotrexate via the umbilical arteries has also been described [139]. Its use preoperatively, or alternatively the use of actinomycin D, has been proposed to destroy trophoblastic activity in cases with an established fetal death [140].

15.3.7 Prognosis

15.3.7.1 Maternal Outcome

Abdominal pregnancy poses a serious threat to the survival of equally the mother and the fetus. Hence, it is vital that the diagnosis is made early in the pregnancy. Maternal mortality ranges 6–30 % [103, 104, 127]. This is principally because of the risk of massive hemorrhage from incomplete or entire placental separation. The placenta can be attached to the uterine wall, bowel, mesentery, liver, spleen, bladder, and ligaments, which can separate at anytime during pregnancy leading to heavy blood loss.

15.3.7.2 Fetal Outcome

The fetal outcome tends to be poorer than the mother's with perinatal mortality in range 40–95 % [126, 141]. Fetal abnormalities (congenital malformations) range 20–40 %, mostly because of associated oligohydramnios [142]. However, with advanced pregnancy and if the fetus is surrounded by a normal volume of amniotic fluid, fetal outcome tends to be better [127].

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Spontaneous Uterine Rupture 16

16.1 History

In James Dowling Trask's (1821–1883, one of the founders of the American Gynecologic Society) monograph on rupture of the uterus, 303 cases are recorded from 1700 to 1848; of these, only 38 are classified as ruptures during pregnancy, the others being cases of rupture during labor. On a careful examination of the notes in each of these 38 cases, it appears that the number must be considerably reduced – first, elimination of cases where the evidence that they were really cases of rupture of the uterus and not some other condition, for instance, abdominal extrauterine pregnancy and, second, by removing those cases which were really cases of premature labor, the pregnancy having advanced nearly to term. When this reduction has been made, there remain 14 cases [1]. Lustgarten quoted one case in the *British and Foreign Medico-Chirurgical Review*, one in the *Glasgow Medical Journal* in 1861, and 17 cases by Lewers in 1887 [2]. Nevertheless, in 1903, Baisch was able to record 37 instances of nontraumatic uterine rupture which occurred in the first 6 months of pregnancy [3].

16.2 Incidence

16.2.1 Developed/Undeveloped Country

Rupture of the uterus of pregnant women is one of the most serious obstetric complications. In spite of the recent advances in modern obstetric practice, it remains a life-threatening complication of pregnancy and labor especially in the developing world [4]. Table 16.1 shows the incidence rate differences between countries:

The problem with true incidence rates especially in Africa is that registration of births occurring at home is incomplete, although it is our impression that the number of patients who deliver at home and only seek medical attention when problems occur is decreasing. Also, a number of maternal deaths occur in the rural areas before hospital admission. More importantly, patients are transferred from peripheral hospitals and clinics, where the numbers of deliveries are unknown. Recent reports suggest that the incidence particularly of a spontaneous rupture may be on the increase in industrialized countries [39]. Widespread antenatal care and hospital deliveries made the maternal and fetal morbidity and mortality rather low.

16.2.2 Decade Dependency

Incidence is decade dependent. Incidence of uterine rupture in the United States between 1967 and 1978 was 1/1,000–1/1,500 deliveries, but spontaneous ruptures accounted for 25 % of the total and only 17 % of these occurred before the onset of labor [40]. After two decades, the incidences of spontaneous rupture of the unscarred uterus ranged from 1/8,000 to 1/15,000 deliveries [41]. The incidence is not strictly decade dependent, but due to the rarity of the spontaneous

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Table 16.1 (Spontaneous) uterine rupture incidence rates across the world (in decreasing incidence)

Country	Incidence
Ethiopia [5, 6]	1/38–1/175
Pakistan [7]	1/100
Nigeria (rural) [8]	1/112
Yemen [9]	1/159
Ibadan [10]	1/167
Guinea [11]	1/199
Uganda [12, 13]	1/93–1/200
Morocco [14]	1/222
Sudan [15]	1/246
Nigeria [16]	1/258
India [17, 18]	1/357–714
Lagos [19]	1/416
Kenya [20]	1/425
Libya [21]	1/585
Iraq (Basra) [22]	1/801
Turkey [23]	1/966
Saudi Arabia [24]	1/1,011
Nepal [25]	1/1,100
Australia [26]	1/1,163
Zimbabwe [27]	1/1,285
Republic of South Africa [28]	1/1,362
Trinidad [29]	1/1,500
Bahrain [30]	1/2,213
Tunis [31]	1/2,581
Kuwait [32, 33]	1/1,851–1/3,333
Canada [34]	1/3,333
Taiwan [35]	1/3,871
Ireland [36]	1/4,348
Qatar [37]	1/4,968–1/6,843
Singapore [38]	1/6,331
United States [39]	1/8,000–1/15,000

uterine rupture, most studies have a study interval of around a decade to collect enough number of patients sufficient for the analysis and comparison. With the progress of medicine and knowledge of the risk factors, the incidence is decreasing (Fig. 16.1).

16.3 Risk Factors

Most cases of spontaneous uterine rupture in undeveloped/developing countries is due to rupture of the unscarred uterus secondary to neglected obstructed labor, while previous Cesarean section scar (scarred uterus) rupture is the most common cause in developed countries [43–45]. On the contrary, in developed countries, rupture of unscarred uterus is severalfold lower than that of scarred uterus involving 1/17,000–1/20,000 deliveries [46]. Schrinsky and Benson in 1978 classified causes of uterine rupture during pregnancy [40] and here is updated and expanded version (Table 16.2):

16.3.1 Scarred Uterus (Previous Cesarean Delivery)

Various reports have shown that previous Cesarean section is the most important predisposing factor for the occurrence of uterine rupture [4, 47, 48], and so-called scarred uterus (uterine scars from any type of operation) is present in up to 65 % of cases [24, 47–49]. The rate of Cesarean delivery has risen from 5 % in 1970 to 26 % in 2003 despite improvement in obstetric procedures such as classic Cesarean section, internal version, total breech exaction, etc. [50]. Relevant to this issue of vaginal birth after Cesarean section (VBAC) is that the overall rate in the United States increased from 3.4 % in 1980 to a peak of 28 % in 1996. Commensurate with this eightfold increase in the VBAC rate, reports of maternal and perinatal morbidity also increased, in particular with reference to uterine rupture. By 2007, the VBAC rate in the United States had fallen to 8.5 %. Not surprisingly, the Cesarean delivery rate also reached an all-time high of 32 % in 2007. In its most recent guidelines pertaining to VBAC in August 2010, the *American Congress of Obstetricians and Gynecologists* (ACOG) adopted the recommendation not to restrict women's access to VBAC [51]. This occurred after the *National Institutes of Health Consensus Development Conference Panel* reviewed the totality of the evidence concerning maternal and neonatal outcomes relating to VBAC in March 2010 [52]. The recurrence rate for uterine rupture is reported to be between 4.8 and 19 % with the highest rates of recurrence seen in women with a history of a ruptured upper uterine segment (classic scar). All studies recommend planned Cesarean delivery [53–55].

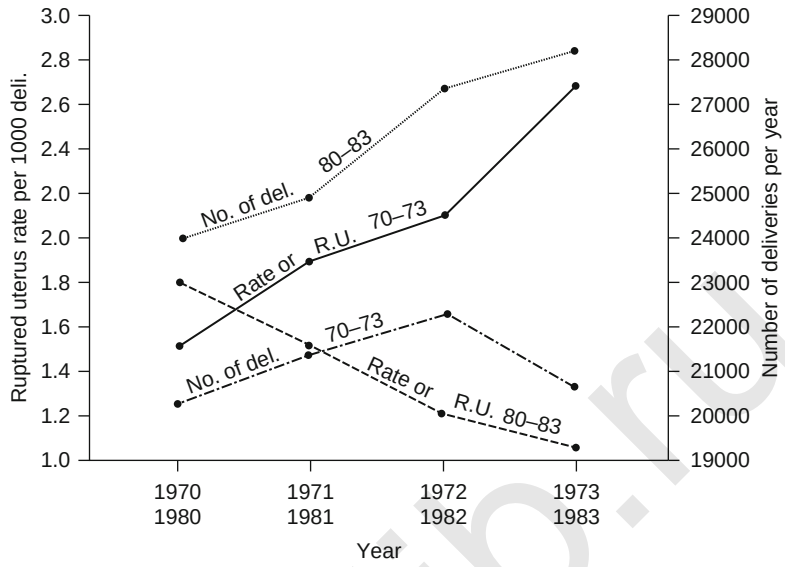

Fig. 16.1 Comparison between the total number of deliveries in 1970–1973 and 1980–1983 in relation to the rate of ruptured uterus per 1,000 deliveries in those years. (The numbers for 1983 are a multiplication of the first 6 months) (*R.U.* rupture of the uterus) [42]

16.3.1.1 Previous Classic Cesarean Delivery

Classic Cesarean delivery via vertical midline uterine incision is currently infrequently performed and account for 0.5 % of all births in the United States [56]. There is 11.5 % absolute risk of uterine rupture in women with classic vertical Cesarean scars who underwent an unplanned TOLAC [57]. For women who underwent repeat Cesarean section, the uterine rupture rate for women with prior classical uterine Cesarean scars was 0.64 %. All patients in that study underwent repeat Cesarean delivery, but a high rate of preterm labor resulted in 49 % of the patients being in labor at the time of their Cesarean delivery [56]. Landon et al. reported a 1.9 % absolute uterine rupture rate in women with a previous classic, inverted *T*, or *J* incision that either presented in advanced labor or refused repeat Cesarean delivery [58]. These rates of frank uterine rupture in women with classic Cesarean deliveries are in contrast to the higher rates of 4–9 % that the ACOG had historically reported for women with these types of uterine scars [59]. However, there is a 9 % rate of asymptomatic uterine scar dehiscence observed [56]. This result suggests that disruptions of uterine scars might have been misclassified as true ruptures instead of dehiscences in previous studies; this error may explain the bulk of the discrepancy.

16.3.1.2 Previous Low-Vertical Cesarean Delivery

A meta-analysis demonstrated a 1.1 % absolute risk of symptomatic uterine rupture in women undergoing a TOLAC with a low-vertical Cesarean scar [58, 60–63]. Compared to women with low-transverse Cesarean scars, these data suggest no significantly increased risk of uterine rupture or adverse maternal and perinatal outcomes. Interpretation of these studies is hampered by inconsistencies in how high the lower uterine segment could be cut before it was considered a classic incision. Even when the lower uterine segment is already well developed as a result of active labor, a low-vertical incision of adequate length is often impossible to permit fetal delivery. Naef et al. arbitrarily defined a 2 cm extension into the upper segment as a classic extension, and the overall rate of uterine rupture was 0.62 %. This rate could be further divided as 1.15 % for women who underwent a TOLAC compared with no ruptures among women who underwent elective repeat Cesarean delivery [60].

16.3.1.3 Unknown Uterine Scar

In many instances, the type of incision used for a prior Cesarean delivery cannot be confirmed due to unavailability of the operative report. Under these circumstances, the assessment of

Table 16.2 Classification of causes of uterine rupture during pregnancy

1. Traumatic rupture
A. Instrumental
(i) Uterine sound or curette
(ii) Manual removal of placenta
(iii) Various tool for induction of legal or criminal abortion
B. Violence: direct or indirect
C. Obstetric
(i) Oxytocins, forceps (low, mid, failed), breech extraction
(ii) Intrauterine manipulation: internal version, forceps rotation, shoulder dystocia
(iii) Fundal pressure
(iv) Craniotomy (hydrocephalus)
(v) Neglect: cephalopelvic disproportion, transverse lie
2. Spontaneous (prior to or during labor) rupture
A. Previous uterine surgery
(i) Cesarean section (low segment vs. classical)
(ii) Myomectomy
(iii) Salpingectomy
(iv) Ventrofixation
(v) Curettage or manual removal of the placenta
B. No previous surgery
(i) Congenital uterine abnormality
(ii) Cornual pregnancy
(iii) Hydatidiform mole or chorioadenoma destruens
(iv) Placenta percreta
(v) Genetic susceptibility for rupture (Loeys-Dietz syndrome)
(vi) No apparent cause
3. Combinations

uterine rupture risk may sometimes be guided by the obstetric history to infer the most probable type of uterine scar. For example, a patient with a history of a preterm Cesarean delivery at 28 weeks' gestation has a much higher likelihood of having had a vertical uterine incision than a patient who underwent a Cesarean section for an indication of arrest of fetal descent at term. It has been argued that because most Cesarean deliveries in the United States are accomplished via low-transverse uterine incisions, the risk of uterine rupture for patients with an unknown scar is similar to that for women who have previously undergone a low-transverse hysterotomy. This logic depends on the high ratio of low-transverse to vertical incisions performed for Cesarean section, but it ignores the varying probability with which different types of uterine incisions are made under different obstetric circumstances, as well as differences that occur due to varying medical resources and the prevailing local practitioner practices in countries other than the United States (e.g., practices that occur in other countries, such as Mexico or Brazil). An estimated 20,000 African refugees enter the United States each year, 80 % from countries were upper uterine segment Cesarean delivery is not an uncommon practice. Immigration of African refugees to Europe is becoming increasingly common [64]. Nevertheless, the vast majority of Cesarean deliveries performed in the United States are accomplished via low-transverse uterine incisions.

In a small case-control study of 70 patients, no association was found between an unknown uterine scar and the risk of uterine rupture; however, given the rarity of uterine rupture, this study was vastly underpowered to detect such a difference [65]. Two additional, but similarly underpowered, case series have also reported comparable rates of uterine rupture and VBAC success in women with unknown uterine Cesarean delivery scars versus those with documented previous low-transverse hysterotomies [66, 67]. The *Maternal-Fetal Medicine Units Network Cesarean Delivery Registry* reports a 0.5 % risk of uterine rupture for patients who underwent a TOLAC with an unknown uterine scar [58]. For cases in which there are one or two unknown prior uterine incisions, there is a single small, randomized, controlled trial by Grubb et al. that compared labor augmentation with oxytocin with no intervention in women with prior Cesarean deliveries involving either one or two unknown uterine incisions. Four uterine dehiscences and one uterine rupture occurred, all in the group that underwent labor augmentation [68].

16.3.1.4 Previous Low-Transverse Cesarean Delivery

The risk of uterine rupture after a low-transverse Cesarean delivery varies depending on whether patients undergo a TOLAC or an elective repeat

Cesarean delivery and on whether labor is induced or spontaneous, as well as other factors. The vast majority of Cesarean deliveries in the United States are of the low-transverse type. For women who have had one previous Cesarean delivery, examining the various risk factors for uterine rupture is instructive. These absolute risks for uterine rupture are discussed below.

16.3.1.5 Previous Cesarean Delivery Without a Subsequent Trial of Labor

In a large study, the spontaneous uterine rupture rate among women with a single Cesarean delivery scar who underwent scheduled repeat Cesarean delivery without a TOL was 0.16 % [69]. This finding indicates that uteri with Cesarean scars have an intrinsic propensity for rupture that exceeds that of the unscarred organ during pregnancy, which is 0.012 % (OR 12). Therefore, all other uterine rupture rates in women with a previous Cesarean delivery should be referenced to this expected baseline rate.

16.3.1.6 Previous Cesarean Delivery with Subsequent Spontaneous Labor

The uterine rupture rate among women with a single previous Cesarean delivery who labored spontaneously during a subsequent singleton pregnancy is in the range of 0.45–0.72 % [69–71]. This rate of uterine rupture implies an increased relative risk (RR) of three to four for women who labor spontaneously compared with women who undergo elective repeat Cesarean delivery.

16.3.1.7 Previous Cesarean Delivery with Subsequent Augmentation of Labor

Despite the clinical heterogeneity and different VBAC success rates for women undergoing spontaneous labor rather than either labor augmentation or induction, very few studies have stratified their data by labor augmentation versus labor induction, and the data that do exist are conflicting. There is wide variance in the frequency of clinical use of oxytocin as well as in the dose and dosing schedules of oxytocin that are used. As a result, there is a paucity of specific evidence-based clinical guidelines for the use of oxytocin in VBAC trials. In a study by Blanchette et al., the rate of uterine rupture in women who underwent oxytocin augmentation of labor after a previous Cesarean delivery was 1.4 %, compared with 0.34 % in women who underwent a trial of spontaneous labor. This finding suggests a fourfold increased risk of uterine rupture in women who undergo labor augmentation with oxytocin compared with spontaneous labor after a previous Cesarean delivery.

In another study, the rate of uterine rupture with oxytocin augmentation was 0.9 % versus 0.4 % without oxytocin use [52]. Zelop et al. also found that labor augmentation with oxytocin did not significantly increase the risk for uterine rupture [70]. However, the conclusions to be drawn from this are both limited and suspect because, in general, no proper adjustment has been made for the potential (and very likely) confounding by indication that occurs in the observational studies that attempt to compare the rate of uterine rupture for women receiving treatment with oxytocin versus those who do not (e.g., proper propensity score matching has not been performed). Tahilramaney et al. found that neither the administration nor the duration of oxytocin had an impact on dehiscence or rupture [72]. Phelan found that when oxytocin is used in a judicious manner, there is no increased risk of uterine dehiscence or rupture in the scarred or unscarred uterus [73]. Therefore, the duration of labor and not oxytocin use itself may predispose the patient with or without a uterine scar to rupture. The problem in some studies from developing countries is high percentage of its use; 41.7 % of the respondents were given this drug (all but one had it through intravenous infusion) [9]. Oxytocin was used for augmentation of already prolonged and obstructed labor rather than for active management of labor concluding that the supervision and control over this drug is missing.

In this regard, assessment of the safety of oxytocin use in VBAC trials must consider both the dosage and the time of exposure. These issues were addressed by Cahill et al. in a multicenter, retrospective cohort with at least one prior

Cesarean delivery who underwent a TOLAC. At an intravenous oxytocin dosage range of 6–20 mU/min, a more than threefold increased risk of uterine rupture was associated with oxytocin use. At a dosage range of more than 20 mU/min, a nearly fourfold increased risk of uterine rupture was noted. The attributable risk of uterine rupture associated with oxytocin use was 2.9–3.6 % for the maximum oxytocin dose ranges of more than 20 mU/min and more than 30 mU/min, respectively. The authors did not find a significant risk association between time (in terms of both duration of oxytocin exposure and duration of labor) and uterine rupture risk. They suggest an upper limit of 20 mU/min of oxytocin for use in VBAC trials and a judicious approach to the use and monitoring of oxytocin for both labor augmentation and induction.

The benefit of intrauterine pressure catheter (IUPC) monitoring of uterine contractions in VBAC trials is unclear, with only a single small case series failing to detect differences in fetal or maternal morbidity/mortality associated with uterine rupture when an IUPC was used instead of external tocodynamometry. Nevertheless, many institutions have found the IUPC useful in allowing careful titration of oxytocin dosing, especially when maternal habitus poses a limit to the accurate external monitoring of uterine contractions in women undergoing a TOLAC.

16.3.1.8 Previous Cesarean Delivery with Subsequent Induction of Labor

Emerging data indicate that induction of labor after a prior Cesarean delivery appears to be associated with an increased risk of uterine rupture. Zelop et al. found that the rate of uterine rupture that underwent labor induction after a single previous Cesarean delivery was 2.3 % compared with 0.72 % for women who had labored spontaneously [71]. In a study by Ravasia et al., the uterine rupture rate was 1.4 % compared with 0.45 % for women who labored spontaneously [70]. Blanchette et al. found that the uterine rupture rate after previous Cesarean delivery when labor was induced was 4 % compared with 0.34 % for women who labored spontaneously [74]. This last finding suggests a 12-fold increased risk of uterine rupture for women who undergo labor induction after previous Cesarean delivery.

Data on mechanical methods of labor induction for cervical ripening are limited but reassuring. In a small case series, Bujold et al. found no statistically significant difference among the uterine rupture rates of 1.1 % for spontaneous labor, 1.2 % for induction by amniotomy with or without oxytocin, and 1.6 % for induction by transcervical Foley catheter [75]. Conversely, Hoffman et al. reported a 3.67-fold increased risk of uterine rupture with Foley catheter use for preinduction cervical ripening. Importantly, however, many of these patients received concomitant oxytocin together with application of the transcervical Foley catheter [76]. Of particular note is that a recent randomized controlled trial by Pettker et al. found that the addition of oxytocin to the use of a transcervical Foley catheter for labor induction does not shorten the time to delivery and has no effect on either the likelihood of delivery within 24 h or the vaginal delivery rate [77]. In light of these findings, induction of labor with a transcervical Foley catheter alone may be a reasonable option for women undergoing a TOLAC with an unfavorable cervix.

16.3.1.9 Prostaglandins for Cervical Ripening and Induction of Labor After Previous Cesarean Delivery

Current ACOG guidelines discourage the use of prostaglandins to induce labor in most women with a previous Cesarean delivery. This recommendation is based on considerable evidence for an increased risk of uterine rupture associated with prostaglandins. Several studies found a severalfold (3–5 % compared to <1 %) increased risk for uterine rupture when prostaglandins were used in gravidas who underwent a TOLAC [69, 70, 78]. In contrast, two studies did not show significant difference (in both studies, patients with induction of labor had higher percentage of spontaneous uterine perforations) [79, 80]. Landon et al. reported no uterine ruptures among 227 patients who underwent induction with prostaglandins alone. Although the study was

underpowered to detect small differences, the particular type of prostaglandin administered did not appear to significantly affect the uterine rupture rate (52 patients received misoprostol; 111, dinoprostone; 60, PGE_2 gel; and 4, combined prostaglandins) [58].

16.3.1.10 Previous Cesarean Delivery with Previous Successful Vaginal Delivery

Several studies have shown a protective association of previous vaginal birth on uterine rupture risk in subsequent attempts at vaginal birth after previous Cesarean delivery with around one-fourth to one-fifth of the risk [81–83]. A Maternal-Fetal Medicine Units Network study found that in women with no prior vaginal delivery who underwent a TOLAC, there was an increased risk of uterine rupture with induction versus spontaneous labor (1.5 % vs. 0.8 %, $p = 0.02$). In contrast, no statistically significant difference was shown for women with a prior vaginal delivery who underwent spontaneous TOLAC compared with labor induction (0.6 % vs. 0.4 %) [84].

16.3.1.11 Previous Cesarean Delivery with Subsequent Successful VBACs

Multiple studies suggest a protective advantage with regard to the uterine rupture rate if a woman has had a prior successful VBAC attempt. Multiple potential explanations exist, but the two most obvious are that a successful prior VBAC attempt assures that (1) the maternal pelvis is tested and that the bony pelvis is adequate to permit passage of the fetus and (2) the integrity of the uterine scar has been tested previously under the stress/strain conditions during labor and delivery that were adequate to result in vaginal delivery without prior uterine rupture. Mercer et al. found that the rate of uterine rupture decreased after the first successful VBAC, but that there was no additional protective effect demonstrated thereafter: the uterine rupture rate was 0.87 % with no prior VBACs, 0.45 % for those with one successful prior VBAC, and 0.43 % for those with two or more successful prior VBACs [85]. Pooled data from five studies indicate an increased uterine rupture rate of 1.4 % (1/73) in failed VBAC attempts that required a repeat Cesarean section in labor [58, 74, 86–88].

16.3.1.12 Interdelivery Interval

Several studies found an interpregnancy interval between Cesarean delivery and a subsequent pregnancy of <6 months that was nearly three to four times as common among patients who had uterine rupture than in control subjects [89, 90]. Shipp et al. similarly found that the risk of symptomatic uterine rupture was increased threefold in women with interdelivery intervals of <18 months when they underwent a TOLAC after one previous Cesarean delivery [91]. The authors controlled for maternal age, public assistance, length of labor, gestational age of 41 weeks, and induction of augmentation of labor with oxytocin. In additional support of this observation, a Canadian study on women who underwent a TOL after a single previous low-transverse Cesarean delivery found that 2.8 % of patients who had an interdelivery interval of ≤24 months had a uterine rupture compared with 0.9 % for those with an interdelivery interval of >24 months (OR 2.65) [92]. In a follow-up study, the same authors examined the risk of uterine rupture between 18 and 24 months. After adjustment for confounding factors, they found that an interdelivery interval shorter than 18 months was associated with a significant increase of uterine rupture (OR 3), whereas an interdelivery interval of 18–24 months was not (OR 1.1). The conclusion is that an interdelivery interval shorter than 18 months but not between 18 and 24 months should be considered as a risk factor for uterine rupture [93].

The authors speculated that a prolonged interpregnancy interval may allow time for the previous Cesarean delivery scar to reach its maximal tensile strength before the scar undergoes the mechanical stress and strain with a subsequent intrauterine pregnancy. Interestingly, the authors also observed that the combination of a short interdelivery interval of ≤24 months and a single-layer hysterotomy closure was associated with a uterine rupture rate of 5.6 %, a rate approximately three times higher than patients without this combination. This is comparable to the rate of uterine

rupture for patients undergoing a TOLAC with a previous classic midline Cesarean scar [92]. There were no comparisons of single- or two-layer suture in these studies.

16.3.1.13 One-Layer Versus 2-Layer Hysterotomy Closure

Bujold et al. found a four- to fivefold increased risk of uterine rupture for women who had a previous single-layer uterine low-transverse closure compared with those having a two-layer closure for Cesarean hysterotomy. Uterine rupture occurred in 3.1 % of previous single-layer closure versus 0.5 % of two-layer closure (OR 3.95) [94]. The other studies had similar results with conclusion that single-layer closure should be avoided in women who contemplate future VBAC delivery [95, 96]. One study states that locked but not unlocked single-layer closures were associated with a higher uterine rupture risk than double-layer closure in women attempting a TOL [97].

16.3.2 Multiple Cesarean Deliveries

Most large-scale studies showed that multiple Cesarean sections carry a higher risk for uterine rupture than a previous single Cesarean section. Ten studies published from 1993 to 2010 showed that the risk of uterine rupture in a subsequent pregnancy ranged from 0.9 to 6.0 % (1/17–1/108). This risk is increased 2–16 times compared to women with only a single previous Cesarean delivery [98–100]. A study by Caughey et al. confirmed these results and also found that women with a previous vaginal delivery were about one-fourth as likely to have a uterine rupture as women without a previous vaginal delivery (OR 0.26) [82].

A 2004 ACOG guideline suggested that in women with two previous Cesarean deliveries, only those with a previous vaginal delivery should be considered candidates for a TOLAC [101]. This ACOG recommendation was subsequently revised in an updated 2010 guideline to suggest that women with two previous low-transverse Cesarean deliveries may be considered candidates for TOLAC regardless of their prior vaginal delivery status [51]. The only study with findings contrasting with all these reports where there was no statistically significant difference in uterine rupture between single and multiple previous Cesarean sections was by Landon et al. [102].

16.3.2.1 Previous Uterine Myomectomy

Nearly all uterine ruptures that involve uteri with myomectomy scars have occurred during the third trimester of pregnancy or during labor [103, 104]. Only one case of a spontaneous uterine rupture has been reported before 20 weeks of gestation [105]. Brown et al. reported that among 120 term infants delivered after previous transabdominal myomectomy, no uterine ruptures occurred and 80 % of the infants were delivered vaginally [106]. In contrast, Garnet identified uterine rupture rate of 4 % in women who had scars from a previous myomectomy and who underwent elective Cesarean delivery because of previous myomectomy [107]. Such reports do not often delineate the factors that were deemed important for assessing the risk of subsequent uterine rupture (e.g., number, size, and locations of leiomyomas; number and locations of uterine incisions; entry of the uterine cavity; type of closure technique).

Dubuisson et al. reported a uterine rupture rate of 3 % in patients who underwent previous laparoscopic myomectomy [104]. Only one rupture occurred at the site of the previous myomectomy scar, resulting in the conclusion that the risk of pregnancy-related uterine rupture attributable to laparoscopic myomectomy is 1 %. However, the rarity of spontaneous uterine rupture raises the issue of whether the two uterine ruptures at sites that were not coincident with previous myomectomy scars were attributable to the previous myomectomies. Others reported no pregnancy-related uterine ruptures in women who previously underwent laparoscopic myomectomy [108–111]. However, the number of patients who were allowed to labor was low, and a high percentage of deliveries were by scheduled Cesarean delivery (80, 79, 75, and 65 %, respectively). In a prospective study from Japan, there were no uterine ruptures among 59 patients with a successful vaginal delivery after a prior laparoscopic myomectomy [112]. In a multicenter study in Italy with 386

patients after laparoscopic myomectomy, there was one recorded spontaneous uterine rupture at 33 weeks' gestation (rupture rate 0.26 %) [113]. Uterine rupture has been reported to occur as late as 8 years after laparoscopic myomectomy [114]. This finding suggests that additional investigations with long-term follow-up are needed.

16.3.2.2 Medical Abortion

Medical abortion was started in the late 1980s, becoming more widely used in the late 1990s with mifepristone and misoprostol being the most used. It came as an alternative for the dilatation and curettage which caused more complications, resulting in 50,000–100,000 maternal deaths every year [115, 116]. In 2006, the total number of abortions for women residing in England and Wales was 193,700 compared with 186,400 in 2005, a rise of 3.9 %. Of these, medical abortions accounted for 30 % of the total compared with 24 % in 2005 [117]. No randomized controlled trial has been powerful enough to properly compare medical and surgical abortions in relation to the possible adverse effects of these two treatments. Misoprostol alone for termination of pregnancy was described for the first time in 1994. It has been used widely in the normal uterus [115, 116].

The absence of previously reported cases of gemeprost-associated uterine rupture may reflect the rarity of this method of pregnancy termination in the second trimester. Fourth case was notable because of the absence of risk factors for uterine rupture. It is unlikely that routine amniocentesis or chorionic villus biopsy would have predisposed this patient to uterine rupture [118]. Initially, higher doses were administered and the conclusion was that smaller doses may lessen the risk of uterine hypertonus and decrease the risk of uterine rupture. There is a case of combined use of oral mifepristone and intravaginal misoprostol (prostaglandin E_1 analog) causing uterine rupture [119]. Additional risk factor in such cases is scarred uterus [120–122], but there are cases with this uterine rupture in unscarred uterus [123, 124]. The only systematic review on the subject from 2009 found a seven times higher incidence of uterine rupture of scarred uterus (0.28 %) in comparison with unscarred uterus (0.04 %), but authors found the incidence acceptable to both patients and health-care providers [125]. Rupture in an unscarred uterus is possibly related to the dose, dose interval, gestation, and parity. Based upon pharmacokinetics of misoprostol, a dosage interval of 6 h is common (range 3–12 h) [126]. Uterine rupture occurred in one case with lower accumulated dose of misoprostol (1,200 Ag/30 h) than in some reported regimens (2,400 Ag/24 h) [126]. There is even a case of spontaneous rupture of the unscarred uterus in the first trimester using mifepristone/misoprostol for medical termination of pregnancy [127].

Corticosteroid therapy is listed as a contraindication to mifepristone (but not misoprostol), possibly because of its glucocorticoid antagonistic effect. Whether prolonged corticosteroid therapy can result in a weakened myometrium susceptible to rupture remains to be determined.

The incidence of uterine rupture among women with a prior Cesarean delivery during second trimester pregnancy termination with prostaglandin E_2 or oxytocin is 3.8 % [128]. The risk is even higher when oxytocin is used with prostaglandins [129]. The incidence of this complication with misoprostol was difficult to define because of paucity of its use. There was no set regimen protocol for intravaginal misoprostol in second trimester pregnancy termination, and all studies have used a different regimen. Mostly the initial dose was 400 Hg repeated every 4–6 h, up to a maximum of 1,200–1,600 Hg per 24 h. Some studies have augmented misoprostol with either oxytocin or mifepristone [120, 123, 128]. Recently, FIGO has recommended the regimen protocol for second trimester pregnancy termination with 100–200 Hg intravaginal misoprostol, repeated 6 hourly till maximum four doses/24 h [129], and its use should be with care in a previously scarred uterus.

Four cases of rupture of an unscarred uterus in the second trimester following MTOP were found. Only two of these cases used mifepristone and misoprostol [120, 130]. The other women found do not follow the MTOP protocol but contain information relevant to this case. The first was an MTOP using mifepristone and gemeprost. The rupture was found by ultrasound scan the

morning after commencing prostaglandins [119]. The second case was a grand multiparous patient [122]. The rupture was found by ultrasound scan following one dose of misoprostol (200 μg) followed by oxytocin 12 h later. Although high doses of prostaglandins is a known risk factor, the above two women were treated for over 24 h, raising the possibility that duration of prostaglandin treatment is a risk factor. Other agents, such as ethacridine lactate, have been linked to uterine rupture, although this is very rare and the case was relating to the second trimester [131].

Cases of uterine rupture have been reported involving small doses of misoprostol. One case involved an endocervical rupture in the second trimester following two doses [132]. Another was a scarred uterus, and the patient was being prepared for surgical management [133]. A similar case to this was of a first trimester rupture following one dose of misoprostol in preparation for surgical termination [134].

There is no evidence that pretreatment with mifepristone might increase the chance of uterine rupture. It is thought that the chance might actually be reduced as mifepristone increases cervical compliance; however, as it increases uterine sensitivity to the action of exogenous prostaglandins [119], the risk benefit is not known. Previous Cesarean sections are thought to be a risk factor for uterine rupture. One trial of second trimester abortion using misoprostol in 720 women with one or more previous Cesarean deliveries has been carried out and concluded that the use of misoprostol was not associated with an excess of complications compared with women with unscarred uteri [135].

16.3.3 Unscarred Uterus

An unscarred prelabor primigravid uterus can show a very thin uterine wall, compatible with incomplete uterine rupture, without apparent etiological or risk factors. Walsh and Baxi [136], reviewing the literature over six decades (1946–2006), found 36 primigravid uterine ruptures, and Matsubara et al. have found a further 21 cases [137–141]. Of these 21 cases, 15 were reported in a case series from Nepal [140], with all ruptures occurring after labor of >48 h, and 12 having received no antenatal care. Of 57 (36 + 21) cases previously reported, 55 women had some discernible etiological or risk factors for rupture, including a past history of uterine surgery, congenital uterine anomaly, adherent placenta, labor, or oxytocin and/or prostaglandin use [136–142]. The etiological factors were described as indiscernible in the remaining two cases; one of which was described in a case series and lacked detailed data [143]. In the remaining case – that of a 21-year-old Indian woman – she had stated that she was primigravida, but she had received no antenatal care until rupture, and no further evaluation to identify any underlying condition was performed [144]. Therefore, the data was insufficient to claim "unknown etiology." There have been no reported cases of primigravid unscarred uterine rupture of unknown etiology, employing its strict definition.

16.3.3.1 Oxytocin

PGE_2 is a potent oxytocic agent and rupture of the unscarred uterus has been reported with vaginal and intracervical applications [41, 145–147]. PGE_2 should be used with caution particularly in multiparous patients and in combination with oxytocin [39]. Uterine hyperstimulation was not observed and rupture occurred more than 4 h after administration [39].

16.3.3.2 Vacuum-Assisted Vaginal Delivery

One rupture was encountered after vacuum-assisted vaginal delivery. Application of external force in the second stage of labor [148], vacuum forceps, and breech extraction are all possible causes of uterine rupture [41].

16.3.3.3 Parity and Age

> *High multiparity carries with it certain inherent risks … it can be very unforgiving of any carelessness, incapacity or neglect.*
>
> John Kevin Feeney, 1935

The high parity observed by John Kevin Feeney (Professor of Gynecology and Obstetrics in University College Dublin and Master of the Coombe Hospital in Dublin) in 1953 is recognized

as major risk factor of spontaneous uterine rupture in unscarred uterus in most studies [149, 150]. Some authors have reported that the uterus may have been weakened by thinning and stretching of the muscle fibers during labor, especially with aging and repeated childbearing [39]. There are several studies that show the mean parity at the time of rupture was between 5 and 6 [151–155]. Grand multiparity predisposes to malpresentation and unstable lie, a significant risk factor for ruptured uterus [32, 156]. Grand multiparas attended antenatal clinics sparsely (due to heavy domestic commitments), and consequently, malpresentations were diagnosed late, during labor. However, Beacham et al. [157] and Mennon [158] reported that 56–75.6 % of uterine ruptures occurred in women with a parity of between 1 and 4, while 38 % (69/184) with parity between 5 and 9 had ruptures. Nevertheless, recent evidence suggests that with proper antenatal care, modern obstetrics, and advanced neonatal services there is no difference in outcome between grand multiparous women and women with low parity [159]. Gardeil et al. found only two women with uterine rupture among 39,529 multigravidas who had no previous uterine scar (0.005 %) [160]. Uterine overdistension due to the presence of twin pregnancy was not proven to be the risk factor. Fetal weight in singleton pregnancy is a risk only when it contributes to cephalopelvic disproportion [9].

Age and parity are interrelated risk factors. Women older than 35 and women having their fifth or later birth are at greatest risk for uterine rupture, and the importance of fertility regulation and contraception usage could be clearly concluded [9]. Others state the peak incidence in the 26–35-year age range [157], while one Nigerian study showed peak incidence in 25–29 age group. Probably, it is related to reproductive and life span in developing countries with significantly lower incidence of older parturient women.

Unfortunately, these two factors are prominent features in obstetric practice in Qatar where repeated pregnancies continue into middle age. In their study, 56.9 % cases of uterine rupture were grand multiparous (para 5 or more), and nine patients 39 % were >35 years of age. These findings and review of the literature suggests some additional risk factors that warrant consideration.

Other etiological factors classically recognized as contributing to a rupture of unscarred uterus are as follows: obstetric maneuvers, malpresentations especially transverse fetal position, cephalopelvic disproportion, excessive uterine expressions, abnormal placentation (placenta percreta mainly), trauma due to uterine curettage, and uterine abnormalities [31, 161]. Connective tissue diseases [142] may also induce uterine rupture. In some cases, the rupture of gravid uterus has no obvious cause even before labor [162]. In the series of 40 uterine ruptures, Schrinsky and Benson [40] found ten spontaneous ruptures without any predisposing factors.

16.3.3.4 Congenital Uterine Anomalies

Congenital uterine anomalies affect approximately 1/200 women [163]. In such cases, the walls of the abnormal uteri tend to become abnormally thin as pregnancies advance, and the thickness can be inconsistent over different aspects of the myometrium [164–167]. Ravasia et al. reported an 8 % incidence of uterine rupture in women with congenitally malformed uteri compared with 0.61 % in those with normal uteri who were attempting VBAC [168]. Both cases of uterine rupture in the women with uterine anomalies involved labor induction with prostaglandin E_2. In contrast, a study of 165 patients with Müllerian duct anomalies who underwent spontaneous labor after one prior Cesarean delivery reported no cases of uterine rupture [169]. Of note, in this study 36 % had only a minor uterine anomaly (arcuate or septate uterus), and 64 % had a major uterine anomaly (unicornuate, didelphys, or bicornuate uterus). Moreover, only 6 % with Müllerian duct anomalies underwent induction of labor.

For pregnancies that implant in a rudimentary horn of a uterus, a particularly high risk of uterine rupture (≤81 %) is associated with the induction of labor [170]. Importantly, 80 % of ruptures involving these types of rudimentary horn pregnancies occurred before the third trimester, with 67 % occurring during the second trimester.

The decision for induction of labor in women with a congenitally anomalous uterus, especially in cases of a previous Cesarean delivery, must be carefully considered, and given the higher

incidence of uterine rupture reported in this patient population. Although the uterine rupture rate for unscarred anomalous uteri during pregnancy is increased relative to that for normal uteri, the precise increase in risk associated with the different types of uterine malformations remains uncertain.

16.3.3.5 Uterine Sacculation

A thin uterine wall, as a result of uterine sacculation [171, 172] or uterine diverticulum [173] may induce uterine rupture. Uterine sacculation is defined as a transitory pouch or saclike structure developing from a portion of the gravid uterus [172]. The typical form of sacculation results from an incarcerated retroverted uterus [171, 172]. A ventrally located cervical ostium and vagina may cause physicians to suspect this diagnosis. Magnetic resonance imaging (MRI) may provide a preoperative diagnosis [171]. In this condition, the anterior uterine wall becomes stretched and thinned. Other conditions, such as previous surgery, a primary myometrial defect, uterine malformation, or placental abnormalities, are listed as possible causes of uterine sacculation [172, 174].

16.3.3.6 Uterine Diverticulum

Uterine diverticulum is frequently misunderstood and reported as uterine sacculation [173]. Uterine diverticulum has a narrow connection with the uterine cavity and a thicker wall than in sacculation [173]. While uterine sacculation is usually observed during pregnancy [172, 174], diverticulum is usually detected in nonpregnant women. Uterine diverticula as complications during pregnancy are rare. Rajiah et al. [173] reported a primigravid woman in whom an MRI revealed uterine diverticulum in the 22nd week of gestation. A Cesarean section was performed in the 31st week. The diverticulum originated from the posterolateral wall of the uterine body and did not contain the fetus. The diverticulum was not excised due to surgical risks. In the postpartum period, the diverticulum was observed via ultrasound. The authors considered that the underlying etiology for the diverticulum may have been congenital because this patient was primigravida with no prior cervical or uterine procedure. Sun et al. [175] reported a case in which the gestational sac implanted in a diverticulum: the pregnancy was terminated at an estimated 7–8 weeks. The authors considered that abnormal development of the paramesonephric duct may cause a congenital uterine deformity, leading to a formation of diverticulum.

Midforceps delivery and breech version extraction have been implicated as potential causes of uterine rupture [176]. Whether or not the manipulation causes the rupture is unclear. Epidural anesthesia has also been linked to uterine rupture; however, in those patients with uterine rupture, the incidence of epidural use is small and ranges from 6 to 21 % [28, 177, 178].

Prelabor uterine rupture in primigravid women was identified in 24 cases up to 2011. In almost half of them, partial wall defect was the principal recognizable risk factor before the onset of labor. It is interesting to note that 52 % of women with specific available information had a history of infertility. A possible explanation could be that infertile patients more frequently undergo diagnostic/operative procedures on their uterus during diagnostic investigation or treatment resulting in a likelihood of iatrogenic damage [179]. It is important that the majority (67 %) of the women did not attend antenatal care [12].

16.3.3.7 Genetic Susceptibility for Rupture

Loeys-Dietz syndrome is a syndrome caused by heterozygous mutations in the genes encoding type 1 or 2 transforming growth factor-β receptor (TGF-$\beta_{R1/2}$). The obstetric manifestations are risk of rupture of the gravid uterus and the arteries, either during pregnancy or in the immediate postpartum period, and damage to the vagina, the perineum, and the colon [180].

16.3.3.8 Sexual Intercourse

There are three case reports describing uterine rupture following sexual intercourse [181–183]. The topic for discussion could be is the uterine rupture spontaneous after sexual intercourse of should this mechanism be included in the group of traumatic uterine ruptures. Also it is not known whether intercourse was before cases of other reports of spontaneous uterine rupture.

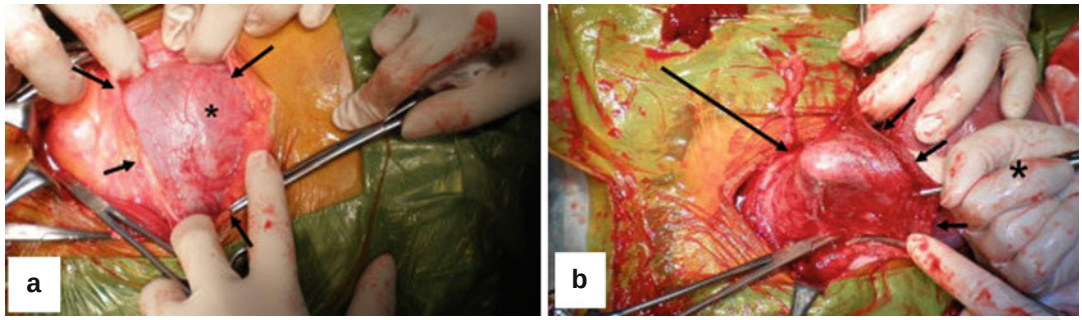

Fig. 16.2 Operative findings during a Cesarean section. (**a**) The *asterisk* indicates the thin anterior uterine wall, seen with a bulge caused by fetal parts from the inside. *Arrows* indicate the peritoneum. The left side of the photograph is the caudal side of the patient. (**b**) After delivering the fetus and removing the placenta, the thin wall was gently pushed from inside the uterus with a finger. The finger tip (*large arrow*) is clearly visible through the thin wall. The *asterisk* indicates the surgeon's right hand. *Small arrows* indicate the uterine incision site [184]

16.3.3.9 Antenatal Care

The prenatal care in Yemen is very poor. According to the last published data, only 44 % of pregnant women had ever been to any prenatal clinic, with the frequency of visits during a pregnancy ranging from one to four. Women visit antenatal clinic mostly when they encounter a complication and very rarely for a routine antenatal care (13 %). In Yemen, 56 % of pregnant women have never had any antenatal care. Home delivery is still common in Yemen. About 78 % of women deliver at home, 16 % at state hospitals, and about 5 % at private hospitals. The home deliveries are usually attended by midwives with minimal training or relatives who have had some experience of labor. Some of the women will still deliver at home completely alone [9].

16.4 Prevention

The most direct prevention strategy for minimizing the risk of pregnancy-related uterine rupture is to minimize the number of patients who are at highest risk. The salient variable that must be defined in this regard is the threshold for what is considered a tolerable risk. Although this choice is ultimately arbitrary, but safety threshold is chosen as 0.5 % (1/200), therefore the categories of patients that exceed this critical value are those with the following:

- Multiple previous Cesarean deliveries
- Previous classic midline Cesarean delivery
- Previous low-vertical Cesarean delivery
- Previous low-transverse Cesarean delivery with a single-layer hysterotomy closure
- Previous Cesarean delivery with an interdelivery interval of less than 2 years
- Previous low-transverse Cesarean delivery with a congenitally abnormal uterus
- Previous Cesarean delivery without a previous history of a successful vaginal birth
- Previous Cesarean delivery with either labor induction or augmentation
- Previous Cesarean delivery in a woman carrying a macrosomic fetus weighing >4,000 g
- Previous uterine myomectomy accomplished by means of laparoscopy or laparotomy

16.5 Mechanisms and Classification

16.5.1 Definition

Uterine rupture is defined as a disruption of the uterine muscle and visceral peritoneum or a uterine muscle separation with extension to the bladder or broad ligament found at the time of Cesarean delivery or laparotomy following vaginal birth after previous Cesarean section. Rupture can be incomplete or complete.

Incomplete uterine rupture is present when the uterine wall is extremely thinned and the uterine muscular layer is lost but the uterine serosa (parietal peritoneum) is preserved (Fig. 16.2). It

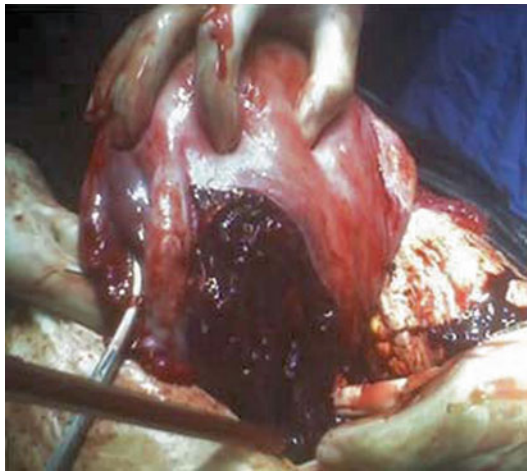

Fig. 16.3 Complete uterine rupture with a large left broad ligament hematoma with multiple small bleeding points from the branches of the uterine artery is seen [148]

is mostly seen with scar dehiscence. Incomplete rupture is also referred to as uterine dehiscence. In contrast to frank uterine rupture, uterine scar dehiscence involves the disruption and separation of a preexisting uterine scar. Uterine scar dehiscence is a more common event than uterine rupture and seldom results in major maternal or fetal complications. Importantly, when the defect in the uterine wall is limited to a scar dehiscence, it does not disrupt the overlying visceral peritoneum, and it does not result in clinically significant bleeding from the edges of the preexisting uterine scar. In addition, in cases of uterine dehiscence (as opposed to uterine rupture), the fetus, placenta, and umbilical cord remain contained within the uterine cavity. If Cesarean delivery is needed, it is for other obstetric indications and not for fetal distress attributable to the uterine disruption.

Complete uterine rupture is present when rupture occurs through all layers of the uterine wall including serosa with or without accompanying bleeding or hematoma (Fig. 16.3). Therefore, the amniotic cavity directly communicates with the abdominal cavity. In the study by Padhye, 70 % had complete rupture and 25 % incomplete rupture. Seventy percent of scar rupture presented with complete rupture [25].

16.5.2 Classification

Rickards in 1938 described five types of rupture of the scarred uterus during pregnancy [185]:

Type I: In this group, the rupture occurs through an old upper segment incision, and the placenta is situated away from the uterine scar. Characteristics include:

- Rupture tends to take place during labor.
- Little or no hemorrhage occurs, and therefore the pulse remains good.
- The pain may become niggling in type after the scar has started to give way.
- The bulging bag of membranes may sometimes be palpated through the abdominal wall.
- Prognosis is good provided that suitable treatment is available.

Type II: It consists of cases in which the rupture occurs through an upper segment incision and the placenta is situated underneath the old scar. This type of case is more serious and presents a different clinical picture. When the placenta is situated underneath the old scar, a gradual erosion of fibrous tissue by the placental villi occurs [186]. This erosion is an insidious one and may cause marked attenuation of the scar during the latter part of pregnancy. In this type, rupture is more liable to occur before the onset of labor. The eating away of the scar may be associated with vague pains in the lower abdomen [187]. As the process is gradual, hemorrhage is seldom severe. Characteristics include:

- Gradual rupture tends to occur toward the end of pregnancy. This may be accompanied by vague pain in the lower abdomen. Such pain should therefore never be ignored.
- After the onset of labor, hemorrhage occurs and may be of considerable severity.
- Prognosis will not be so favorable as in type I and will depend very largely on the amount of intra-abdominal hemorrhage.

Type III: The uterine rupture occurs after a previous lower segment Cesarean section. Characteristics include:

- Rupture is said to take place during labor.
- Hemorrhage may occur, due to the extension of the laceration laterally into the uterine arteries.

- The bladder may be involved (rarely), giving rise to hematuria.

Type IV: The rupture is complete, through an upper segment incision, and the child, within its bag of membranes, is expelled into the abdominal cavity, the placenta remaining in situ. The uterine scar gives way along its entire length, the contractions persist, and the child is extruded into the abdominal cavity. The fetal heart sounds almost invariably disappear and fetal movements cease. The physical signs are characteristic. The uterus is felt to be pushed over to one side, and the child, floating in the abdominal cavity, is very easily palpable. Characteristics include:

- Fetal heart sounds cease as a rule.
- Fetal movements usually stop.
- The uterus is pushed over to one side.
- The fetus, lying free in the abdominal cavity, is easily palpable.

Type V: The rupture is complete, through an upper segment incision, and the child, with its placenta, is extruded completely into the abdominal cavity. Characteristics include:

- Often associated with severe intra-abdominal hemorrhage.
- Fetal heart sounds are absent.
- Fetal movements are absent.
- The uterus is pushed over to one side.
- The fetus, lying free in the abdominal cavity, is easily palpable.

16.5.3 Pathophysiology

16.5.3.1 Scarred Uterus

Patients who had a previous uterine scar were more likely to rupture in the hospital as a result of attempted trial of scar and the poor monitoring of labor [12]. In scarred uteri, the vast majority of uterine dehiscence and ruptures will occur via the uterine scar. The atrophic, inelastic nature of the scar renders it less adaptive to forces in labor, predisposing to scar rupture. However, a particularly rigid anterior lower segment may cause abnormal distribution of force. During retraction, the posterior wall may be excessively shortened and thinned due to the rigid anterior uterine scar,

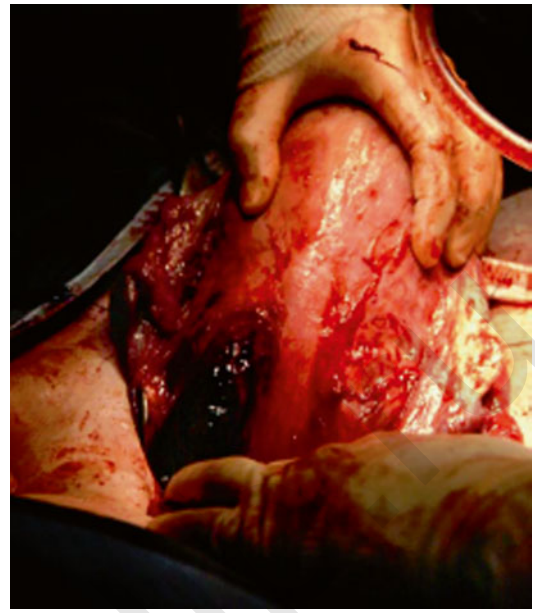

Fig. 16.4 Vertical posterior rupture of scarred uterus due to occipitoposterior position of the fetus [191]

catalyzing atypical uterine rupture via healthy tissue. Any factor compromising uterine structural integrity or causing abnormal distribution of force can precipitate uterine rupture. The site of uterine rupture is unpredictable and may be atypical. The most common location is lower anterior uterine segment.

There are only six cases of posterior uterine rupture complicating vaginal birth after Cesarean section in the period 1997–2011 [147, 188–192]. Fetal malposition with an occipitoposterior position has previously contributed to posterior uterine ruptures (Fig. 16.4), as has malpresentation with a transverse lie and dead fetus [190–192]. Malposition alters the distribution of contractile force and increases labor dystocia; certain malpresentations cause uterine hyperdistension, which may also precipitate atypical uterine rupture.

Prostaglandins generating excessive uterine activity have been assumed to be the cause of uterine rupture. Buhimschi et al. suggested that prostaglandins induce local biochemical modifications that weaken the scar, predisposing it to rupture [193]. Figueroa et al. [189] proposed that prostaglandins might have caused excessive uterine activity that resulted in a posterior wall sacculation

in the face of a strong anterior scar. During the second stage of labor, with the fetus undergoing cardinal movements, uterine rupture occurred through the weakened posterior wall. But in the five instances of rupture through posterior uterine wall in the presence of anterior scar, only in two cases was labor induced by prostaglandin, suggesting other factors may play a role. The presence of an inelastic scar comprised of fibrous tissue on the anterior wall prevents even distribution of forces of contraction. As uterine muscle undergoes retraction during active phase of labor, the healthy posterior wall may undergo excessive shortening and thinning compared to inelastic anterior wall, which could have predisposed to rupture.

The lower segment uterine rupture is the most common (60 %) site of rupture [46, 194–196] with anterior transverse location being the most common [16]. The second most common location is extension to broad ligament, and other locations have an incidence of around 5 % [16]. The study did not differentiate between rupture caused by obstructed labor and scarred uterus. Rupture is complete in around 73 % cases and incomplete in 27 % [46, 194, 196, 197].

16.5.3.2 Unscarred Uterus

Obstruction as a cause of uterine rupture and the delay in accessing qualified care is found in developing counties with patients without antenatal care. The causes of rupture during labor may briefly be described as follows: some obstruction exists opposing the advance of the child; whether the obstruction is pelvic contraction, unusual size of the child, or malpresentation does not matter – the uterus continuing to contract, thickening of the upper part of the uterus occurs, while its lower segment becomes thinned. If assistance is not given, the lower segment becomes more and more thinned and finally ruptures. It is to be noted that rupture of the uterus during labor almost always begins in the lower segment. These may be complete or incomplete, according as they involve the entire thickness of the organ, or only extend to the peritoneal covering; they may extend to the vagina.

It is the most common cause of spontaneous rupture during pregnancy and labor ranging from 68.5 to 73.2 % [5, 12] in developing countries. In developed countries, it is significantly lower starting from 13 % [159].

16.6 Clinical Presentation

16.6.1 Symptoms and Signs

The signs and symptoms of uterine rupture largely depend on the timing, site, type, and extent of the uterine defect. Classical signs and symptoms of uterine rupture have been reported by many authors ranging back to 1881 [198]. Sudden, severe, shearing abdominal pain with the absence of fetal heart sounds and cessation of uterine contractions in conjunction with vaginal bleeding and shock is classical presentation. Overall, only 45 % of cases reviewed had the classical signs and symptoms of uterine rupture [8, 13, 21, 158, 176, 199–202]. Commonly reported signs and symptoms related to uterine rupture are abdominal pain and tenderness, shock, vaginal bleeding, undetectable fetal heart beat, palpable fetal body parts, cessation of contractions, and signs of intraperitoneal bleeding. One study showed that severe abdominal pain was present in 13.4 % of patients with uterine rupture, shock in 21.3 %, bleeding in 16.8 %, disappearance of fetal heart sounds in 8.9 %, and cessation of contractions in 5.6 % [201]. Less commonly associated with uterine rupture are epigastric pain, shoulder pain (right sided or bilateral), abdominal distention and paralytic ileus, hematuria, hypertonic uterus, altered uterine contour, and fluid thrill. Fetal distress, manifested by fetal bradycardia and absence of fetal movement, is also reported.

16.6.1.1 Labor

Rupture of the uterus during labor is also associated with cessation of labor pain, recession of presenting fetal body parts, cervical lacerations, and vaginally palpable uterine defect. The most common sign is the sudden appearance of fetal distress during labor. One series reported that 81 % of patients with uterine rupture during labor have evidence of fetal distress prior to the onset of bleeding or abdominal pain [178], while

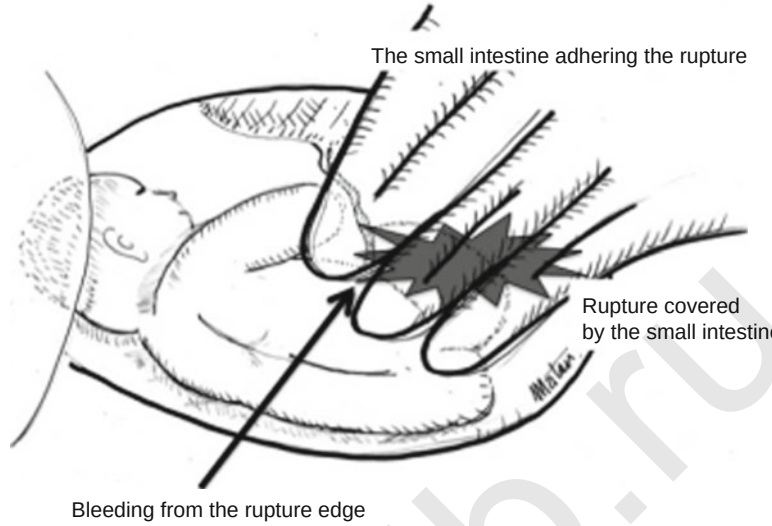

Fig. 16.5 Schematic diagram of the laparotomy findings. The uterine rupture was not initially discernible. Bleeding was observed from the rupture edge (*arrow*). The small intestine tightly adhered to the anterior uterine wall over the uterine rupture. After separating the small intestine, uterine rupture became evident. Amniotic membrane beneath the rupture site remained intact [203]

in another study the most common manifestation of uterine rupture were fetal heart abnormalities present in 43.5 % [24]. The observation of sudden fetal heart irregularity in laboring women should be taken as a potential sign of danger [37].

16.6.1.2 Scarred Uterus

The signs and symptoms of uterine rupture in patients with a previously scarred uterus differ from patients without a uterine scar [200]. Uterine rupture at the site of a previous uterine scar is typically less violent and less dramatic than a spontaneous or traumatic rupture because of their relatively reduced vascularity. The most common sign in women with previous uterine scar is lower abdominal tenderness. In women without a scar, shock is the most common sign, followed by uterine bleeding, severe abdominal pain, and easily palpable fetal parts. Severe abdominal pain is common to both groups of women with and without a uterine scar.

16.6.1.3 Incomplete and Silent Rupture

In incomplete rupture, the symptoms can be minimal and so obscured as to lead us to almost inevitable diagnostic errors. Silent antepartum rupture of the uterus is usually associated with a previous uterine scar, produced by Cesarean section, myomectomy, or perforation of the uterus at the time of curettage. Spontaneous silent rupture of the intact uterus is exceptionally rare in the antenatal period, and if it occurs the rupture usually involves the uterine fundus in patients of high parity. In one study, 4.5 % of patients in this study had no signs and symptoms and were incidentally found to have a ruptured uterus [201].

16.6.1.4 Delayed Presentation

Delayed presentation is possible if uterine perforation is "covered." The rupture may be covered by small intestine, therefore preventing acute massive bleeding. Therefore, vital signs and laboratory data could be stable. Covering by the small intestine may also prevent amniotic rupture or amniotic cavity protrusion, which may explain the initial absence of a fetal heart rate pattern indicative of cord troubles (Fig. 16.5). In this case, the pouch of Douglas was closed, possibly due to the previous laparotomy, prohibiting blood retention [203].

One article described uterine rupture occluded by "fetal legs." Blihovde et al. [204] described a prelabor primiparous uterine rupture at the 32nd week of gestation, with the ruptured site being occluded by the fetal legs. There was abdominal pain but without vaginal bleeding, hemodynamic instability, or fetal compromise. CT revealed the uterine rupture occluded by the protruding fetal legs from the ruptured site, which was confirmed

by laparotomy. The fetal legs, protruding through the rupture and occluding it, masked the symptoms and signs of the rupture, delaying the diagnosis.

16.6.1.5 Spinal Anesthesia

There have been concerns that the use of epidural analgesia may mask clinical symptoms (mostly abdominal pain) causing delayed diagnosis of uterine rupture [188]. The most common sign of uterine rupture is non-reassuring fetal heart rate pattern with variable deceleration [205]. Other findings are more variable and include abdominal pain, vaginal bleeding, and hypovolemia. Epidural analgesia rarely masks the signs and symptoms of uterine rupture, and in fact sudden development of "breakthrough pain" under epidural analgesia may improve the specificity of abdominal pain as a symptom of uterine rupture in patients attempting vaginal birth after previous uterine surgery [205].

16.6.2 Physical Examination

A physical examination reveals tenderness in the middle of lower abdomen with or without guarding. Vaginal bleeding can be present. Blood pressure depends on the rate of uterine bleeding, and the patient can be hypotensive with increased pulse rate. There is recommendation that *clinicians should consider the diagnosis of uterine rupture when a patient presents with abdominal pain, even without evidence of hypovolemia, vaginal bleeding, contractions, or fetal compromise* [203, 204].

Shoulder pain (*Kehr's sign*) is a valuable sign of intraperitoneal blood in subdiaphragmatic region. Even a small amount can cause this symptom, but it is important to realize that it may be 24 h or longer after the bleeding has occurred before blood will track up under the diaphragm, and some cases of acute massive intraperitoneal bleeding may not initially have shoulder pain. Sooner or later, however, shoulder pain will usually appear, and it is in the doubtful cases with a slow leak of blood into the peritoneal cavity over a period of 2 or 3 days that such referred pain is of great diagnostic value.

If there is sufficient cervical dilatation, the vaginal examination may reveal intestinal loops or parts of the greater omentum in the uterine cavity. There is also considerable abdominal distension with dyspnea, caused by the compression of the thoracic cavity.

Postpartum fever ≥38 °C after Cesarean delivery is associated with an increased risk of uterine rupture during a subsequent trial of labor [206].

Antepartum hemorrhage (APH), often indicates uterine rupture [192] and may occur in association with shoulder tip pain due to hemoperitoneum. APH was documented in 33 % (2/6) of posterior uterine ruptures [191]. With posterior uterine rupture, bleeding may be concealed, as described in two earlier cases where signs of hypovolemia developed, each with a large concealed hemoperitoneum [147, 188]. It should be kept in mind that maternal pulse and blood pressure remained could remain within normal limits despite massive uterine rupture, demonstrating the potentially misleading capacity for compensation in an otherwise fit patient. In 33 % (2/6) of posterior uterine ruptures, women reported persistent abdominal pain [147, 191].

If the fetus is partly or completely outside the ruptured uterus, especially if the rupture is on the anterior wall, hard mass can be palpated [184].

16.7 Diagnosis

Around 30 % of patients are diagnosed with uterine rupture preoperatively [37, 157]. Laboratory findings should include hemoglobin which is lowered, and the exact value and dynamics of its decrease depend on the intensity of uterine wall bleeding. Since fetal heart abnormalities are one of the most common features in patients during labor [24], measurement of possible fetal heart abnormalities in laboring patients should be taken as a potential sign of danger [178].

16.7.1 Transvaginal/Transabdominal Ultrasound

A transvaginal and transabdominal ultrasound should be performed to search direct and indirect findings of suspected uterine rupture. Direct signs

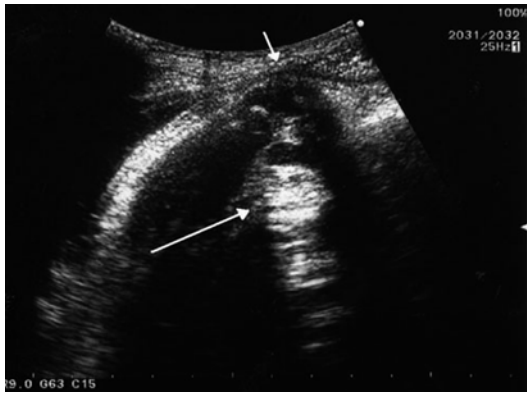

Fig. 16.6 An abdominal ultrasound image of the uterine wall and the fetal minor part. *Small arrow* indicates a thin uterine wall, which is slightly bulging. Beneath the thin uterine wall, a fetal minor part (*large arrow*) is visible, which was palpated as a hard mass through the abdomen [184]

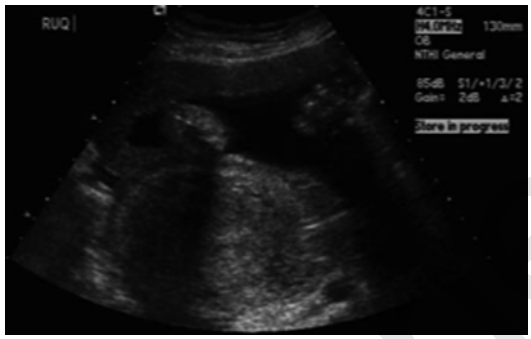

Fig. 16.7 Ultrasound image demonstrating contracted uterus (lower) with fetal extremities and amniotic sac outside the uterus [183]

are thinned wall with bulging of fetal parts (Fig. 16.6) or for visualization of the rupture. The fetus can be partly or completely out of the uterus (Fig. 16.7). Indirect signs are free peritoneal fluid (blood) especially in the pouch of Douglas, extraperitoneal hematoma, intrauterine blood, empty uterus, gestational sac above the uterus (Fig. 16.8), and large uterine mass with gas bubbles [183, 184, 207].

16.7.2 Abdominal CT

Abdominal CT scan should be done in unequivocal cases such as intestinal adhesions over uterine rupture delaying diagnosis. It is seen as focal disruption of the myometrium along with

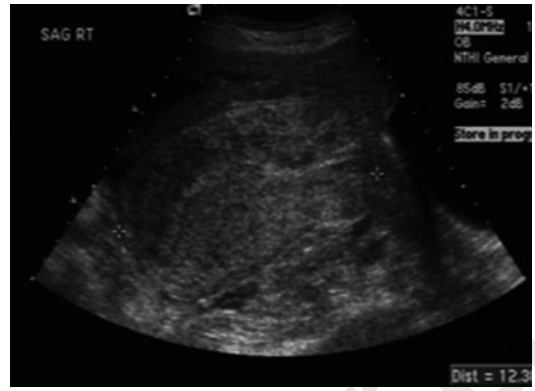

Fig. 16.8 Ultrasound image demonstrating contracted uterus, endometrial stripe, and no intrauterine gestation, with the placental tissue above and bladder to the right [183]

hemoperitoneum (Fig. 16.9). Other signs (see direct and indirect signs) such as fetal parts or hemoperitoneum outside of the uterus can be seen (Figs. 16.10, 16.11 and 16.12).

16.7.3 Magnetic Resonance Imaging

The MRI appearance consists of a focal myometrial defect which may be filled with hematoma and an associated hemoperitoneum (Fig. 16.13). Uterine rupture is a surgical emergency, and MRI should only be considered when the diagnosis is inconclusive and the patient is hemodynamically stable [212].

Scar dehiscence is a separation that involves only a portion of the uterine scar in the lower uterine segment after Cesarean delivery; in these cases, an extensive fluid collection with air bubbles in the bladder flap as a sign of local infection can be seen. The differential diagnosis should consider bladder flap hematoma, endometritis, and normal Cesarean delivery incision changes, which are better depicted with MR imaging.

16.7.4 Uterine Tone Monitoring

Uterine tone monitoring is mandatory in patients with clinical presentation described. External monitoring (external tocodynamometer) demonstrate the classic sign of complete loss of uterine

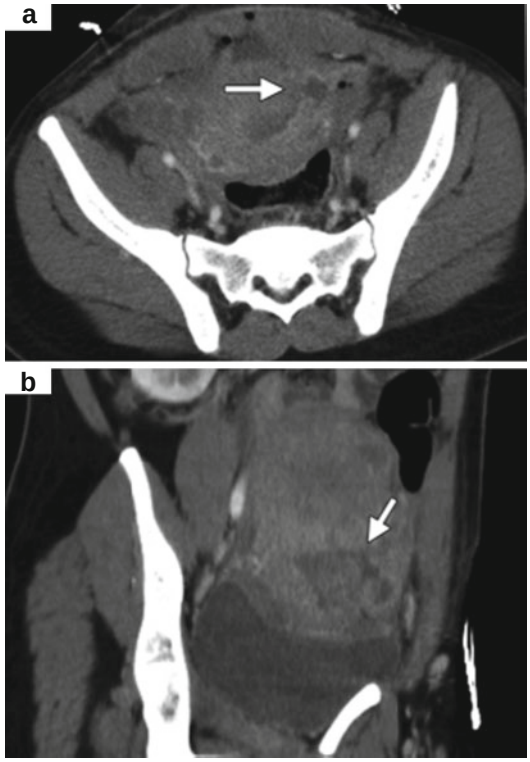

Fig. 16.9 Partial uterine rupture in a 29-year-old woman. Axial (**a**) and coronal oblique (**b**) contrast-enhanced CT images obtained 4 days after Cesarean delivery show disruption of the myometrium (*arrow*) in the left side of the lower uterine segment, a finding depicted as a hypoattenuating band in the myometrium connecting the uterine cavity with a fluid collection in the left broad ligament and pelvis [208]

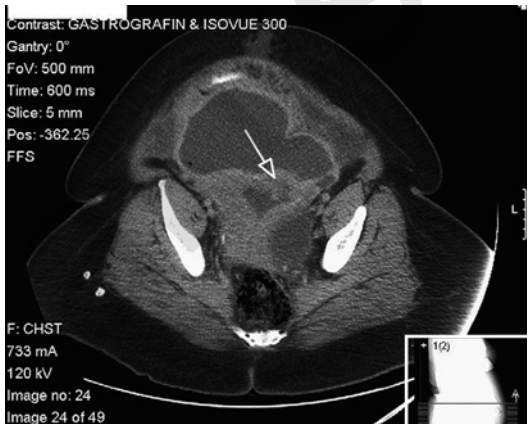

Fig. 16.10 Contrast CT scan of abdomen and pelvis of another patient showing a defect in the anterior wall of the uterus (*arrow*) and fluid collection with wall enhancement and adjacent fluid collection 2 weeks after elective Cesarean section with normal postoperative course [209]

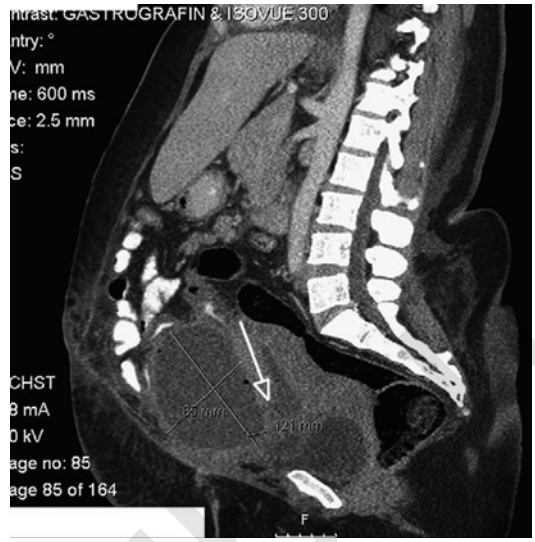

Fig. 16.11 Axial CT scan of abdomen (the same patient as in Fig. 16.10) showing the measurement of fluid collection anterior to the uterus (*arrow*) [209]

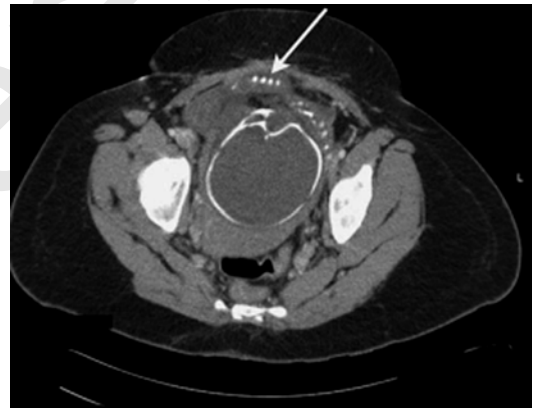

Fig. 16.12 A 34-year-old woman with seven previous Cesarean deliveries and a history of scant prenatal care presented at 32 weeks. The CT scan revealed a fetal hand protruding through the lower uterine segment (*arrow*) [210]

tone. In contrast, internal monitoring (internal pressure transducer) demonstrated an increase in uterine resting tone. Both techniques reveal a stepwise gradual decrease in contraction amplitude followed by a sudden onset of profound and prolonged fetal bradycardia in patients with rupture of an unscarred uterus at term – so-called staircase sign (Fig. 16.14) [213]. When internal monitoring was used, the intrauterine pressure

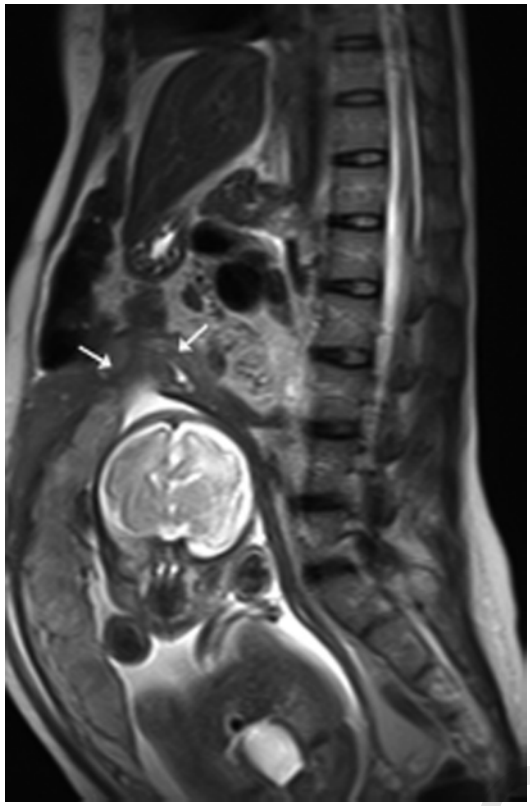

Fig. 16.13 A 35-year-old female patient in her third trimester with lower abdominal pain and with prior history of Cesarean delivery. Sagittal T2-weighted image shows a focal disruption at the fundus of the uterus (*arrows*) with associated hematoma. No part of the fetus protruded into the abdominal cavity [211]

catheter did not show a complete loss of resting tone (Fig. 16.15). In general, internal monitoring has better sensitivity for the detection of both fetal heart rate and uterine contraction, consistent with the published reports of the persistence of uterine contraction and increased resting tone in cases of rupture monitored by intrauterine catheter – findings that were not observed with external monitoring [39, 178]. However, few papers in the literature actually documented the type of uterine monitoring used. Furthermore, the uterine contraction pattern may differ depending upon the presence or absence of a uterine scar, or with the site and direction of rupture.

Bradycardia is the most common fetal heart rate abnormality seen in cases of uterine rupture [178, 214–216] and may occur as a result of cord compression within the uterine rupture, loss of uterine perfusion, or placental abruption. This staircase pattern appears to be a unique combination of fetal heart rate pattern and uterine contraction pattern that may be of value in diagnosing uterine rupture. Fetal bradycardia starts right after or several minutes after staircase sign [213]. CTG abnormalities are associated with 55–87 % of uterine ruptures [217]. Other recognized signs of uterine rupture include loss of station of presenting part and new inefficient contractility [218].

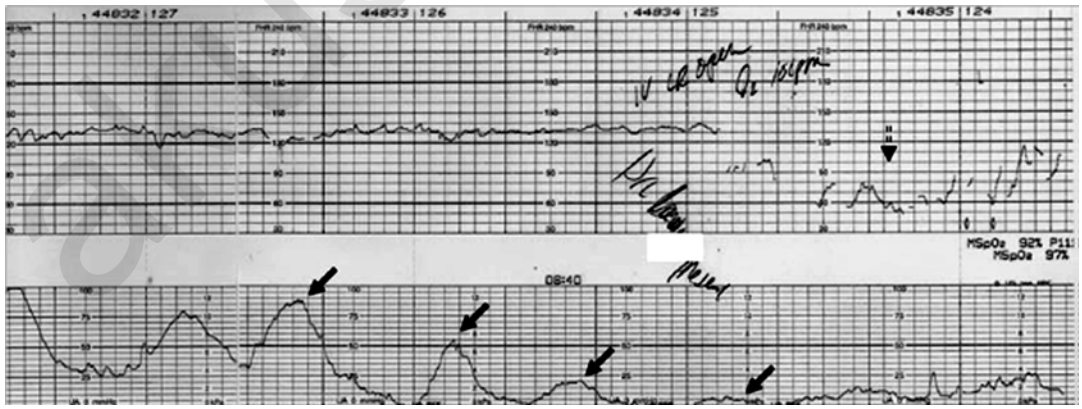

Fig. 16.14 Uterine contraction pattern during rupture of an unscarred uterus at term. External cardiotocogram was used for the tracing. *Black arrows* show the gradual decrease of the amplitude of uterine contractions (*staircase sign*). *Black arrowhead* with dashed body shows prolonged fetal bradycardia [213]

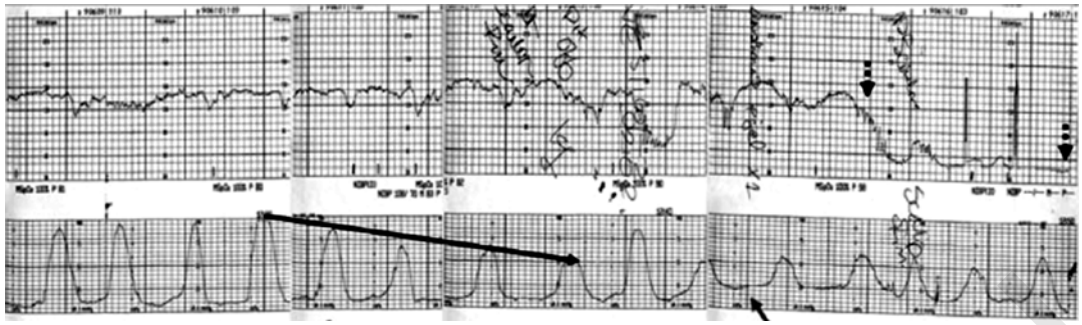

Fig. 16.15 Uterine contraction pattern of another case during term rupture of an unscarred uterus. Intrauterine pressure catheter was used for the tracing. *Black arrow* shows the gradual decrease of the amplitude of uterine contractions (*staircase sign*). *Black arrowheads* with dashed body show prolonged fetal bradycardia. *Gray arrow* shows increased resting tone [213]

16.8 Treatment

16.8.1 Perioperative Management

Once a diagnosis of uterine rupture is established, the immediate stabilization of the mother and the delivery of the fetus are imperative. After securing the airway and adequately ventilating the patient with oxygen, careful and immediate attention must be paid to correct hypovolemia. Patients should have multiple, preferably large-bore, intravenous catheters placed with vigorous fluid resuscitation and blood product replacement. In a study from Yemen, antibiotics were used in 100 %, 32.4 % received prophylaxis against gas gangrene, and 32.4 % received antitetanic serum [9].

The use of prophylactic antibiotics is controversial; Schrinsky and Benson state that they have no value [40], while others recommend their use because 30 patients (23 %) in one series (19 with an unscarred uterus and 11 with a previously scarred uterus) had intraperitoneal sepsis at the time of laparotomy [42]. More importantly, Gaffin et al. state that hypovolemic shock may lead to invasion of gram-negative bacteria from the ischemic bowel mucosa to the bloodstream, complicating the picture with endotoxemia and septic shock [219].

16.8.2 Operative Treatment

In 1932, Mahfouz urged conservative treatment whenever possible [220], but nowadays the key to successful treatment is early surgical intervention.

The time available for successful intervention after frank uterine rupture and before the onset of major fetal morbidity is only *10–37 min* [49, 74, 216, 221, 222].

After the fetus is successfully delivered, the type of surgical treatment for the mother should depend on the following factors:

- Type of uterine rupture
- Extent of uterine rupture
- Degree of hemorrhage
- General condition of the mother
- Future childbearing

16.8.2.1 Suture Repair

Uterine bleeding is typically most profuse when the uterine tear is longitudinal rather than transverse. Conservative surgical management involving uterine suture repair (Figs. 16.16 and 16.17) should be reserved for women who have the following findings:

- Desire for future childbearing [223]
- Low-transverse uterine rupture
- No extension of the tear to the broad ligament, cervix, or paracolpos
- Easily controllable uterine hemorrhage
- Good general condition
- No clinical or laboratory evidence of an evolving coagulopathy

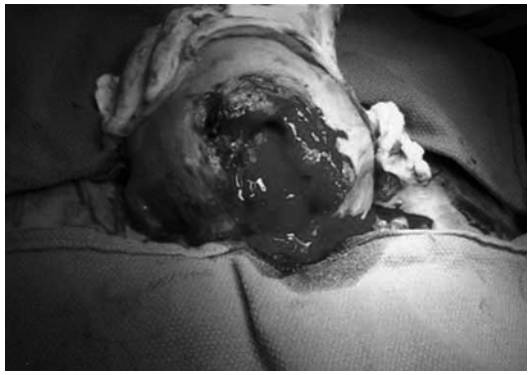

Fig. 16.16 The ruptured and contracted uterus found during emergent exploration [183]

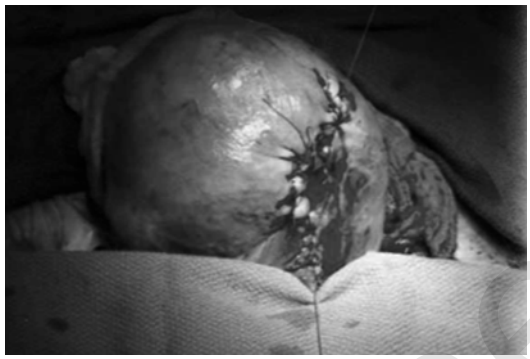

Fig. 16.17 The line of uterine rupture, extending inferiorly from the left side of the previous lower segment scar [183]

Repair of a ruptured uterus is achieved in 13–74 % of cases [4, 28, 177, 178, 224]. Suture repair in general carries a recurrence risk of uterine rupture of 4–19 % at a subsequent pregnancy [31, 225, 226]. Therefore, it is recommended that women with a previous suture repair of uterine rupture undergo an elective Cesarean delivery as soon as fetal lung maturity can be demonstrated [227–230]. There are cases where pregnancy was undisturbed until 37 weeks and then Cesarean section performed [231]. Recommendations are not strong because there are no prospective studies. The type of rupture dictates the type of uterine repair. In one study, the percentage of patients with simple repair of the uterus was significantly higher in the previously scarred uterus group (90.2 %) when compared to the previously unscarred uterus group (57.5 %). Hysterectomy was performed in 25 % of the patients with previously unscarred uterus, which was significantly higher than the 9.8 % in patients with previously scarred uterus [33].

16.8.2.2 Hysterectomy

Hysterectomy should be considered the treatment of choice in several indications:

- Intractable uterine bleeding
- Uterine rupture sites – multiple, longitudinal, or low lying
- Placenta percreta
- Irremediable uterine atony/accreta
- Probability of cervical cancer

Total Abdominal Hysterectomy

Total abdominal hysterectomy is definitive procedure unless cardiovascular decompensation necessitates subtotal abdominal hysterectomy or simple suture repair with/without bilateral tubal ligation [232–234]. Previous studies support total hysterectomy because of the probability of cervical cancer in the cervical stump and increased rate of bleeding and discharge [235, 236]. The cervical malignancy rate was 0.39–1.9 %. Their rate has currently decreased to 0.1–0.15 % due to cytological surgery [237]. It was also found that although the difference was not statistically significant, the amount of blood loss, duration of operation, and rate of maternal deaths, ABO need for blood transfusion and reoperation were higher in the total hysterectomy group [237]. Hysterectomy rate differs significantly in the range of 6–83 % [4, 28, 74, 143, 177, 178, 224, 238, 239]. In a study by Leung et al., 19 % of patients required hysterectomy. Sixty-eight percent of hysterectomies were performed because the uterus was not deemed repairable, 21 % for irremediable uterine atony, and 5 % because of placenta accreta [49].

Placenta percreta is additional therapeutic problem if present during spontaneous uterine rupture. Up to 1966, there were 33 cases published [240], and in the period from 1966 to 2000, there were only 40 cases reported worldwide [241]. In cases of spontaneous rupture of the uterus due to placenta percreta, partial manual removal and hysterectomy showed 20 %

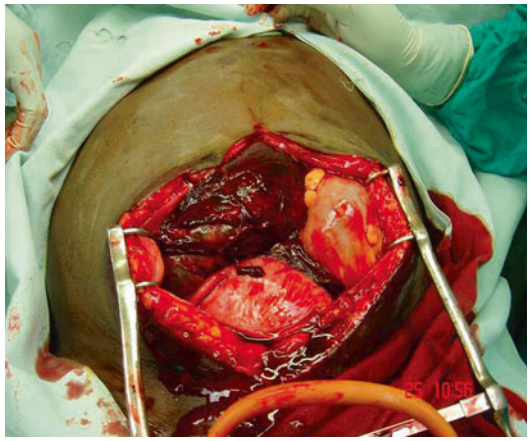

Fig. 16.18 Intraoperative photograph showing the uterus (lower part of operative field), the gestational sac (on the *left*), and the placenta (*upper right*) after opening the abdomen [246]

mortality, while hysterectomy with no attempt at manual removal resulted in 100 % survival. When the adherent placenta was left in situ, 67 % succumbed. Clearly, the treatment of choice is total abdominal hysterectomy with no attempt at manual removal [240, 242–245].

Subtotal Hysterectomy

Subtotal hysterectomy is the preferred operation when shorter operation is indicated, as in hemodynamic instability or cardiovascular decompensation to minimize mortality and morbidity [237]. In this study by Özden et al., this recommendation was for general emergency hysterectomies, not only spontaneous uterine ruptures which represented 10 % of cases [237]. In patients with spontaneous uterine rupture, studies show that total abdominal hysterectomy was done in 14 % women, subtotal hysterectomy in 5–22 %, uterine repair with bilateral tubal ligation in 25–45 %, and uterine repair without bilateral tubal ligation in 39 % of patients [9, 12].

During operation, the placenta should be examined and evacuated. It can be found in the abdominal cavity or placed intrauterine. The amniotic sac can be intact (Fig. 16.18) [223, 246] or disrupted.

16.8.2.3 First Trimester

Case reports on the management of uterine rupture in the first trimester are limited. Often, the clinical condition of the patients requires an emergency hysterectomy. However, there have been reports with conservation of the uterus. A midgestational uterine rupture was repaired using fibrin-coated collagen fleece, allowing the successful continuation of the pregnancy [247].

16.8.2.4 Elective Cesarean Section

A recurrent uterine rupture rate of 4–19 % has been noted in patients with a prior repair [28, 54, 248, 249]. For this reason, it has been recommended that women with a previous uterine rupture undergo an elective Cesarean delivery as soon as fetal lung maturity can be demonstrated [224, 250]. All studies recommend planned Cesarean delivery [64, 156, 228, 251]. Delivery between 37 and 38 weeks is recommended for patients with a history of ruptured lower uterine scar, while those with a history of ruptured classical scar or previous uterine rupture, the opinion varies as to the time of delivery. Some surgeons deliver at 35 weeks, while others recommend admission to the hospital 1 week prior to the gestational age at which labor started in the previous pregnancy [54, 55].

On the contrary, a case series described 18 pregnancies, occurring in 15 patients in whom a simple repair of a ruptured gravid uterus had been previously performed. Seventeen of these pregnancies had a successful outcome, and there were no cases of recurrent rupture [252]. Therefore, there is evidence that a patient with previous uterine rupture can carry another pregnancy. This chance appears to increase if the uterus is closed with a double-layer suture [94]. It is also important to note that Weingold et al. in 1966 found that 29 % (2/7) of patients who underwent repair of a ruptured uterus later presented with another rupture in a subsequent pregnancy [199]. In the last 50 years, there is a significant improvement in diagnostic accuracy due to modern imaging modalities and diagnostic laparoscopy; therefore, this outcome should be analyzed cautiously.

16.9 Prognosis

Maternal and perinatal mortality vary significantly between developed and developing countries. Also these rates are highly variable in the

same country especially between cities and rural areas. Due to the rarity of the disease and improvement in diagnostic and therapeutic modalities, the mortality was also decade dependent.

16.9.1 Maternal Outcome

16.9.1.1 Maternal Morbidity

The maternal morbidity rate ranges from 11.8 to 46.2 % [40, 202, 253]. Commonly reported maternal morbidity includes hemorrhage and shock, overall 46 %; infection (wound infection, 13.8 %; peritonitis, 10.2 %; tubo-ovarian abscess or urinary tract infection, 19.8 %; pelvic inflammatory disease, 4.3 %; respiratory infections including pneumonia, 2.2 %; and tetanus, 2 %); vesicovaginal fistula, 6.6 %; pelvic hematoma (mostly in the broad ligament), 19.2 %; fever, 21.7 %; and paralytic ileus, 18.9 %.

Complications of surgery such as injury to the bladder and ureter, dehiscence, and hernia have been described. Less commonly, hematuria, renal failure, disseminated intravascular coagulation (DIC), atelectasis, thrombophlebitis, pulmonary and cerebral embolism, and intestinal obstruction are reported as complications of uterine rupture.

In a series reported by Eden et al., 58 % of patients with uterine rupture required five or more units of blood [4]. In the study by Weingold et al. in 1966, 29 % (2/7) of patients who underwent repair of a ruptured uterus later presented with another rupture in a subsequent pregnancy and one of these women died [199].

16.9.1.2 Maternal Mortality

Maternal mortality as a consequence of uterine rupture occurs at a rate of 0–1 % [90] in developed countries, but the mortality rates in developing countries are 2–8 % [8, 12, 194, 196, 233, 254–257] and even 11 % reported in one Ethiopian study from 2002 [258]. The availability of modern medical facilities in developed nations is likely to account for this difference in maternal outcomes.

Maternal mortality depends on several other factors. In a South African study from 1976, with the mortality rate 8.5 % due to the rupture of an unscarred uterus, deaths could be further subdivided into mortality for women with longitudinal uterine tears (8.2 %), transverse tears (4 %), posterior wall tears (13 %), and multiple uterine tears (25 %). Golan et al. reported no deaths among 32 mothers who experienced rupture of a scarred uterus compared with 15 % (9/61) of women with an intact uterus [28]. Mokgokong and Marivate noted that the maternal mortality rate associated with uterine rupture largely depends on whether the diagnosis is established before (4.5 %) or after delivery (10.4 %) [238].

16.9.2 Fetal Outcome

16.9.2.1 Fetal Morbidity

It has been shown that significant neonatal morbidity occurred in women with uterine rupture when more than 18 min elapsed between the onset of prolonged decelerations and delivery [49]. Others claim that the time available for successful intervention after frank uterine rupture and before the onset of major fetal morbidity is 10–37 min [49, 74, 216, 221, 222].

Fetal Hypoxia or Anoxia

Leung et al. found that 5 % of neonates born to women who had uterine ruptures developed neonatal asphyxia (defined as umbilical-artery pH <7 with seizures and multiorgan dysfunction). No neonate had clinically significant perinatal morbidity when delivery was accomplished within 17 min of an isolated and prolonged deceleration of fetal heart rate. If severe late decelerations preceded prolonged deceleration, perinatal asphyxia was observed as soon as 10 min from the onset of the prolonged deceleration to delivery [49]. In a study by Menihan, 55 % (6/11) of fetuses born after uterine rupture had bradycardias between 18 and 37 min prior to delivery. Although the rate of fetal acidosis was high (91 %), no permanent neurological injuries or neonatal deaths occurred [216]. Bujold and Gauthier found that, even with rapid (<18 min) intervention between prolonged deceleration in fetal heart rate and delivery, 10 % (1/10) of neonates developed hypoxic-ischemic encephalopathies with impaired motor development. They concluded that, though

rapid intervention did not always prevent severe metabolic acidosis and serious neonatal disease, it probably did limit the occurrence of neonatal death [92]. The incidence of hypoxic-ischemic encephalopathy associated with uterine rupture in another study was 5 % (1/20) [58].

Fetal Acidosis

In 99 cases of uterine rupture, Leung et al. found that 43 % had an umbilical-artery pH <7, and 58 % of these newborns had a pH <6.8. In association with these pH levels, 39 % had 5-min Apgar scores of <7, and 12 % of whom had 5-min Apgar scores of <3 [49]. Menihan found that 91 % who were born after uterine rupture had an umbilical-artery cord pH level <7.0, and 45 % had 5-min Apgar scores <7. The most important factor for the development of fetal acidosis was complete extrusion of the fetus and placenta into the maternal abdomen [216].

16.9.2.2 Fetal Mortality

Fetal mortality is reported in the range of 54.3–81.7 % [9, 40, 194, 196, 233, 257], and 91–93 % found in Pakistan and Uganda [7, 12]. In the study by Al Salem et al., the perinatal mortality rate was two times lower (157/1,000) in the scarred uterus group, which is significantly lower than the perinatal mortality (372/1,000) in the unscarred uterus group [33]. Smith et al. found that the overall risk of perinatal death due to uterine rupture was 1/2,100 and uterine rupture was three times more likely to result in death of the infant if the delivery took place in a hospital with <3,000 births a year (1/1,300) compared to 1/4,700 in hospitals with >3,000 births a year [259].

Fetal distress and neonatal demise resulting from uterine rupture is related to placental abruption and hypovolemia resulting in placental hypoperfusion, which develops rapidly as is evident from previous instances of posterior rupture. Prompt delivery resulted in fetal salvage before fetal compromise could develop.

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Torsion of the Gravid Uterus 17

17.1 History and Incidence

No tumor, no torsion.
Barozzi, 1907
No uterine abnormality, no torsion.
Robinson and Duvall, 1931

17.1.1 History

The earliest report of this condition in pregnancy was made by an Italian veterinarian Columbi in 1662 [1]. Almost 200 years later, in 1863, Virchow reported the first case of torsion of nongravid uterus in a human observed at postmortem examination [2]. In 1876 this abnormality was described in a living woman for the first time by Labbe [3, 4].

17.1.2 Incidence

Nesbitt and Corner reviewed this subject in 1956 and found only 107 cases in the world's literature [5]. Jensen, during the long period between 1876 and 1992, found 212 cases [6]. Between 1996 and 2006, Wilson et al. found 38 cases [7]. A Medline search revealed only 46 cases reported since 1985 and none with a rotation ≥270° [8]. Therefore, there are less than 300 cases published in the last 150 years.

The majority is found in the third trimester [7]. The earliest reported age for uterine torsion during pregnancy is in the 6th gestational week; the latest is in the 43rd week. The majority of the torsions diagnosed at term are noted during the first stage of labor. There are only several cases in the puerperium [9, 10].

17.2 Etiopathogenesis

Uterine torsion is defined as rotation of the uterus on its long axis ≥45°. In most cases, the degree of torsion is approximately 180° [1]. However, there are two cases published with rotation of 540° which was associated with uterine necrosis [1, 11]. Torsion of the gravid uterus is extremely rare [12–14] but is more common than in nongravid uterus. The uterus in its normal state has little motility and is firmly held in place by the broad ligaments and the uterosacral ligaments. These widely distributed supports resist any tendency to torsion. But, for example, a large heavy fibroid of the subperitoneal type attached near the fundus of the uterus and well above the pelvic brim may rotate and exert traction on the uterus. It has inertia and a wide field of movement, and the more spherical its shape, the more easily it can rotate.

Physiological dextrorotation occurs commonly in pregnancy being the normal orientation of the myometrium fibers. In approximately 80 % of cases, dextrorotation is present and levorotation in the other 20 % [1]. A minor degree of rotation of the uterus is common but insignificant, especially in pregnancy, and is not sufficient to obstruct the blood supply in the normal uterus [15]. Pregnancy exaggerates the congenital and physiological rotations and obliquities of the

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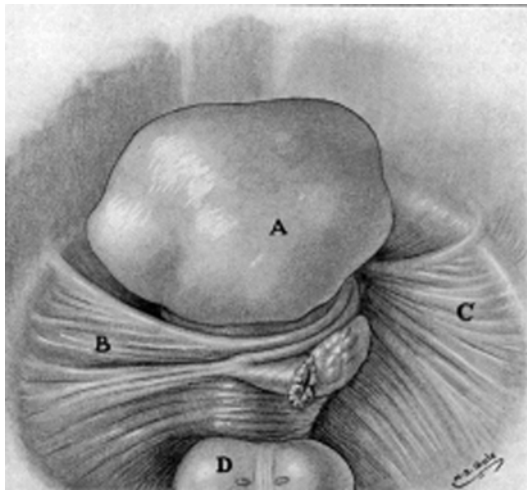

Fig. 17.1 Posterior view of the uterus. (*A*) Fibroid situated upon the fundus of the uterus; (*B*) left broad ligament (wrapped around body of the uterus); (*C*) right broad ligament; (*D*) rectum [16]

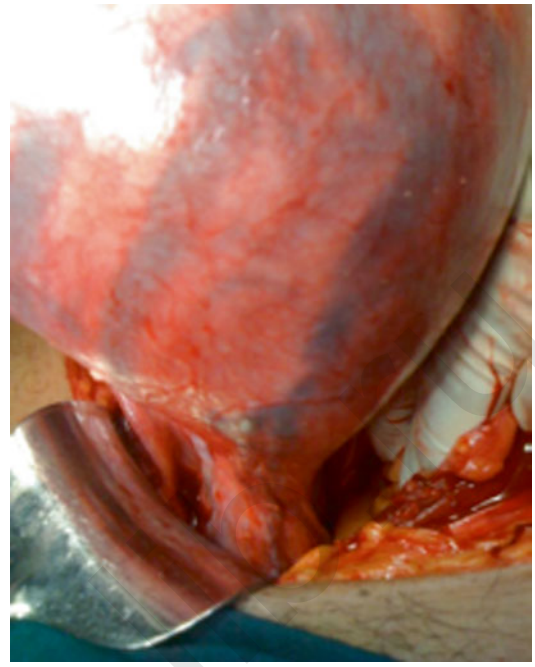

Fig. 17.2 Untwisted 180° levorotated gravid uterus with venous engorgement [18]

normal uterus. Changes due to pregnancy play an important role, but the phenomenon is more common in nulliparous women (Fig. 17.1), while Jensen states that maternal age and parity seem to play no part in causing the torsion [6]. According to Rabbiner, a kyphotic pelvis is an occasional cause of torsion of the pregnant uterus [17].

When the leiomyoma is sessile, torsion of the uterus occurs at the same time as that of the leiomyoma [16]. The point of torsion of the uterus occurs usually at the level of the uterine isthmus [16]. If the torsion of pregnant uterus occurs to such an extent that the uterine circulation is arrested, venous engorgement ensues (Fig. 17.2).

The presence of a uterine tumor was once believed to be the main etiological factor in the development of torsion of the uterus, and in 1907 Barozzi made the statement "no tumor, no torsion" [19]. Robinson and Duvall in 1931 modified that statement to "no uterine abnormality, no torsion," and they presented the hypothesis that uterine rotation in the absence of gross disease was due to a developmental asymmetry of the myometrium [20]. However, in 1935, Reis and Chaloupka reviewed the literature and found 15 cases of torsion of the uterus unassociated with any uterine abnormalities [21]. MRI studies proved that defective isthmic healing after lower uterine segment Cesarean section may result in suboptimal restoration of normal cervical length [22]. This may result in an elongated cervix with structural weakness and angulation in the isthmic region and may predispose to torsion of the uterus. Nicholson et al. [23] showed an X-shaped configuration of the upper vagina instead of H-shaped, but the plane should be at the level of the vagina on abdominal MRI [24]. In approximately 20 % of cases of uterine torsion, no causative factor is apparent. It has also been suggested that peristaltic movements of the sigmoid colon may cause uterine torsion [16]. The causative factors mentioned by Nesbitt and Corner in their review of the condition are listed in Table 17.1.

A recent review of published cases from 1966 to 2006 has not shown this to be the case, but rather uterine torsion occurs during a normal pregnancy and within a typical pelvis [8]. Authors claim that the common risk factors reported in association with uterine torsion are often nonspecific and therefore not always useful in heralding this uncommon complication of pregnancy.

Table 17.1 Causes of torsion of the gravid uterus [5]

Cause	%
Uterine myomas	31.8
Uterine anomalies, especially bicornuate uterus	14.9
Pelvic adhesions	8.4
Ovarian cysts	7.0
Abnormal presentation and/or fetal anomalies	4.6
Abnormalities of the spine or pelvis	2.8
No discoverable cause	30.5

Table 17.2 Presenting symptoms of torsion of the gravid uterus [5]

Symptoms	%
Pain	95
Shock	8–27
Intestinal obstruction	11–27
Urinary symptoms	9–12
Bleeding	6–13
Obstructed labor	14–29
Asymptomatic	6

17.3 Clinical Presentation

17.3.1 Symptomatology

17.3.1.1 Pregnancy

In general, symptoms are related to the degree and duration of torsion and may be designated as acute, subacute, chronic, or intermittent. The presentation of the patient may be in spectrum ranging from asymptomatic to mild abdominal pain and cramping to shock and maternal death. In about 11 % of cases, torsion is asymptomatic [5]. The main clinical features are pain, shock, intestinal and urinary symptoms, obstructed labor, and secondary vaginal bleeding. In many cases the clinical features exacerbate progressively, resulting in a diagnosis of "acute abdomen." Rarely does torsion of pregnant uterus occur to such an extent that the uterine circulation is arrested leading to acute maternal symptoms and also threaten fetal survival. Thus, it is usually associated with placental abruption. Pyrexia found on two puerperal torsions was due to degeneration of red fibroids that caused uterine torsion [9, 10].

The presenting symptoms depend upon the degree of rotation and are listed in Table 17.2.

Urinary symptoms include urgency, frequency, nocturia, oliguria, and hematuria. According to Siegler and Silverstein, there is, up to 1948, no instance of this condition having been diagnosed preoperatively [25]. Often it presents as an acute abdominal crisis, and differential diagnosis is presented in Table 17.3.

Table 17.3 Differential diagnosis of torsion of the gravid uterus [1, 12]

Ectopic pregnancy
Abdominal hemorrhage
Torsion of a pelvic tumor
Peritonitis
Obstructed labor
Placental abruption
Concealed accidental hemorrhage
Tonic uterine contraction
Degenerating fibromyomata
Acute hydramnion

17.3.1.2 Puerperium

The clinical presentation of puerperal uterine torsion is nonspecific and may differ from the symptoms of torsion in pregnancy. Symptoms at presentation could suggest an adnexal torsion or other colicky abdominal pain. The most common symptom is abdominal pain varying from mild abdominal tenderness to symptoms of an acute abdomen, making diagnosis difficult. In the puerperium a significant decrease of postpartum discharge (*lochia*) as well as a sudden complete stop of vaginal bleeding and discharge several days after delivery is highly suggestive of uterine torsion [26].

17.3.2 Physical Examination

On abdominal examination, the round ligament is palpably stretched across the maternal abdomen.

On pelvic examination, the uterine artery is perceived as pulsating anteriorly; on per speculum examination, the vagina and/or the cervical canal is distorted. Jensen described four pathognomonic clinical findings in cases of uterine torsion [6]:

- The round ligament palpably stretching across the abdomen
- The uterine artery pulsating anteriorly on vaginal examination
- Twisting of the vagina and/or the cervical canal with the urethra displaced laterally
- Twisting of the rectum

17.4 Diagnosis

Preoperative diagnosis of uterine torsion is difficult to establish. In most cases, the diagnosis is made intraoperatively.

The diagnosis can be confounded by other diagnoses, such as abnormal fetal heart rate [2, 4, 22, 27–30], failure to progress in labor [27, 29, 31, 32], or suspected placental abruption [4].

Radiologically, gas in the uterine cavity – on plain radiographs and CT scanning – has been described as a feature of uterine torsion in a nongravid patient but probably can be applied to gravid uterus also [33].

Ultrasound is not specific for this kind of diagnosis. In some cases, if previous ultrasound scans revealed fibroids that have changed position, torsion of a myomatous uterus may be suspected [33]. It can be detected by MRI if the equipment and personnel are present in emergency departments. The first case of uterine torsion detected by MRI is by Nicholson et al. in 1995 [23].

17.5 Treatment

17.5.1 Surgical Treatment of Uterine Torsion

17.5.1.1 Detorsion

The only therapy for a successful maternal and fetal outcome is laparotomy and correction of the torsion (Figs. 17.3 and 17.4). Whether any procedures should be performed to fix the uterus in the usual anatomic position is uncertain.

17.5.1.2 Hysterotomy

If detorsion is impossible, the posterior approach is used with a transverse incision. After deliberate *posterior transverse Cesarean hysterotomy*, the round ligament plication may prevent recurrent torsion in the immediate puerperium [24, 36]. Incorporating into routine practice the palpation of round ligaments at the time of Cesarean section would most likely prevent inadvertent hysterotomy at sites other than the anterior lower segment [7].

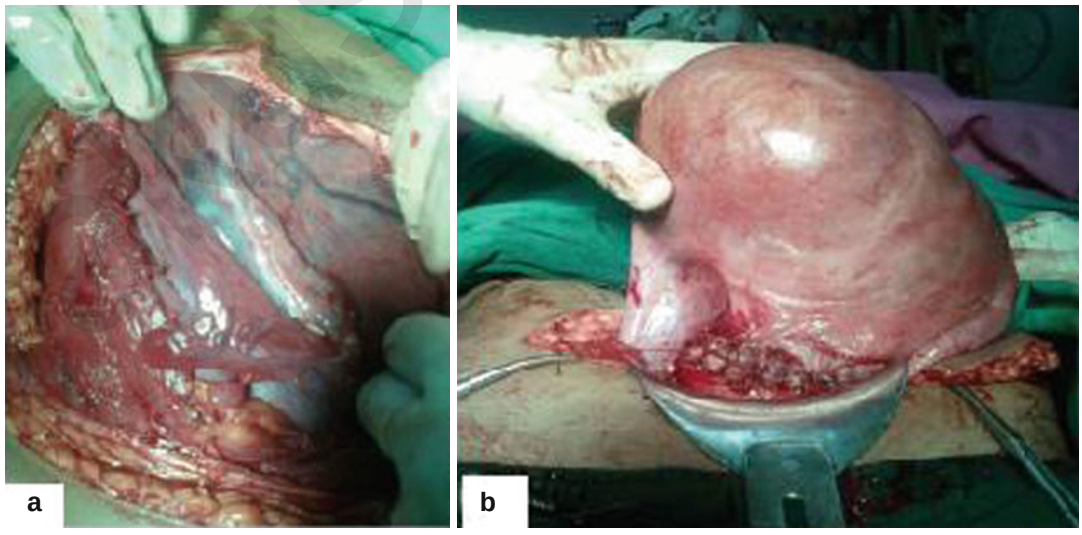

Fig. 17.3 (**a**) posterior wall uterus with left adnexa turned to right; (**b**) detorsioned uterus with myoma after suturing [34]

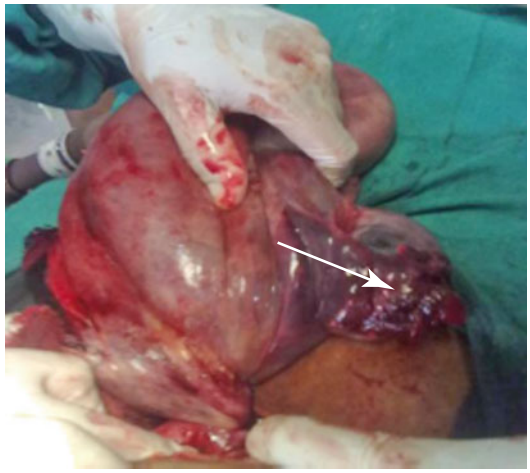

Fig. 17.4 Uterine torsion of 720°. Left ovary and tube enlarged congested free swinging (*arrow*) [35]

17.5.1.3 Hysterectomy

If the uterus is not viable or in women who are past the reproductive age or do not desire more pregnancies, hysterectomy is indicated [37]. It is, however, very difficult to determine whether the ischemic injury affecting the uterus is reversible or not, especially because puerperal torsion is a rare pathologic condition [26].

17.5.2 Obstetric Management

Obstetric decisions depend on the gestational age. At or near term (beyond 34 weeks), Cesarean section is the procedure of choice. At an earlier stage (before 23–24 weeks), the causative factor should be corrected if present or if possible and the pregnancy be allowed to continue to term. In the interval between the limit of fetal viability at 23–24 weeks' gestation and the 34th week or in the rare instance when the diagnosis is securely established by MRI or another study before a laparotomy and signs and symptoms are not compelling, the best management is unclear. If the abdomen has been opened and the uterus successfully rotated into the anatomic position, apparently relieving the torsion, the gynecologist must balance the unknown risk of a maternal and/or fetal complication if the delivery is not accomplished against the immediate risk of substantial prematurity.

17.6 Prognosis

17.6.1 Maternal Outcome

17.6.1.1 Maternal Mortality

The overall maternal mortality rate associated with torsion of the gravid uterus is about 13 % and is directly related to the duration of the gestation. Under 5 months it is 0 %, whereas at term it reaches 18.5 % [2, 6, 17]. Maternal mortality rate is also directly related to the degree of twisting. In 1951, it was 7.4 % in torsions of 90–180° and increased to 50 % when the rotation is 180–360° [38]. These findings were confirmed by Jensen [6]. Jensen stated that in the period 1960–1992, there is only one maternal death [6]. After 1976, maternal mortality was 0 % [23].

17.6.1.2 Future Pregnancy

There are no evidence-based recommendations for women who have had a uterine torsion and who wish to have future pregnancies. The risk of uterine rupture with a prior posterior lower segment incision compared with the risk following an anterior lower segment incision remains unknown. In the absence of evidence, Wilson et al. recommend a Cesarean section for any subsequent deliveries. Theoretically, a repeated Cesarean section is safer because it avoids the possibility of a labor-associated uterine rupture [7].

17.6.2 Perinatal Outcome

The limited number of cases reported and the lack of accuracy of some clinical records make this figure difficult to estimate with precision. It has been noted that the perinatal mortality increases with the degree of rotation, and whereas it ranges 20–24 % in cases in which the uterus is rotated from 90 to 180°, it may reach as high as 75 % in cases of rotation in excess of 180°. This fetal mortality rate of 18 % in cases from 1996 to 2006 (38 cases) [7] is higher than that reported by Jensen (212 cases) in the period 1876–1992 (12 %) [6].

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Degenerating Uterine Myomas 18

18.1 Classification and Histopathological Features

18.1.1 Considerations in the General Female Population

Uterine fibroids, also known as leiomyomas or myomas, are the most common uterine neoplasms. They are benign tumors of smooth muscle origin, with varying amounts of fibrous connective tissue [1]. Fibroids usually arise in the myometrium but may occasionally be found in the cervix, broad ligament, or ovaries [1, 2]. They are multiple in up to 84 % of women [3]. Fibroids have been reported to occur in up to 70 % of women by the age of 50 years [4] and are especially common in black women, who also often have more severe disease [4, 5]. These benign tumors are hormone dependent, responding to both estrogen and progesterone [6]; they often increase in size during pregnancy and usually decrease in size after menopause. Early age at menarche and obesity are risk factors for the development of fibroids, likely due to the increased exposure to estrogen [7].

18.1.2 Classification

Uterine fibroids in the general female population are classified according to their location as submucosal, intramural, or subserosal [1]. *Submucosal fibroids* are the least common type, accounting for just 5 % of all fibroids [8], but they are the most likely to be symptomatic since they project into the endometrial cavity. Submucosal fibroids can occasionally become pedunculated and prolapse into the cervical canal or vagina [9]. *Intramural fibroids* are the most common type, but they are usually asymptomatic; however, they may cause infertility due to compression of the Fallopian tubes. *Subserosal fibroids* project exophytically into the abdomen or pelvis and can also become pedunculated, which may be confused with ovarian tumors. Pedunculated subserosal fibroids can undergo torsion and consequent infarction and thus be a cause of severe abdominal pain [8, 10]. Large fibroids often degenerate as they outgrow their blood supply. The various types of degeneration include hyaline, myxoid, cystic, and red degeneration [8, 11, 12]. Calcification tends to occur following necrosis [12].

Although the majority of fibroids are benign, it is thought that some uterine leiomyosarcomas arise in a subset of fibroids [13]. Only about 0.23–0.7 % of apparently benign uterine fibroids turn out to be leiomyosarcomas on pathologic examination [14, 15]. Most leiomyosarcomas arise de novo. A leiomyosarcoma can be difficult to distinguish from a benign fibroid, and this possibility should always be considered in a patient with a rapidly growing uterine fibroid. Although red degeneration of a uterine myoma during pregnancy is managed nonoperatively, it is included in this discussion because of its ability to mimic a surgical emergency. A uterine myoma (or fibroid) is a benign tumor composed of smooth muscle. These tumors can exist within the wall

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of the uterus (intramural), within the uterine cavity (submucosal), underneath the serosa (subserosal), or attached to the uterine serosa by a stalk (pedunculated). As a myoma enlarges, it can outgrow its blood supply and undergo degeneration (muscular infarction), which occurs in up to 15 % of pregnant women who have myomas [16].

18.2 Incidence

Uterine leiomyomas occur in 1.6–2 % of pregnancies [17]. According to Spencer from 1920, pregnancy is complicated by fibromyomata in 0.6 % of cases [18]; Monro Kerr and Chassar Moir found the incidence to be 0.8 %. In the series from 1930 to 1954, out of a total of 69,656 deliveries, there were 245 fibromyomata or approximately 0.35 % [19]. Some authors claim that the incidence of uterine fibroids during pregnancy is decreasing especially of larger sizes because these are removed before pregnancy or if indicated hysterectomy is made. Others claim that it is increasing because many women are delaying childbearing. Red degeneration (necrobiosis) is particularly liable to occur during pregnancy. Browne had an incidence of 17.3 % in a series of 121 cases. In a series of 189 cases, necrobiosis occurred in 15.8 and 82 % were primipara [19].

18.2.1 Natural History of the Disease

During pregnancy, 15–30 % of myomas get enlarged due to increased estrogen and progesterone levels but most of them shrink during puerperium [20].

18.3 Clinical Presentation

Although leiomyomas during pregnancy usually remain asymptomatic, they may have complications which are symptomatic. The most common complication of uterine myomas during pregnancy is abdominal pain. The process of degeneration usually begins when the fibroid grows so large that the nearby blood vessels can no longer supply it with oxygen and nutrients. As the cells of the fibroid die, they are often replaced by collagen. This type of degeneration is called *hyaline degeneration*. Degeneration in fibroids may be hyaline (the most common), myxomatous, cystic, fatty, hemorrhagic, or malignant in nature. The type of degenerative change seems to depend on the degree and rapidity of the onset of vascular insufficiency. The pain is often severe and localized to the site of the fibroid, usually somewhere in the pelvic area. The severe pain associated with fibroid degeneration often lasts for 2–4 weeks. Degeneration of uterine myoma can lead to a complaint of sudden, severe abdominal pain. In addition, unlike with torsion of an ovarian mass, there is no direct correlation between the size of the myoma and the degree of pain. Gastrointestinal manifestations could be present such as nausea, vomiting, and diarrhea due to obstructive pressure of myomas on bowel.

18.3.1 Physical Examination

Physical examination will often reveal an exquisitely tender abdomen with signs of localized peritoneal irritation. There is tenderness over the mass attached to the uterus. Vomiting and dehydration for red degeneration is self-limiting.

18.4 Diagnosis

The ultrasound appearance of a degenerating myoma consists of a well-circumscribed uterine mass composed of echodense and echolucent areas (Fig. 18.1).

Because a degenerating uterine myoma does not require surgery and has characteristic sonographic findings, it is important to consider ultrasound examination in any pregnant patient in whom emergent abdominal surgery is being contemplated. In cases which would require myomectomy during pregnancy, the addition of Doppler evaluation is recommended. A sharp drop in residence index in Doppler means an indication of some degree of necrosis [22]. The Doppler is a helpful modality to decide whether to perform myomectomy or not during pregnancy [22].

Magnetic resonance imaging (MRI) can be safely used during pregnancy to evaluate adnexal masses (Fig. 18.2). But only two of 71 cases were evaluated by MRI [23, 24].

18.5 Treatment

18.5.1 Emergent Presentation

Despite an often dramatic presentation, the optimal treatment for a degenerating uterine myoma is a short course of analgesics. Pain will often improve dramatically soon after treatment is initiated. The local release of prostaglandins from a degenerating fibroid can also stimulate uterine contractions and premature labor, so prompt consultation with an obstetrician/gynecologist is strongly advised when this complication is identified.

Sometimes genuine doubt with a right-sided fibroid low in the iliac fossa mimicking appendicitis forces the surgeon to do a laparotomy. The severity of symptoms and suspicion of malignant mass or torsion are key in deciding upon indication for emergent operation. If in doubt, laparotomy or laparoscopy should be done to exclude other causes of acute abdomen.

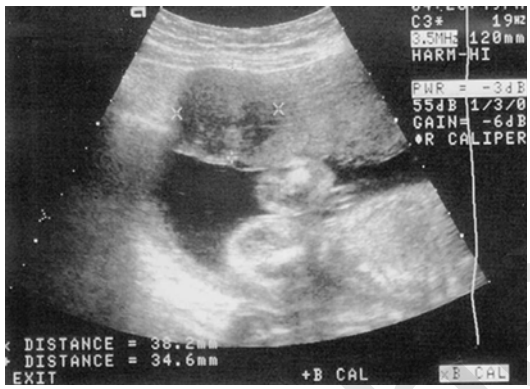

Fig. 18.1 Ultrasound of degenerating uterine fibroid at the uterine fundus (marked with calipers) [21]

> Once the real condition is apparent, usually the abdomen should be closed with no attempt at myomectomy, a particularly bloody operation at this stage of pregnancy.

Kim and Lee recommend cyst aspiration rather than myomectomy in a myoma with cyst degeneration and pain [23]. Occasionally a well-pedunculated fibroid may be easy to remove, but no attempt should be made to dissect out sessile or buried tumors.

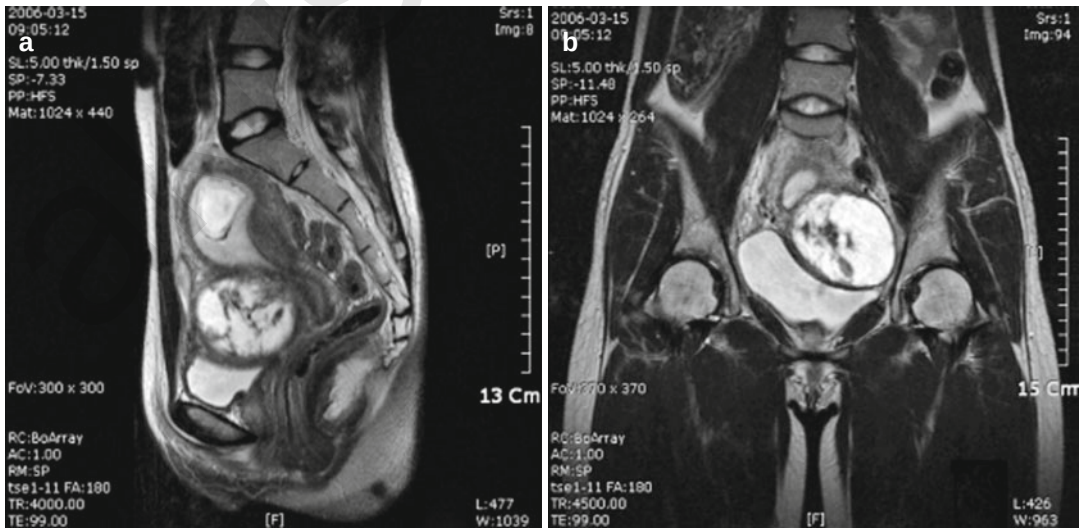

Fig. 18.2 T2-weighted image of MRI findings of a 27-year-old 12-week pregnant woman shows an 8 × 7 × 6 cm cystic and solid mass with septa. (**a**) sagittal view; (**b**) coronal view [23]

There has been only one successful case of a gasless laparoscopic myomectomy [25]. In this case, it could be difficult to differentiate a complex ovarian mass from cystic degeneration of the myoma.

18.5.2 Elective Presentation

Treatment depends upon the location of the tumor, but unless it is cervical, there may be no more difficult question to answer. Four options are available:

- Hysterectomy
- Abortion with removal of the tumor subsequently
- Myomectomy with or without removing the fetus
- Progress of pregnancy and meeting emergencies if they arise

18.6 Prognosis

18.6.1 Maternal Outcome

18.6.1.1 Maternal Mortality

In all published cases, mortality was 0 %.

18.6.1.2 Maternal Morbidity

There was one large prospective study. Among 15,579 women registered at the prenatal clinic, severe abdominal pain was seen in 16 patients; in 13 cases myomectomy was done. Twelve cases had live birth; 13 cases had no blood transfusion and other complications [26].

18.6.2 Neonatal Outcome

In 71 cases, only two pregnancies were terminated after myomectomy [27, 28], and two cases had preterm labor and preterm delivery, respectively [26, 29]. One case had intrauterine growth retardation [27]. In one large prospective study, in 13 cases myomectomy was done, and there were 12 cases of live births [26]. These series show excellent neonatal survival in the range of 92–97 %.

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Pelvic Inflammatory Disease and Tubo-ovarian Abscess

19

19.1 Considerations in General Female Population

19.1.1 Tubo-ovarian Abscess

Despite an increase in the number of effective broad-spectrum antibiotics, pelvic inflammatory disease (PID) and the complications arising from the disease continue to reach epidemic proportions into the 1990s. Acute salpingitis and PID account for more than 350,000 hospital admissions and 150,000 surgical procedures per year [1]. In addition, some report that nearly one-third of patients hospitalized for PID develop some degree of pelvic abscess [2]. Other sequels such as ectopic pregnancy, salpingitis isthmica nodosa, tubal infertility, chronic pelvic pain syndromes, and pelvic adhesions are other consequences of PID. Tubo-ovarian abscess (TOA) is the most serious manifestation of salpingitis because the intra-abdominal rupture of a TOA is potentially life-threatening, with mortality rates as high as 8.6 % [3]. Pelvic inflammatory disease and subsequent TOA may result whenever bacteria gain access to the upper female genital tract. Under normal circumstances, the Fallopian tubes and related pelvic structures are sterile. However, access of bacteria into the upper genital tract either via sexually transmitted diseases or through instrumentation of the uterus may inoculate the uterus with bacteria from the vagina, causing infection. It has been suggested that passive transport and vectors such as spermatozoa and *Trichomonas* assist in establishing the ascending infection from the polymicrobial vagina and cervix [4]. Once present in the upper genital tract in sufficient numbers and virulence, these bacteria initiate an inflammatory reaction (endometritis-salpingitis-peritonitis) that results in the signs and symptoms of PID. The rate of a TOA developing from typical PID is in the range of 1–4 % [5].

TOA is usually a polymicrobial infection, whereas general pelvic infections may often be monomicrobial. Tubo-ovarian abscesses are usually a mixture of anaerobic, facultative anaerobic, and aerobic organisms, with the purest isolated generally being anaerobes. The most frequent isolates from TOAs include a variety of *Enterobacteriaceae*, such as *Escherichia coli* (37 %), *Bacteroides fragilis* (22 %), other *Bacteroides* species (26 %), *Peptostreptococcus* (18 %), and *Peptococcus* (11 %) [3, 6].

The sexually transmitted organisms such as *Neisseria gonorrhoeae* and *Chlamydia* are usually not present in the abscess but may be recovered from the cervix in one-third of cases. The emergence and recognition of *Prevotella bivia* (formerly *Bacteroides bivius*) and *Prevotella disiens* as major pathogens in upper female genital tract infection, combined with data suggesting that increased concentration of anaerobic organisms in the vagina is a risk factor for PID, point toward an anaerobic-predominant mixed infection as a cause of PID and TOA. These anaerobic bacteria such as *Bacteroides* species and *Peptostreptococcus* species are commonly found in high concentrations in the vagina of women with bacterial vaginosis [4].

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Standardized diagnostic criteria for TOA do not exist. The clinical diagnosis of TOA has the same diagnostic difficulties of PID. Women presenting with PID and a pelvic mass may have a TOA, or it could be a hydrosalpinx, tubo-ovarian complex, or other complex adnexal mass. Patients with TOAs typically present with a history of pelvic or abdominal pain and fever. A history of PID may be present in only 50 % of patients. The majority of patients also have a leukocytosis [2]. A significant proportion of women with TOA is afebrile (20–30 %) and has normal WBC counts [2]. Other laboratory studies that may help in the diagnosis are an elevated erythrocyte sedimentation rate (ESR) and elevated C-reactive protein (CRP), which was found to be more sensitive than elevated WBC or ESR. Pelvic examination usually reveals extreme pelvic tenderness (cervical motion tenderness), and a mass may be present. If rupture has occurred, typical signs and symptoms of peritonitis are present and may lead to shock and death if not treated immediately. Ultrasonography is very helpful in the diagnosis of TOAs and in following TOAs that are managed conservatively. Ultrasonography has proven to be very reliable in the diagnosis of TOA [6]. The expected typical appearance of a TOA on ultrasonography is a complex or cystic adnexal mass with multiple internal echoes and septations. The "gold standard" for diagnosis has always been laparoscopy; however, as ultrasound technology continues to improve, laparoscopy may be reserved for patients in whom the diagnosis is questionable.

Indications for surgical intervention in the treatment of TOA include:

- Questionable diagnosis, when another surgical emergency may exist
- Rupture of abscess
- Failure of medical therapy with or without a drainage procedure

The first two are indications for immediate surgical intervention. Intraperitoneal rupture of a TOA represents a true surgical emergency. Delayed interventions may increase the risk of septic shock and even death. There is general agreement that acute rupture of a TOA requires immediate surgery, but the extent of the surgery required to achieve a cure is controversial [6, 7]. Traditionally, aggressive surgical extirpation, usually consisting of total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) and drainage of all pockets of infection, was the treatment of choice in TOAs. This radical approach was used largely because of the inadequacies of antibiotics of that time. This procedure dropped the mortality rate from 100 to 12 % [8] and is probably the procedure of choice in a patient who has completed childbearing or in those who are postmenopausal. However, most women who present with a TOA are in the peak of their reproductive years, and fertility is a major issue. Conservative therapy of an unruptured TOA consists of appropriate intravenous antibiotic therapy, close monitoring of the patient, and possible drainage of the abscess via posterior colpotomy [9, 10], CT- or ultrasound-guided percutaneous drainage, or drainage via laparoscopy. The posterior colpotomy approach has largely been abandoned because of a high rate of complications, including peritoneal sepsis and death. Success rates of CT-guided percutaneous drainage have been in the range of 77–94 %, and this technique may play more of a major role in the future [11]. Early drainage of abscess and irrigation via laparoscopy in addition to antibiotics achieved a success rate of 95 % by Reich and McGlynn's series of 21 patients [12]. These latter approaches have shown initially promising results but still need to be studied prospectively in a controlled randomized fashion. It does appear that drainage of a TOA in combination with antibiotic therapy is much more successful than conservative management. It has been shown that 50 % of patients treated with antibiotics alone eventually require surgical treatment for the disease [2, 13]. Others report a success rate of 70 % when TOAs are treated with antibiotics alone [4].

Approximately 19 % of patients treated with conservative surgical therapy require reoperation at a later date [2, 13, 14]. In cases of grossly apparent bilateral disease, a somewhat conservative approach of bilateral partial adnexectomy without hysterectomy may be performed.

Patients without adnexa are still able to conceive via in vitro fertilization and donor eggs. One must always use clinical judgment, however, and in patients with severe pelvic disease, TAH-BSO may be necessary despite the patient's reproductive status. In patients who have completed childbearing, TAH-BSO is standard therapy. It should also be noted that when a TOA is present in a postmenopausal woman, associated underlying malignancies are found in 25–50 % of cases, and conservative surgical therapy has no role [15]. Antibiotic therapy should include a broad-spectrum cephalosporin such as cefoxitin or cefotetan. Anaerobic coverage with clindamycin or metronidazole should also be added, as these have been shown to have the best ability to penetrate an abscess [6].

19.1.2 Ovarian Abscess

Ovarian abscess is a primary infection of the parenchyma of the ovary, an entity distinctly different from tubo-ovarian abscess. Tubo-ovarian abscess, by contrast, involves the ovary by secondary spread from the infected Fallopian tube [16]. Ascending infection is the most important mode of infection in nonpregnant women. Cases of ovarian abscess have also been reported due to non-gynecologic conditions such as ruptured appendicitis or diverticulitis or secondary to infection at distant sites as in tonsillitis, typhoid, parotitis, and tuberculosis. Association of ovarian abscess with intrauterine device (IUD) has been noted, and some of them may be secondary to *Actinomyces spp*. It may also occur due to secondary infection in a dermoid cyst, serous cystadenoma, or simple ovarian cyst. Ovarian abscess is also a known complication of transvaginal oocyte retrieval or transcervical embryo transfer, occurring in approximately 0.2–2.2 % [17]. Aitken is attributed to give the earliest description of primary ovarian abscess in 1869 [18, 19] and then Coe in 1891 [20]. Black presented the first major series of 42 cases in 1936. Wetchler and Dunn have reported 120 cases in literature till 1985 [16].

19.2 Incidence

19.2.1 Tubo-ovarian Abscess

Pelvic inflammatory disease in the form of pelvic and peritoneal abscess complicating pregnancy is rare. Blanchard et al. found that acute salpingo-oophoritis during pregnancy occurs more commonly in first trimester [21]. Sherer et al. have reported a recurrent pelvic abscess in pregnancy and in their review noted that the pelvic infection and pelvic abscess are less common in the second and third trimesters than in cases diagnosed in the first trimester [22]. By 1977, only 12 cases of tubo-ovarian abscess occurring late in pregnancy had been described in the literature [23]. Auguste Brindeau (Fig. 19.1) in 1917 is thought to have described the first such case [23]. In addition to 12 personal cases of salpingo-oophoritis during pregnancy, he has collected 81 more cases, of these 44 were operated on. There are several newer cases in late pregnancy [24, 25]. On the other hand, pelvic infection readily occurs in the puerperium if there is infection of the birth canal during or following parturition.

Up to 2003, there were only 26 reported cases of tubo-ovarian or pelvic abscess during pregnancy published [27]. The incidence of PID after oocyte retrieval is 0.12 % [28]. Pelvic infection after transvaginal oocyte retrieval for IVF-ET is <1 % [17, 29–31]. In less than half of these cases, a pelvic abscess develops.

19.2.2 Ovarian Abscess

There are only several case reports of true ovarian abscess during pregnancy [16, 18, 32, 33], and although the true incidence is unknown, it seems that it is extremely rare in pregnancy.

19.2.3 Intramyometrial Abscess

This entity is not described as part of PID, but it is mentioned here due to the same possible etiological factor. It is the rarest entity. Only one report with two cases was found [34].

Fig. 19.1 Auguste-Marie-Joseph-Victor Brindeau was a French gynecologist who worked in Paris [26]

19.3 Etiopathogenesis

19.3.1 Tubo-ovarian Abscess

During pregnancy, pelvic infection occurs quite independent of the gravid state or the infection may exist before the pregnancy. The etiologies may include non-gynecologic conditions such as ruptured diverticulitis or appendicitis; tubo-ovarian abscess of unknown origin has also been reported [35]. Friedman and Bobrow have proposed four mechanisms for infection of the ovaries or tubo-ovarian abscess during pregnancy [36]:

- Hematogenous spread as in pelvic tuberculosis
- Lymphatic spread especially from vagina and cervix
- Infection of a previously existing ovarian cyst
- Flare-up of old infection

Similar mechanisms are described by Merzer [37]:

- Infection at the time of fertilization
- Infection soon after fertilization before the uterine cavity has become closed by conception (12 weeks)
- Vascular or lymphatic spread (from a septic focus in the vagina or cervix)
- Flare-up of preexisting infection
- Instrumentation sufficient to overcome natural barriers
- Ascending infection associated with threatened abortion and intrauterine bleeding

Pelvic inflammatory disease, previous laparotomy, structural genital anomalies, and IVF-ET are known risk factors for pelvic abscess during pregnancy [27].

Why some tubo-ovarian abscesses are unilateral may be explained by a “flare-up” of an already preexisting but latent salpingitis [24].

This possibility would seem to necessitate either a low-grade infection of the tube in the first instance leaving sufficient patency to permit the passage of a fertilized ovum. After nidation, the infection may then become acute probably because of the congestion produced by the gestation or unilateral salpingitis, the other tube being patent and functioning [38].

19.3.1.1 In Vitro Fertilization-Embryo Transfer

Pelvic abscess formation is a rare complication of oocyte retrieval, which usually results in failure of the procedure. It is reported to occur in 0.2–0.5 % of transvaginal oocyte retrievals [17, 39]. Inoculation of vaginal bacteria and anaerobe opportunists is suggested to be the cause of PID following oocyte retrieval [30]. Microorganisms of the vagina are suggested to be the etiological pathogens in pelvic abscesses when transvaginal oocyte retrieval is used [30]. El-Shawarby et al. in 2004 described three different pathways for such infections. Direct inoculation of vaginal microorganisms may occur by puncture through the non-sterile vagina. The risk of pelvic infections after oocyte retrievals seems also related to the history of pelvic inflammatory disease. Reinfection may occur through puncture of chronically infected ovaries [40]. Although least likely, infection may occur through direct puncture of the bowel with an inflammatory or infectious spillage [41]. However, no pelvic infection has been reported with laparoscopic or abdominal oocyte retrievals in the 1990s [30].

The most well-established and well-accepted technique to decrease the risk of pelvic infection is using the fewest possible vaginal punctures [39, 42]. Serour et al. emphasized the importance of the fact that most patients in their study had a maximum of only two vaginal punctures [42]. Vaginal preparation has been made by different methods including the use of saline or povidone-iodine. In reports by Meldrum [43] and Evers et al. [44], no cases of PID in small group of patients were diagnosed. The former study used intravenous cefazolin and vaginal irrigation with povidone-iodine and the latter using only 10 % povidone-iodine. Larger series report rare cases of serious infections using sterile saline (0.5 %) [45] and Earle's balanced salt solution (0.4 %) [39].

19.3.1.2 In Vitro Fertilization-Embryo Transfer and Endometriosis

IVF-ET is now a recognized treatment for refractory endometriosis-associated infertility. On the other hand, endometriosis is proposed to be a risk factor for pelvic inflammation and abscess development following transvaginal oocyte retrievals [46, 47]. The presence of old blood in endometrioma is suggested to provide a culture medium for bacteria to grow slowly after transvaginal inoculation which may explain the role of endometriosis in predisposing the patients with PID [46]. Among its risk factors, incidental aspiration of an ovarian endometrioma during the process of oocyte retrieval is believed to be a common cause for developing the pelvic infection [46, 48, 49]. In one study 80 % (8/10) of PID following oocyte retrieval had underlying endometriosis [28].

There have been some case reports on the coexistence of endometriosis [46, 48] or its history [47] in patients with PID following assisted reproductive technology treatment. Younis et al. [46] presented three cases of severe pelvic abscess following oocyte retrievals for IVF-ET in whom stage IV endometriosis or ovarian endometrioma was previously diagnosed as the sole reason for infertility. In contrast, Ashkenazi et al. [17] failed to show a higher incidence of endometriosis among their patients: two cases of endometriosis in 28 PID patients among 4,771 ovum pickups. It has been suggested that both the pseudocapsule of endometrioma and its inside old blood may prevent antibiotic prophylaxis from overcoming the transvaginal bacterial inoculation [46]. In other cases of endometriosis, small pools of old blood may act as culture media for the inoculated bacteria. Deposit of TOA is an uncommon complication in pregnant women,

leading to serious complications such as surgery, ICU admission, and preterm delivery; only one subject developed a TOA during pregnancy following IVF-ET in this report.

The presence of endometrioma is a risk factor for the development of a TOA or an ovarian abscess [50]. Whether operative treatment of recurrent ovarian endometriosis improves the prognosis of IVF is still open to debate [51]. Previous reports have indicated that aspiration of endometriotic cysts before ovulation induction for in vitro fertilization resulted in a better clinical outcome [52]. However, studies have also indicated that pretreatment for endometrioma before IVF could potentially reduce the number of retrieved oocytes [53]. In order to prevent infection in patients with endometrioma for oocyte retrieval, previous reports have suggested the aspiration of endometrioma before oocyte retrieval [53]. However, Tsai et al. found these endometriotic cysts re-expanded quickly after aspiration and it was difficult to harvest some oocytes without puncturing through these chocolate cysts. In addition, the chocolate content of the follicular fluid is sometimes found incidentally after the aspiration [54]. Since endometrioma was considered a risk factor for the development of a TOA or an ovarian abscess [50], infection-preventing measures should be applied not only prior to but also immediately before oocyte retrievals.

19.3.1.3 Pelvic Inflammatory Disease

The risk of infection has been shown to be higher in cases of PID [27, 30, 40].

19.3.1.4 Postpartum

The postpartum period appears to be the least likely time to develop a TOA because ascending infection, which is the major pathophysiology in developing PID in most women, rarely occurs during this phase.

19.3.1.5 Tubal Sterilization

Particularly in women who have had tubal sterilization, the incidence of TOA is minimal because the procedure blocks communication between the genital tract and the pelvic cavity [55]. Theoretically, this blockage should prevent an ascending transmission of any organisms, if present, from the genital tract proximal to the site of tubal sterilization into the peritoneal cavity. This view is supported by clinical evidence that a complete or even partial occlusion of tubes appears to lessen the severity of infection when it occurs [55]. Three possible explanations of TOA after previous occluded tubes (TOAPOT) have been proposed [55]. The most likely cause is the persistent tract or reconnection between the two tubal segments. Secondly, factors related to the operative procedure are possible. Lastly, systemic factors such as a hematogenous or lymphatic bacterial spread with a compromised immunological status of the patient are possible. Time intervals from tubal occlusion to TOAPOT had been reported to range from as early as 36 h to up to 12 years [55].

19.3.2 Ovarian Abscess

The etiology of ovarian abscess in pregnancy is uncertain and in all probability is different from that in nonpregnant state. Ascending infection is the most important mode of infection in nonpregnant women. Barriers to ascending infection in pregnancy include cervical mucus plug, intact fetal membranes, and the decidua covering the openings of the Fallopian tubes. Friedman and Bobrow [36] have proposed four mechanisms for infection of ovaries during pregnancy (see section Tubo-ovarian Abscess). Data that confirm these facts are that ovarian abscess readily occurs in the puerperium if there is infection of the birth canal during or following parturition. Also it is likely that the ovary becomes infected quite independently of the gravid state or that the infection exists before the pregnancy.

19.3.3 Intramyometrial Abscess

The etiology in one published report of two cases is failed instrumental delivery in the second stage of labor [34].

19.4 Microbiology

Up to 2003, in only several cases, bacterial etiology of pelvic infections is available after transvaginal punctures such as *E. coli* [56] and a subclinical infection with *C. trachomatis* [57] and rare isolate in general population *Atopobium vaginae* [58], *S. aureus*, and mixed anaerobic bacteria [47]. Anaerobic opportunists of the vagina are found to be etiological agents in pelvic abscesses after transvaginal oocyte retrieval. *Escherichia coli*, *Bacteroides fragilis*, *Enterococcus*, and *Peptococcus* are commonly found microorganisms [30, 31]. There are also case reports with other microorganisms such as *Fusobacterium necrophorum* during puerperium [59]. In a case by Navada and Bhat, at laparotomy there was no clear-cut evidence of spread of infection from adjacent organs, but the preexisting salpingitis or previously ruptured tubo-ovarian abscess could not be ruled out. Thus, the proposed mechanism in the case by Navada and Bhat could be flared up of old infection [60]. Intraoperative finding of adhesion between the loops of intestine, the uterus, and the tubo-ovarian tissue indicates the chronic nature of the disease. Hence, she might have contracted the pelvic infection before pregnancy following the first Cesarean section.

Patients who suffer from ovarian abscesses almost always have a history of salpingitis, endometriosis, pelvic adhesion, hydrosalpinx, or pelvic surgery [30, 46].

19.4.1 Ovarian Abscess

An ovarian abscess is defined as a primary infection of the ovary without the involvement of the Fallopian tube, whereas a tubo-ovarian abscess involves both the Fallopian tube and the ovary. Since 1869, only 125 cases of primary ovarian abscesses have been reported in the related English literature. Wetchler and Dunn reviewed 120 cases up to 1985, [16] and Stubblefield in 1991 added five cases [61]. The possible factors for the cause of ovarian abscess are disruption of the ovarian capsule, giving bacteria access to the ovarian stroma, and hematogenous and lymphatic spread [16]. Nevertheless, the most common mechanism is considered to be alteration of the ovarian capsule at the time of ovulation or by penetration during surgery or surgical procedures. The interval between capsule disruption and clinical presentation may vary, depending on the bacterial inoculum dose, type of bacterium, its virulence and whether the infection occurred secondary to a direct contamination at surgery, or spread through devitalized tissue [62]. The aforementioned complication has been reported to occur after vaginal hysterectomy, ovarian cystectomy, Cesarean section, during pregnancy, and with the use of an intrauterine device [16, 63].

Furthermore, transvaginal or percutaneous needle aspiration of an endometrioma has been considered in the causation of this rare phenomenon [48, 64]. Ultrasonically guided vaginal oocyte collection is a relatively atraumatic method with rare complications. This technique has now become the method of choice in most IVF-ET programs, because it results in excellent oocyte yields, with increased speed and excellent follicle, as well as major pelvic vessel visualization, thereby decreasing the probability of vessel puncture [65]. Nevertheless, despite the advantages, there are some inherent risks, such as injury to blood vessels and hemoperitoneum, trauma to pelvic organs, infection or exacerbation of pelvic inflammatory disease, rupture of endometriotic cystic masses, urinary tract infections, and hyperstimulation [31, 66–68]. Reports on the formation of an ovarian abscess after ovum retrieval for IVF are scant [48]. Moreover, the case reported by Padilla in 1993 occurred during ovum retrieval while an endometriotic cyst was punctured [48], thus making the case by Dicker et al. of ovarian abscess to occur after follicle aspiration without any subtle pelvic pathology [31].

19.5 Clinical Presentation

19.5.1 Tubo-ovarian Abscess

Pregnancy is said to protect against pelvic infections. Clinicians are therefore unlikely to suspect a pelvic abscess as a cause of an acute abdomen

in pregnancy. The first signs of the disease are sometimes mild and not specific [46]. Recurrent symptoms of abdominal pain in the postoperative period and interpregnancy period suggest the chronic nature of the disease. However, the courses of antibiotics and the low virulence of the organisms resulted in chronic pelvic infection. The infection might have flared up recently and presented in the third trimester of pregnancy with some acute symptoms like abdominal pain with giddiness and vomiting to suggest peritonitis. Patients with PID during pregnancy may present with wide range of clinical symptoms, and the findings may be altered significantly by the size of the gravid uterus [22]. With no classical clinical features of acute peritoneal or pelvic infection, it was not suspected preoperatively and was detected only during Cesarean section [69]. Jafari et al. in the English literature review of 19 cases found that in only one case, the diagnosis was made preoperatively [23].

Diagnosis of PID after IVT-ET with underlying endometriosis was based on the signs of peritonitis on physical examination, cervical and adnexal tenderness, rise of body temperature to >37.8 °C for 48 h, cervical discharge, leukocyte count above 12,000, and elevated ESR. The PID was usually diagnosed 4–7 days after the procedure [28]. Of special interest is the delayed presentation of the infection in pregnancy [46, 70]. A pelvic infection becomes clinically evident within hours up to a few days after oocyte retrieval. The time from oocyte retrieval to the manifestation of a frank pelvic abscess is much longer. In the majority of cases, diagnosis will be made within 3 weeks after oocyte retrieval, but an interval of 56 days has been reported [30, 46] and a case described where the diagnosis was made in the second half of pregnancy [47].

19.5.2 Ovarian Abscess

Women with ovarian abscess during pregnancy may present with a wide range of clinical symptoms. A woman with a ruptured ovarian abscess presents with features of diffuse peritonitis. An unruptured abscess is more difficult to diagnose because of variable clinical presentation. The most common presenting symptom is an indolent onset of abdominal pain. Diffuse lower abdominal pain may worsen to severe pain associated with anorexia, nausea, and vomiting in case of rupture. Low-grade fever may be the only presentation in 50 % of cases.

19.6 Diagnosis and Differential Diagnosis

19.6.1 Differential Diagnosis

- Ectopic pregnancy
- Pelvic neoplasm
- Endometrioma
- Ovarian torsion
- Hemorrhagic cyst
- Ovarian hematoma
- Appendiceal abscess
- Diverticular abscess
- Tubo-ovarian abscess

19.6.2 General Female Population

To make the diagnosis of TOA, the patient must have abdominal pain, cervical motion tenderness, and adnexal tenderness, as well as one of the following:

- Fever >38 °C (101 °F)
- Abnormal cervical discharge
- Elevated ESR or CRP or positive cervical cultures for *N. gonorrhea* or *C. trachomatis*

Ultrasonography should be the first diagnostic imaging examination to be performed in cases of suspected PID in which there are nondiagnostic clinical findings. This modality is readily available and noninvasive and can be performed at the patient's bedside [71–75]. Transvaginal sonography (TVS) allows detailed visualization of the uterus and adnexa, including the ovaries. The Fallopian tubes are usually imaged only when they are abnormal and distended on physical examination, primarily from postinflammatory obstruction. Transabdominal sonography (TAS) is complementary to the endovaginal examination because it provides a more global view of the pelvic contents (Fig. 19.2) whether TAS (bladder

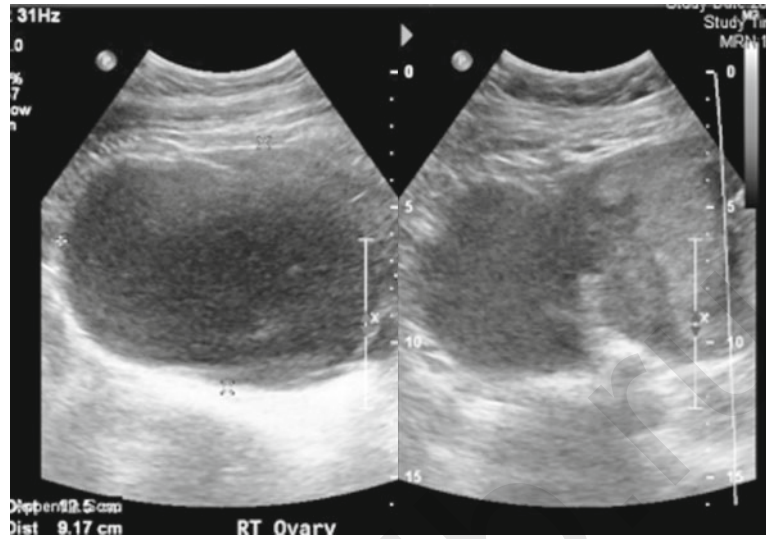

Fig. 19.2 Transabdominal sonography. A 12.5-cm-sized right ovarian cyst in pregnant women [76]

filling required) or TVS (bladder filling not required) is performed first and whether the complementary examination is needed for a final diagnosis is a matter of individual clinical imaging practice [74, 77–79]. The free fluid in the abdomen indicated that rupture of the tubo-ovarian abscess had likely occurred. Lee and Swaminathan described sensitivity of ultrasound for the diagnosis of TOA of 56–93 %, with a specificity of 86–98 % [79]. The wide range is likely due to differences in methods, including variability in the technology used (transabdominal vs. transvaginal), the person performing and interpreting the ultrasound (radiologist vs. gynecologist), the study population (patients with suspected PID and patients with a palpable adnexal mass and suspected PID vs. only patients eventually requiring laparoscopy or surgery in the workup of their PID), the study design (retrospective vs. prospective), and interpretation of positive results (inclusion of any adnexal mass vs. limiting it to those specifically diagnosed as abscess) [79].

Magnetic resonance imaging (MRI) serves as an excellent imaging modality in cases in which the ultrasonographic findings are equivocal (Fig. 19.3). In a study by Tukeva et al., MRI findings with sonograms were compared, and MRI was more accurate than ultrasonography in the diagnosis of PID [80]. However, the study was limited to a selected group of patients [80–82].

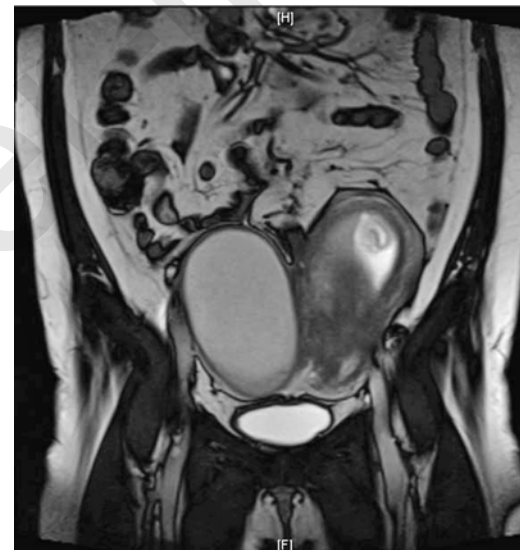

Fig. 19.3 Magnetic resonance imaging findings. Right ovarian cyst and intrauterine pregnancy (T2-weighted image) [76]

19.6.3 Pregnant Patients

There are no studies on the subject, but as for other intra-abdominal infections, ultrasonography might not be as useful in late gestation as in early gestation or the nonpregnant state for detection of adnexal pathologies because of an enlarged uterus.

19.7 Prevention of Infection

19.7.1 Preprocedural Elimination of Endometriosis

Endometriosis may be a predisposing factor for oocyte retrieval-induced PID. In regard to the few investigations available, it is rather soon to conclude a management protocol. However, some precautions may be useful for cases with endometriosis that undergo oocyte retrieval. Full evaluation and removal of endometrioma should be considered for the patients undergoing IVF [27]. However, non-vaginal methods of oocyte recovery like transabdominal approach in cases with endometriosis and pelvic adhesion seem preferable.

19.7.2 Procedural (Vaginal) Antisepsis

Traditionally, the vagina is not prepared with antiseptic solutions (e.g., aqueous povidone-iodine) before oocyte retrieval since these agents are considered to be embryotoxic. Therefore, employing only normal saline irrigation of the vagina is usually the norm prior to oocyte retrieval. However, most believed that using only normal saline rinsing and irrigating the vagina canal can only wash away the vaginal discharge without destroying potentially harmful bacteria preexisting in the vaginal flora. By applying an additional antiseptic solution followed by normal saline solution, as demonstrated in our series with aqueous povidone-iodine, one can eliminate most if not the entire vaginal flora. This process would not jeopardize the development of the oocyte because all the antiseptic solution has been completely flushed away before oocyte retrieval. The comparable clinical outcome of fertilization rate and implantation rate between two groups in our series has also proved this effect.

19.7.3 Prophylactic Antibiotics/ Antifungal Agents

Older studies tend to question their use given the low incidence of pelvic infections [39, 45, 83]. Other investigators, however, do advocate using prophylactic antibiotics as a general rule [31, 42, 43]. Although there is no consensus on the type and protocol for antibiotic use, doxycycline and metronidazole are the common ones. First-generation cephalosporins, which are routinely used as prophylactic antibiotics preoperatively, are another class of antimicrobials that have been used before TVOR [41]. Serour et al. even used fluconazole, an antifungal agent, as part of their protocol prior to oocyte retrieval [42]. Although antifungal prophylaxis may seem excessive, an interesting report by Ibara et al. discussed two cases of systemic *Candida glabrata* infections diagnosed at 34 and 22 weeks gestation following IVF [84]. The yeast was isolated from both the mothers and their babies. Another approach can also be to reserve prophylactic antibiotics to high-risk patients such as those with history of pelvic inflammatory disease or endometriosis.

Patients who suffer from ovarian abscesses almost always have a history of salpingitis, endometriosis, pelvic adhesion, hydrosalpinx, or pelvic surgery [30, 31]. Prophylactic antibiotics during oocyte retrieval are recommended in these groups of patients with increased risk, but cannot prevent pelvic infection in all patients [30, 46].

19.8 Treatment

19.8.1 Medical Therapy

19.8.1.1 Tubo-ovarian Abscess

Bennett et al. found in their series a minor pelvic infection in 0.3 % of cases defined by pyrexia and pelvic tenderness with no evidence of abscess formation on ultrasound [30]. Therefore, in the early course of infection, all these patients were treated with antibiotic therapy. More severe infections leading to an abscess also occurred in 0.3 % of cases [30]. This incidence is in accordance with the retrospective analyses [17]. However, the preventive treatment with antibiotics does not seem to be helpful and is discussed to be a possible harm for the outcome of IVF cycles.

19.8.1.2 Ovarian Abscess

Ovarian abscess after ovum retrieval may be a severe complication that requires accurate diagnosis and prompt intervention. Initial treatment is with intravenous antibiotics effective against gram-positive, gram-negative, and anaerobic bacteria.

19.8.2 Surgical Therapy

19.8.2.1 Tubo-ovarian and Ovarian Abscess

In both TOA and ovarian abscess, surgical therapy is indicated when:

- There is no response to antibiotics within 72 h.
- If the abscess or adjacent organ ruptures.
- If surrounding organs are affected by the inflamed mass.
- There is unsuccessful drainage of the abscess.
- Uncertainty about the diagnosis.

In general population, there are two surgical options available: laparoscopy and laparotomy, both with removal of the ovary as the treatment of choice. Sometimes it is possible to drain the abscess by laparoscopy, but severe pelvic adhesions secondary to abscess formation can prevent completion of the laparoscopic procedure and then conversion to laparotomy is indicated.

As most of the patients are young, we should attempt conservative surgery if the pathology is limited to one adnexa [35]. Surgical drainage of ovarian abscess and conservative surgical approach under antibiotics are recommended during pregnancy albeit there is no consensus on patient management [85]. Drainage could be performed through culdotomy or using laparoscopy (Fig. 19.4) [76, 86] or laparotomy with peritoneal lavage. The drainage can be done percutaneously under ultrasound control. Be cognizant of peristaltic bowel on ultrasound to avoid bowel puncture and subsequent inflammation/infection. In severe cases where one-sided adnexal disease is present, unilateral salpingo-oophorectomy could be done [60] or even hysterectomy with bilateral salpingo-oophorectomy is performed [66]. Kuo et al. [87] found that, among multiparous patients, hysterectomies were more commonly performed. Park et al. collected all cases of tubo-ovarian abscesses after IVF-ET pregnancies up to 2012 (Table 19.1).

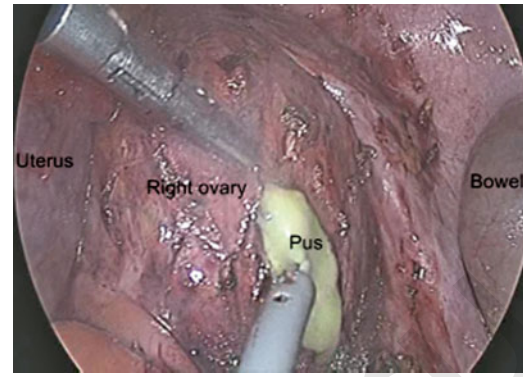

Fig. 19.4 Laparoscopic image of the right ovarian cyst. There was a 10-cm-sized right ovarian cyst including pus, which made severe adhesion with the surrounding pelvic organs and peritoneum. It also had endometriotic lesion [76]

19.9 Prognosis

19.9.1 Tubo-ovarian Abscess

Several possible explanations for the role of infection in reducing pregnancy success have been suggested especially during IVF-ET pregnancy with PID. Introducing endotoxin releasing bacteria into the peritoneal cavity during transvaginal oocyte retrieval may induce abortion by promoting the release of prostaglandins as well as catecholamines and cortisol which play some role in the termination of pregnancy. Moreover, local inflammatory reaction and fever may also affect the success rate of pregnancy [88]. Due to the adverse effect of endometriomas on IVF outcome, it is suggested that endometrioma should be removed in patients with endometriosis prior to IVF admission. Preconception evaluation and treatment should be considered for such condition [27].

Table 19.1 Clinical features of nine cases of tubo-ovarian abscess in pregnancy after IVF-ET [76]

Case	Vaginal preparation method[a]	Interval from IVF to symptom (wk)	History of endometriosis	Time of OP[b] (wk)	WBC[c]	Symptoms and signs[c]			Procedure	Pregnancy outcome
						Pain	BT (°C)	Mass (cm)		
Padilla [48]	Bethadine (irrigated)	3	+	GA 5	12,400	+	38.5	CDS, 5	Laparoscopic drainage	Ongoing singleton IUP, GA 7 week
Zweemer et al. [6]	NA	42[d]	NA	GA 38[d]	18,700	+	38.6	Right, 16	Laparotomic removal	Healthy singleton baby 3,240 g under Cesarean section at GA 38 week
Younis etal. [5]	IV antibiotics	3	+	Operation was not done	21,000	+	38.9	Bilateral, 6	Antibiotics treatment	Healthy singleton baby 2,850 g at full term
den Boon etal. [7]	NA	23	+	GA 25	17,700	+	38.0	NA	1st drainage 2nd diagnostic laparotomy	Delivery at GA 26 week 1st baby: 876 g, Apgar 3/7 live 2nd baby: 915 g, Apgar 1/3 expire at 9 week
Matsunaga et al. [8]	NA	14	+	GA 22[e]	Raised	+	38.1	Left, 8	Laparotomy-LSO	Vaginal delivery at GA 22 week, Apgar 1/3 expired
Jahan and Powell [10]	NA	3	+	GA6	Raised	+	39.0	Left, 7.8	Laparoscopic drainage (2 times)	Elective Cesarean section at GA 37 week (fetal cardiac anomaly)
Sharpe et al. [4]	Saline PO antibiotics	11[f]	+	GA 31	30,600	–	–	Right, 10	Cesarean section and drainage	Healthy twins, GA 31 week
Al-Kuran etal. [11]	Saline	7	–	GA9 GA21[g]	15,000	+	+	Left, 5	Laparotomy-Appendectomy drainage (2 times)	Spontaneous abortion at GA 21 week
Current case	Saline PO antibiotics	12	+	GA 14	10,330	+	–	Right, 12.5	Laparoscopic drainage	Ongoing singleton IUP GA 25 week

IVF in vitro fertilization, *ET* embryo-transfer, *OP* operation, *WBC* white blood cell count (/mm3), *BT* body temperature, *GA* gestational age, *CDS* cul-de-sac, *IUP* intrauterine pregnancy, *NA* not available, *IV* intravenous, *LSO* left salpingo-oophorectomy, *PO* per oral

[a]It contains vaginal irrigation method in oocyte retrieval and use of peri-retrieval antibiotics

[b]It is time of first operation for tuboovarian abscess

[c]All data are in time of diagnosis

[d]Symptom was developed 45 days after Cesarean section at 38 weeks

[e]Operation was done 15 days after delivery at 22 weeks

[f]She had only painless vaginal discharge at the first time

[g]The second operation was done 24 h after delivery at 21 weeks

The successful culmination of pregnancy is quite unusual when it is complicated by PID even in the first trimester and almost unheard when a tubo-ovarian abscess is present in late pregnancy. However, in a series published by Jafara et al., the fetal survival rate of those pregnancies complicated by a TOA late in the second trimester was surprisingly approximately 33 % [23].

19.9.2 Ovarian Abscess

A delay in diagnosis may be associated with risk of maternal death and can be detrimental to the fetus as well. Fetal loss rate of 50 % has been reported most often as spontaneous septic abortions.

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