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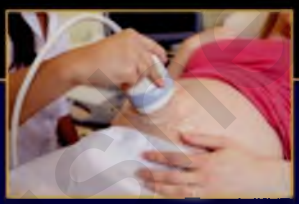
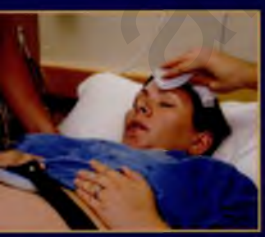
Obstetric Triage and Emergency Care Protocols

Second Edition





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SECOND EDITION

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To my husband, David.
—D.J.A.

To all my patients—I hope I have taught them as much as they have taught me. And to John, Trini, and Jack—my work would be meaningless without their love and support.
—D. L.

To my daughters, Anna and Juliana—you keep me smiling, curious, and loving life.
— B. C.

To my beautiful daughter, Annie.
—E.D.H.

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Foreword

That the second edition of *Obstetric Triage and Emergency Care Protocols* is being published just 4 years after the very successful prize-winning first edition illustrates how rapidly the field is advancing. As institutions recognize the unique importance of urgent care for pregnant women and develop units dedicated to providing that care, this book has become increasingly relevant. As current and past chairs of obstetrics and gynecology at the Warren Alpert Medical School of Brown University and Women & Infants Hospital, we are extremely proud of the efforts of our faculty in developing this area of care. Our obstetric triage unit has morphed from a labor evaluation site and little else in the 1980s to its present sophisticated evaluation and stabilization unit for a growing variety of medical problems in pregnant women.

The editors have been involved in this development from its inception. Dr. Angelini came to Providence in 1990 with the charge to begin a midwifery service that would be devoted to training residents and providing collaborative care to our patients. Dr. LaFontaine was one of those residents, graduating in the 1990s. After 13 years in private practice, she returned to our department to take charge of our obstetric triage unit. The two associate editors joined the faculty subsequently—Dr. Cronin, after completing her residency with us; and Dr. Howard, who arrived in 2004 and assumed the leadership of the nurse-midwifery program upon Dr. Angelini's retirement in 2014. All have been intimately involved in developing our triage unit.

The Women & Infants Hospital Emergency Care Unit provides multidisciplinary, collaborative care for approximately 29,000 patients each year. Certified nurse-midwives, obstetrician/gynecologists, nurses, and social workers, as well as residents in obstetrics and gynecology, family medicine, and emergency medicine, function as a team. The team is valued as a clinical resource locally and as an expert resource nationally in providing emergency obstetric care.

The first edition of this book has been very well received; this new edition adds chapters on acuity tools for triage units and on diagnosis and management of sepsis in triage units. All chapters have been updated and refined in order to cover such recent problems as Zika and Ebola virus infections. Most importantly, the chapters are written by clinicians who confront these various problems every day, working in an emergency care unit as well as in triage. The material is written in easily comprehensible prose, and the book should

be in the pocket of every clinician involved in urgent and emergent visits of obstetrics patients in a triage or emergency setting.

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Preface

Obstetric triage has proliferated as a subspecialty in today's practice setting of obstetrics and gynecology. Many centers are now incorporating separate obstetric triage and emergency care units as part of their overall obstetric services to patients. Pregnant women, many with complex and emergent issues, are evaluated more comprehensively within an obstetric triage unit, which provides a full-spectrum approach to care in one setting, including imaging, laboratory services, specialized providers, and access to consultative services.

Historically, the first edition of this book began with the two editors, who practiced collaboratively in a large obstetric triage facility for two decades, dating back to their initial working relationship as resident and midwife. Over time, they saw the need for a reference/handbook on obstetric triage for new learners as well as clinicians. Their collaborative, interprofessional approach to the book chapters and contributor selection culminated in the first edition of *Obstetric Triage and Emergency Care Protocols*. This text was one of the first books to primarily address obstetric triage content. It subsequently won a book award in 2013 from the *American Journal of Nursing*, placing second in the Maternal–Child Health category.

The rapid growth of obstetric triage, coupled with the success of the first edition of the book, prompted the development of this second edition. New to this edition are two chapters: Sepsis in Pregnancy and Triage Acuity Tools. All prior chapters have been updated—some with new imaging and others with updated national guidelines and recommendations. An added feature of the second edition is the inclusion of clinical pearls in each chapter, highlighting special content and key phrases. In addition, two new associate editors have been added to the second edition to more fully address the expansion of triage content and to direct future editions of this handbook.

The continued use of narrative protocols as the primary format is enhanced in this new edition. The content is again partitioned by timing within pregnancy and by topic. The second edition continues the tradition of being robust in both images and tables. Quick access to the best clinical practices is partitioned by timing in pregnancy. The introductory section expands the overview of triage with new content, updates legal considerations, and presents acuity tools essential in the triage and emergency setting. In the section on early pregnancy (less than viability), new content and images have been added to select chapters and the chapter on periviable obstetric management in the emergent setting has been completely revitalized. The section on obstetric conditions (greater than viability) includes updated content. In the section on management of common obstetric conditions, the chapter on biohazardous

exposures includes information on Ebola, and the chapter on infections now adds data on Zika and other travel-related illnesses. Sepsis has been added as a stand alone chapter, given its increased prevalence in the emergency setting. The section on postpartum complications includes updated guidelines.

This book is geared to the primary provider in obstetric triage, including OB/GYN hospitalists; emergency and family practice physicians; midwives; nurse practitioners; obstetric, emergency, and family practice residents; medical, midwifery, and nurse practitioner students; clinical nurses; radiologists; and others. In handbook and e-book formats, it provides expanded content within an interprofessional approach to clinical conditions in the obstetric triage setting. This second edition offers an easy-to-use print or online resource at the bedside or a consult text at the point of care. We hope you find this book invaluable and informative as you provide care using a best practices approach to obstetric triage and emergency care.

Diane J. Angelini

Donna LaFontaine

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We would like to thank the following people who assisted in bringing the second edition of this book to completion:

- Dr. Liz Lazarus, from the Department of Radiology, at Women & Infants Hospital in Providence, Rhode Island, who supplied multiple images to support each chapter in this book, and without whose assistance we could not have completed this work.
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- Dr. Michael Beninati, Maternal Fetal Medicine Fellow, who assisted in reviewing selected manuscripts.

Overview of Obstetric Triage

Diane J. Angelini and Elisabeth D. Howard

The application of triage concepts to obstetric care is well documented in the literature and in numerous editorials (Angelini, 2006, 2010; Angelini & Howard, 2014; Simpson, 2014). The establishment of obstetric triage units across the United States reflects the growing trend of applying triage principles to the screening and evaluation of obstetric patients. Three of the most common reasons for the development of obstetric triage units in the United States have been (a) decompression of labor and birth settings (which have become burdened by numerous non-labor-related patient evaluations), (b) evaluation of labor complaints specifically when delivery is not imminent, and (c) increased demands placed on the obstetric office setting for full evaluations and workups. A review of the literature and core competencies for OB/GYN hospitalists demonstrates the need for triage assessment and evaluation skills as an essential function for obstetric providers, making obstetric triage one of the most critical perinatal services to emerge in the United States (Angelini & Howard, 2014; McCue et al., 2016). In addition, midwives and advanced practice nurses are care providers at the forefront of obstetric triage practice and services in the United States (Angelini, 2010; Angelini, Stevens, MacDonald, Wiener, & Wieczorek, 2009). In one systematic review of obstetric triage (Angelini & Howard, 2014), key categories within the obstetric literature were noted: legal issues and the Emergency Medical Treatment and Active Labor Act (EMTALA); liability pitfalls; risk stratification; clinical decision aids; utilization, patient flow, and patient satisfaction; interprofessional education and advanced practice roles; and management of selected clinical conditions commonly encountered in the obstetric triage setting. Obstetric triage is clearly part of the fabric of obstetric care and is the gatekeeper for initial assessment and evaluation of labor and other obstetric and nonobstetric complaints of pregnant women.

ESTABLISHMENT OF OBSTETRIC TRIAGE UNITS

The increased demand for evaluating urgent and emergent pregnancy and non-pregnancy-related complaints outside the office setting is a key driver in the need for a unit in which all complaints, including labor assessment, can be fully evaluated. Laboring women are more effectively evaluated in a setting that does not utilize a valuable labor bed, particularly if they are not in active labor. The use of an obstetric triage unit improves patient flow, decreases turnover costs, and increases bed capacity in labor and delivery units, which, in turn, enables women in active labor to receive priority for care. In addition, many

EXHIBIT 1.1

Multiple Functions of Obstetric Triage Units

- Labor assessment and evaluation
- Decompression of labor and delivery
- Use as a holding unit (when labor and delivery is at capacity)
- Fetal evaluation and assessment
- Evaluation of medical and obstetric complaints (often after office/clinic hours)
- Initial stabilization of obstetric complications
- Evaluation of referrals/transfers
- Triaging of telephone calls
- Selected obstetric procedures
- Source of obstetric care when normal source of medical care is inaccessible or unavailable

obstetric triage units with large volume may function as a holding unit until inpatient labor beds become available. In some cases, depending on capacity, women may safely labor in the unit if labor and delivery bed capacity is full.

The obstetric triage unit improves efficiency and utilization of both personnel and bed capacity. Such units manage patient volume so that active labor, minor obstetric complaints, non-obstetric-related issues, and obstetric complications can be screened and assessed outside the labor and delivery setting. Triage can also limit diversions from labor and delivery at a time of high census. Multiple functions of obstetric triage units are noted in Exhibit 1.1.

There is wide diversity in the proximity and location of obstetric triage units. For example, some units connect to labor and delivery, whereas others may be remote. The focus is on the process of triage and not just the location, although location can be critical relative to severe complications and the need to transfer the patient to labor and birth or the operating suite. Process is key, and in one study it was suggested that the successful completion of the process is strongly dependent on provider availability to assess, triage, and discharge pregnant patients in a timely fashion (Zocco, Williams, Longobucco, & Bernstein, 2007).

Staff for obstetric triage units may include OB/GYN physicians and residents, midwives, nurse practitioners, staff nurses, and others. Access to direct imaging and laboratory services, fetal assessment, medical and surgical consultations, and immediate care by an obstetric provider makes such units highly valuable in delivering one-stop, comprehensive, and reliable perinatal services. Obstetric triage may also be a setting where women with nonemergent obstetric and medical conditions present when their usual source of medical care is inaccessible or unavailable (Matteson, Weitzen, LaFontaine, & Phipps, 2008).

OBSTETRIC TRIAGE, ACTIVE LABOR, AND EMTALA

EMTALA, part of the original Federal Omnibus Law of 1985, is responsible for the institution of practice mandates within the emergency medical setting. Originally, the law's intent was to prevent private hospitals from transferring or discharging unstable or indigent patients to public facilities. This federal law governs both emergency medical treatment and evaluation of active

labor (EMTALA Regulations, accessed May 2016). Any hospital that accepts Medicare payments is required to adhere to the EMTALA guidelines. Because pregnant women may seek emergency care at labor and birthing units, as well as obstetric triage units, these locations fall under the requirements outlined by the EMTALA law. An emergency medical condition is defined as one that manifests itself in acute symptoms of sufficient severity that the absence of immediate medical attention could reasonably be expected to result in or pose a threat to the health and safety of a pregnant woman.

In brief, the EMTALA law mandates that medical treatment must be provided at the location such that no deterioration of the pregnant condition is likely to result from or occur during transfer from one facility to another. Furthermore, processes that routinely keep patients waiting so long that they leave against medical advice (AMA) may potentially be viewed as a violation of federal law. The law mandates that all pregnant women presenting to an emergency unit or labor/triage setting have a medical screening examination (MSE). The specific types of health care providers capable of performing this screening examination are noted by EMTALA rules. The EMTALA revisions, effective October 1, 2006, specifically state that a woman experiencing contractions is in true labor unless a physician, certified nurse midwife (CNM), or other qualified medical person acting within his or her scope of practice, as defined in hospital medical staff bylaws and state law, certifies that, after a reasonable period of observation, the woman is determined to be in false labor (EMTALA Regulations, accessed May 2016). Therefore, hospital credentialing and bylaws committees must directly identify the providers deemed qualified to perform the MSE at the individual institution. If nurses are performing any initial labor screening or examination, they must be credentialed by the individual facility and be covered in policies and credentialing with appropriate liability coverage.

The EMTALA enforcement process is governed by the Department of Health and Human Services (DHHS), Centers for Medicare and Medicaid, which has the authority to revoke the status and execute fines to both the facility and/or the individual practitioner. Professional organizations have also published obstetric triage care recommendations. The Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN, 2010) recommends that at least for the initial obstetric triage process, one nurse to one pregnant woman is the appropriate staffing ratio. The RN staffing ratio may adjust to 1 nurse to 2 to 3 pregnant women as maternal and fetal status changes. It is recommended that fetal assessment be included in the initial obstetric triage assessment before the level of care is determined. This is in keeping with guidelines from other national professional organizations as well (American Academy of Pediatrics, & American College of Obstetricians and Gynecologists, 2013). These organizations stress that pregnant patients be evaluated in a timely manner and that components of the comprehensive examination be outlined.

The EMTALA law addresses concerns with emergent care provided to active laboring women. As obstetric triage care continues to evolve, a truly collaborative model is likely to emerge in the obstetric triage setting to ensure that all regulations and recommendations are fully addressed in a timely manner (Angelini et al., 2009; Chagolla, Keats, & Fulton, 2013).

CATEGORIES OF RISK IN OBSTETRIC TRIAGE

Major categories of risk liability in obstetric triage primarily focus on patient safety concerns. In a 25-year review (1985–2010) of 100 closed cases of alleged professional liability against obstetricians and neonatal medicine for causation

of poor outcomes, 21% of the allegations involved failure to triage the pregnant woman appropriately (Muraskas, Ellsworth, Culp, Garbe, & Morrison, 2012). Specifically, these allegations involved the following: failure to follow up on test results, failure to administer appropriate drug therapy, misdiagnosis and triage evaluation errors, women sent home at term in active labor, failure to detect ruptured membranes, failure to rule out abruption, diagnostic difficulties secondary to maternal obesity, and a failure of the triage nurse and/or house staff to present an accurate picture of the case (Muraskas et al., 2012). Given this and other liability concerns in the obstetric triage setting, the following categories of risk are reviewed: assessment in a timely manner, discharge from obstetric triage without evidence of fetal well-being, recognizing active labor, inappropriate and incomplete evaluation or documentation, delay in timely response from consultants, and the use and misuse of clinical handoffs.

Assessment in a Timely Manner

Pregnant women who are contracting need to be assessed ahead of other women who present to the obstetric triage setting with less acute complaints. Women who are contracting and could be in active labor come under the purview of EMTALA regulations. Any pregnant woman complaining of uterine contractions, with a gestational age at or greater than viability, requires emergent assessment. Any written patient care policies surrounding this issue need to remain flexible because strict guidelines open the door to liability if they are not implemented for every patient at every encounter. It may become necessary to initiate communication and advance the chain of command when differences in clinical opinion occur in order to prevent any critical delays in treatment.

In a combined OB/GYN triage unit, pregnant women would be assessed ahead of nonpregnant women with less urgent issues. Pregnant women with decreased fetal movement and those with active bleeding are examples of higher acuity patients, along with women in active labor. Use of available standardized acuity tools, guidelines, and staff training is recommended (American College of Obstetricians and Gynecologists [ACOG], 2016). Pregnant women, with a viable or periviable gestation need to be placed on a fetal monitor and a baseline fetal heart rate tracing obtained. If the fetal tracing is nonreactive or is a non–category 1 tracing, further fetal testing measures will need to be implemented depending on gestational age. Initial intrauterine resuscitative measures can be initiated in the triage setting. Notification of maternal and fetal status to the provider who is ultimately responsible for the patient must occur in a prompt and timely manner. Until the responsible provider is located, it is the responsibility of the obstetric triage staff to initiate an action plan and ensure safe transfer of care.

Discharge From Obstetric Triage Without Evidence of Fetal Well-Being

Two commonly noted obstetric triage liability issues regarding fetal status are failure to adequately assess the fetal heart rate tracing and failure to respond to a non–category 1 tracing. Assessment of the fetal heart rate tracing and subsequent action to address any significant changes within the fetal monitor strip are critical even when a pregnant woman is being evaluated in triage for a different complaint. Discharge documentation in the electronic medical record (EMR) must include assessment of fetal well-being.

The EMTALA law addresses the issue of active labor in the triage setting. According to this law, labor or potential labor represents an emergency medical condition that needs to be assessed by a qualified medical provider (QMP). An MSE is required per EMTALA to determine active labor status, especially if patient transfer becomes necessary.

The EMTALA rules state that a woman experiencing contractions is in true labor, unless it is certified that a woman is in false labor. When a QMP makes the diagnosis that a woman is in false labor, that provider must certify this diagnosis in writing prior to the pregnant woman being discharged. If a nurse is to act as a QMP, it is necessary to be specifically credentialed by his or her institution (e.g., hospital bylaws), and to be within the scope of practice to perform this function per state rules and regulations governing nursing practice. In some situations, telephone consultation between the QMP and the responsible obstetric provider may be necessary prior to discharging the pregnant woman from the triage setting.

Inappropriate and Incomplete Evaluation or Documentation

Access to timely laboratory and imaging results is crucial in the obstetric triage setting, so as not to discharge a pregnant woman who might still have an impending, emergent problem. For example, the two most common reasons for nonobstetric surgical intervention in pregnancy, appendicitis and cholecystitis, can be associated with increased maternal/fetal morbidity (Gilo, Amini, & Landy, 2009). Full documentation of all negative findings and counseling efforts is necessary. In addition, it may be clinically prudent to extend observation when clinical findings are unclear or symptomatology is rapidly changing. Failure to follow up on all test results in the triage setting has been a prior liability concern (Muraskas et al., 2012). Failure to perform and/or document an assessment for ruptured membranes is a common liability risk. When an assessment to evaluate membrane status is inconclusive or if the findings are not confirmed in the setting of a reliable history, the assessment can be repeated. After 1 hour, fluid can repool and the examination can be repeated. All findings must be clearly documented.

Differential diagnoses always include conditions both coincidental to as well as exclusive to the pregnancy. Imaging techniques, such as ultrasound, computed tomography, and magnetic resonance imaging, as well as essential laboratory studies and timely access to consultants, are necessary to complete a full and adequate evaluation and assessment. Full medication reconciliation and counseling are needed to complete each triage visit.

Delay in Timely Response From Consultants

An up-to-date list of available on-call consultants is mandated by EMTALA. Reasons for delay in consultant response time include not conveying a sense of urgency to the consultant, miscommunication issues between parties, or unclear consultative relationships. It is critical to document the call-back time or the number of times it took to obtain a response. Excellent record-keeping is an essential component to avoid violating EMTALA rules. Real-time dashboards can facilitate patient care in a triage setting by serving as a visual reminder to all providers to identify those patients who still need to be seen, how long

patients have been waiting, who is off the unit for testing procedures, and other critical quality metrics in the triage setting.

Use and Misuse of Clinical Handoffs

According to The Joint Commission, communication errors account for the vast majority of preventable adverse outcomes in obstetric care (Elixhauser & Wier, 2011). Avoidable communication errors occur across settings as well as providers, contributing to a number of malpractice claims (Riesenberg et al., 2009). To address this issue, hospitals have developed a range of quality improvement strategies, including teamwork and handoff tools for staff (Landrigan & Lyons, 2012). In 2006, The Joint Commission called for a standardized approach to handoffs through communication with an opportunity to ask and respond to questions (The Joint Commission, 2006). One recommended technique, using the concept of situation, background, assessment, recommendation (SBAR), utilizes a framework for communication among members of the health care team regarding a patient's condition (Bello, Quinn, & Horrell, 2011; Freitag & Carroll, 2011).

Patient handoffs involve the transfer of rights, duties, and obligations from one person or team to another. Optimally, it is performed in a private, respectful environment with minimal distractions, via face-to-face communication with the opportunity to ask questions and achieve clarity. There are reports of an increase in handoff errors when trainees are actively participating in patient care. Errors in judgment, teamwork breakdowns, lack of technical competence, and communication errors (Ong & Coiera, 2011) have been reported during handoffs (Kitch et al., 2008), especially with learners (Singh, Thomas, Peterson, & Studdert, 2007). Another potential source of handoff errors occurs during resident signouts (Angelini et al., 2009; Arora, Kao, Lovinger, Seiden, & Meltzer, 2007). The Accreditation Council for Graduate Medical Education (ACGME) now requires that sponsoring institutions and programs ensure and monitor effective, structured handover processes to facilitate continuity of care and patient safety (Starmer & Landrigan, 2015). The use of the emergency medical record (EMR) is helpful to minimize communication vulnerabilities in handoffs (Kitch et al., 2008). Potential errors that can occur during clinical patient handoffs are noted in Exhibit 1.2.

EXHIBIT 1.2

Errors During Clinical Patient Handoffs in Obstetric Triage

- Errors in judgment
- Teamwork breakdowns
- Medication errors
- Lack of technical competence
- Lack of supervision with handoff difficulties
- Increased errors with trainees
- Misdiagnosis and decision making
- Lack of adequate monitoring of the patient or situation
- Miscommunication and communication breakdowns during intra-hospital transfers
- Lack of communication of critical information

Sources: Adapted from Arora et al. (2007), Kitch et al. (2008), Ong and Coiera (2011), and Singh et al. (2007).

Findings from a quality improvement project initiated at one tertiary care center suggest that a CNM-managed obstetric triage unit can improve satisfaction with care during the triage experience and reduce length of stay (Paul, Jordan, Duty, & Engstrom, 2013). Six items were used to measure patient satisfaction: wait time for provider, information provided, amount of time spent with provider, length of visit, overall care received, and overall triage experience. Patient satisfaction was measured before and after implementation of the CNM-managed care unit in an obstetric triage setting. Increased patient satisfaction was reported in five of the six aspects of care. In a 2010 study looking at women's views of a maternity triage service (Molloy & Mitchell, 2010), most pregnant patients were found to be happy with the amount of time they had to wait in triage. Women were satisfied with the amount of time they spent with the midwife and obstetrician in this study, as well as being treated with respect and dignity, although the triage environment presented some problems (not noted in the study). In a systems analysis of one particular obstetric triage setting, it was suggested that the length of stay is primarily dependent on provider availability to assess, triage, and discharge patients when evaluating length of stay and is less dependent on the use of a specific triage room or standing orders (Zocco et al., 2007).

In one qualitative descriptive study (Evans, Watts, & Gratton, 2015), the satisfaction of pregnant women who presented to an obstetric triage unit was reviewed. Recorded telephone interviews with women were performed immediately following the visit. Five themes emerged relative to patient satisfaction with obstetric triage: the triage unit environment, triage staff attitude and behavior, triage team function, nursing care received in triage, and time spent in triage. Overall results demonstrated that women were very satisfied with obstetric triage services. They appreciated the holistic and caring approach of the nurses, being informed about care for themselves and their pregnancy, and having close surveillance as well as effective teamwork. Access to genuine, caring staff was highly valued. Effective interprofessional collaboration was found to contribute to women's satisfaction, warranting more research regarding interprofessional practice and patient satisfaction in the obstetric triage setting (Evans et al., 2015).

QUALITY-RELATED STRATEGIES IN OBSTETRIC TRIAGE

Quality-related issues in obstetric triage involve reducing excessive waiting times, early recognition of significant clinical events, as well as avoidance of overcrowding and delays. The initial person assessing the pregnant woman in the obstetric triage unit is the gatekeeper, and this is the starting place for information acquisition. The use of scripted guides and standardization of assessment questions offers approaches to ensure appropriate assessment of symptoms. Utilizing standardized screening guidelines, protocols, or checklists are other ways to improve reliability of care at the point of service. Knowing the key questions to ask early on can avoid going down the wrong clinical pathway later. Easy access to appropriate databases and reliable on-call lists can improve the timeliness of care performed at the point of patient entry. Early recognition of events in the waiting area or early in the screening process can avoid treatment delays and ensure timely patient care.

Overcrowding can be common in obstetric triage settings. Early in development, most obstetric triage units were primarily initiated to decompress

the overcrowding associated with labor and delivery units. Yet obstetric triage units can themselves become overcrowded. Having a surge policy to effectively manage overcrowding can be invaluable. An early alert system for potential overcrowding is useful so that contingency plans can be implemented. Use of fast-track rooms and/or observational holding rooms can be effective in managing overcrowding and length of stay as long as care providers are readily accessible (Liu, Hamedani, Brown, Asplin, & Camargo, 2013; Zocco et al., 2007). Diversion, if implemented, can trigger strict EMTALA guidelines. If overcrowding occurs frequently, it must be addressed on an institutional level because it will negatively affect decision making or timing of care. If pregnant women experience prolonged waits as a routine, EMTALA violations could be initiated. When labor beds or antepartum beds are at capacity, obstetric triage can easily back up and experience overcrowding. Communication alerts and processes must be developed to ensure all necessary personnel will be readily available in the event an emergency birth occurs.

Obstetric triage care providers need to be knowledgeable regarding standards of care and best practices and be familiar with the EMTALA law as it applies to pregnant women, especially regarding transfer. Evaluating patient status and disposition on a timely basis and initiating a plan for ongoing observation are critical. Communicating plans among all care providers, especially if working in teams, is necessary to improve safety and decrease errors.

Establishing thresholds for care can be useful. Use of a chain of command/communication policy to resolve disputes at certain thresholds and having an escalation policy available are both good administrative directives. When transporting obstetric triage patients, pertinent transfer documents and the appropriate level of personnel to accompany the patient are needed to effect safe transport and comply with EMTALA regulations.

Audits of sentinel events, use of debriefings, mock sessions/drills, and identification of near misses constitute effective quality measures and strategies. Missed opportunities and good catches are to be incorporated into a standardized quality improvement program for obstetric triage (Mahlmeister, 2006). Strategies to promote interdepartmental collaboration and safe triage practices for pregnant women are best implemented by ongoing communications (Chagolla et al., 2013).

Measures to ensure staff competency and competency maintenance programs need to be initiated, documented, and readily available for any review agencies. A specific method that can both remediate issues as well as maintain staff skill sets is through the use of high-fidelity simulation scenarios. In one example using simulation in labor and delivery, it was noted that nurses were not optimally trained to perform focused assessments with regard to nonobstetric medical emergencies (Hoffman, unpublished data, 2012). Use of an obstetric triage nurse competency program can assist in identifying training issues and standardization of performance (Cook, 2013).

In a systematic review of obstetric triage from 1998 to 2013, a best-practices model for obstetric triage was delineated (Angelini & Howard, 2014). Components within this best-practices model include the following items: use of an acuity or risk stratification scale specific to obstetric triage; standardization of assessments; adequate staffing and personnel; measurement of patient flow via analysis of acuity; use of fast-track units; development of clinical and administrative protocols to limit risk; increased use of collaborative, interprofessional practice models and provider mix; identification of liability pitfalls; use of team training and simulation scenarios; and quality metrics that track acuity, length of stay, and patient satisfaction. Use of these multiple measures can enhance the

overall effectiveness of any obstetric triage unit. These best practices provide the gold standard for measuring quality aspects within obstetric triage.

CLINICAL PEARLS

- Obstetric triage is one of the most critical perinatal services to emerge in the past three decades in the United States.
- The EMTALA law pertains to care provided to women who present to obstetric triage with a complaint of labor.
- Use of a best-practices model for obstetric triage can enhance overall effectiveness of any obstetric triage unit.

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2 *Legal Considerations in Obstetric Triage: EMTALA and HIPAA*

Jan M. Kriebs

A pregnant woman presenting to obstetric triage may have a pregnancy-related problem, a medical condition complicating pregnancy, an injury, or simply be anticipating the birth of a healthy child. The Emergency Medical Treatment and Active Labor Act (EMTALA) of 1986 and the Health Information Portability and Accountability Act (HIPAA) of 1996 specifically address the legal requirements for emergency and labor care. Documentation and follow-up care, as essential components of the triage process, are discussed in the context of legal liability.

EMERGENCY MEDICAL TREATMENT AND ACTIVE LABOR ACT

The requirements placed on institutions by EMTALA are possibly the most critical legal concerns specific to obstetric triage. The law was passed to ensure public access to emergency services including labor and birth care. It prevents discrimination based on financial status, that is, whether one has insurance or the ability to self-pay. The guarantee of care extends only to hospitals that accept Medicare; however, virtually all nonmilitary hospitals in the United States meet that criterion and fall under the statute.

The law applies to every person seeking emergency care in a covered facility. The ability to pay for care does not eliminate a hospital's duty to meet the EMTALA standards (Cohen, 2007). Even if an insurance plan requires that care be received in certain hospitals, other facilities cannot turn someone away on that basis. In practice, any claim of discriminatory care (e.g., based on race, religion, lifestyle choices) may be considered under EMTALA. Further, the law does not decide whether care is for an "emergency" based on the patient's location—labor and delivery, procedure rooms used on an outpatient basis, or any other area associated with the hospital falls under the EMTALA requirements (Zibulewsky, 2001).

The burden of EMTALA falls on the hospital, not the provider (Zibulewsky, 2001). This becomes an issue when community providers cover emergency services in rotation or when providers who are not physicians are the primary caregivers in the emergency department (ED). It is the facility's task to maintain adequate staffing within the limits of the hospital's ability to provide care and to ensure that staff members understand the requirements of EMTALA. The

civil penalty to a hospital for a single negligent violation is $50,000 ($25,000 for hospitals with fewer than 100 beds). In addition, any provider who violates EMTALA may be subject to a civil penalty of $50,000. As Bitterman (2002) points out, the Centers for Medicare and Medicaid Services do not care whether harm has come to a woman, but whether the rules concerning care and transfer have been broken. Repeated violations can lead to the hospital's and/or the provider's exclusion from Medicare and Medicaid participation.

The federal EMTALA law does not take the place of state liability tort laws. Failure to diagnose or treat is a medical malpractice issue. A diagnosis rendered in good faith may be in error, leading to an adverse outcome and legal liability for poor care. Simply failing to identify the cause of emergent symptoms does not fall under EMTALA, unless it can be shown that the individual was not screened in the same way as any other patient (Hughes, 2008). Most courts would recognize failure to follow standard practices related to emergency care as a breach for medical liability (Zuabi, Weiss, & Langdorf, 2016). So, for example, the misdiagnosis of an ectopic pregnancy as a spontaneous abortion will generate a liability claim, but in general, not an EMTALA claim. If no imaging studies were performed to identify the pregnancy status, however, that circumstance would potentially be an EMTALA claim.

EMTALA defines an emergency as any health condition producing acute symptoms (including severe pain or psychiatric problems) or in which the absence of immediate medical attention could lead to severe injury, or jeopardize the health of the individual or of a pregnant woman's fetus. For a woman having contractions, either the inability to transport her safely before the birth or the potential for transport to harm the woman or her fetus invokes EMTALA protection (EMTALA, 1986; Zuabi et al., 2016). The use of an obstetric triage acuity tool, such as the Maternal Fetal Triage Index developed by the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN), can provide evidence that all patients presenting to an emergency setting are appropriately assessed (American College of Obstetricians and Gynecologists Committee on Obstetric Practice, 2016; Ruhl, Scheich, Onopise, & Bingham, 2015).

The essential components of the law include medical evaluation and transfer of care. Any person presenting to an ED; or an obstetric triage unit if that is where pregnant women are evaluated, must receive a medical screening examination (MSE) that goes beyond the initial triage (EMTALA, 1986). The woman must then be treated for the emergency condition, including stabilization prior to transport. Nonemergent conditions are not covered under EMTALA solely because someone has been presented to an ED or obstetric suite. An example would be a woman who chose to come to the ED for treatment of a yeast infection, rather than going to her prenatal clinic for care. In practice, however, many facilities provide initial treatment for routine conditions to expedite treatment and provide for patient satisfaction.

Medical Screening Examination

An MSE is different from triage, which determines in what order or how rapidly an individual must be seen. Although triage initiates care, it does not complete the hospital's duty under EMTALA. The MSE is provided by an appropriate licensed provider and is expected to be similar in all women based on initial complaint. It includes the appropriate tests or procedures to identify conditions suspected based on history and physical examination. This requirement speaks to the benefit of standardizing guidelines for common conditions. Clinical

judgment always plays a role in patient evaluation. The rationale for providing care that is different from the norm must be documented. Excluding tests out of a cost or time concern may expose the hospital to an EMTALA claim. In the case of a pregnant woman presenting for emergency care, a second patient (the fetus) is present in every assessment. Documentation of fetal status and well-being is as essential as documentation of maternal well-being and the absence of true labor.

Only in cases of labor are other health care practitioners (certified nurse midwives) specifically mentioned as appropriate providers of a MSE. When a nonphysician provider is assigned to perform the MSE, then the job description and credentialing documents must clearly reflect the facility's approval of this role. Whether or when a physician is expected to review triage decisions made by a nurse or another provider is ideally defined as part of the institution's policies (Angelini & Howard, 2014).

Emergency Treatment

Following the MSE, a hospital is required to ensure that appropriate care is provided to all outpatients in the emergency unit. There is no national standard for care required by EMTALA. The level of care provided varies depending on the availability of services (Cohen, 2007). For example, a hospital that does not offer obstetric care will transfer the woman who presents with possible preterm labor. Another hospital with obstetric practitioners available will evaluate the same woman, treat, and discharge her home.

Treatment includes the provision of appropriate tests and procedures and the follow-up care mandated by the emergency condition. However, if a woman refuses further care or refuses transport, then the EMTALA criteria for discharge have been met. Necessary documentation includes what treatment was recommended and refused, and that risks and benefits of both treatment and no treatment were explained. Just as with anyone leaving "against medical advice" or AMA, having the woman sign a refusal of treatment is best practice.

Transport

Reasons to transfer include need for a higher level of care, lack of capacity at the transferring hospital, and/or patient request for transport (see Exhibit 2.1 for specific transport criteria). Just as a woman can refuse a transfer and decline further treatment, a woman has the right to request transfer away from a facility before stabilizing treatment. This regulation is found at 42 CFR 489.24(e)(1)(ii)(A) (EMTALA.com, 2011).

Under EMTALA, transports must be "appropriate"; that is, the medical benefits have to outweigh the risks. For example, the woman must be stable for transport (e.g., not in active labor) or the danger of remaining in the original location must be greater than the risk of giving birth in an ambulance. The decision that transport is necessary rests with the referring physician, not the receiving physician. As long as the receiving hospital can provide the needed services and has the space to do so, it is obligated under the law to accept transfers. The complete available records from the transporting hospital are to travel with the woman. As long as the emergency condition persists, EMTALA dictates the procedures required. Financial concerns cannot overrule the need for transfer.

EXHIBIT 2.1

Requirements for Transport Under the Emergency Medical Treatment and Active Labor Act (EMTALA)

- Medical screening examination (MSE)
- Stabilization within the abilities of transferring facility
- Need for services not available at transferring facility or medical benefits of transport outweigh risks or patient/responsible person requests transfer
- Contact with receiving hospital to approve/accept transport
- Written certification by physician of need
- Records sent with the patient
- Appropriate method of transport used

Source: EMTALA.com (1986).

Transfer, particularly of an unstable patient, requires documentation of the patient's condition, transfer requirements, and certification that the provider has counseled the woman appropriately (see Exhibit 2.2 for an example of an EMTALA transfer form).

Labor and Birth

Labor is a special case under EMTALA, with a definition that runs counter to both the original title of the act and standard obstetric practice. As defined by EMTALA, labor means the process of childbirth beginning with the latent or early phase of labor and continuing through the delivery of the placenta. A woman experiencing contractions is in true labor unless a physician, certified nurse midwife, or other qualified medical person acting within the scope of practice, as defined in hospital medical staff bylaws and state law, certifies that, after a reasonable time of observation, the woman is in false labor (EMTALA, 1986).

No reference is made to any other specific condition in the law. In the case of childbirth, care to stabilize or resolve (i.e., deliver) the pregnancy is required. Although latent labor is not "false" in a medical sense, a difficulty in interpreting EMTALA arises because the language used in the law is not the same as that used by health care practitioners. Because the law defines labor as the onset of contractions and refers to latent labor, the individual providing the MSE must be able to justify the decision to discharge. A woman with two prior cesarean sections and preterm contractions may need to be admitted as unstable for discharge (or transported to a facility with more appropriate obstetric services), whereas a primigravida at term with the same pelvic examination might not. The normal variation in labor progress and a host of contributing factors—parity, prior surgeries, contraction pattern, fetal well-being, even social factors that might hinder ability to return—make it imperative that the discharge note clearly states the rationale for deciding that a woman is not in active labor. As interpretations of active labor have changed to address the patterns commonly seen today, care is required to avoid discharging women inappropriately. While slow labor progress has been demonstrated to persist

until 5 to 6 cm (Zhang et al., 2010), and 6 cm may be considered an appropriate time for admission to the labor floor, this cannot be used as a blanket justification for turning women away.

EXHIBIT 2.2

Emergency Medical Treatment and Active Labor Act (EMTALA) Transfer Form

Women & Infants Hospital

EMTALA Physician Assessment and Certification

Patient Condition

1. _____ The patient has been stabilized such that, within reasonable medical probability, no material deterioration of the patient's condition or the condition of the unborn child(ren) is likely to result from transfer.
2. _____ The patient's condition has not stabilized.
3. _____ The patient is in labor.

Transfer Requirements

1. _____ The receiving facility, _____, has available space and qualified personnel for treatment as acknowledged by: _____.
2. _____ The receiving facility has agreed to accept transfer and to provide appropriate medical treatment as acknowledged by: _____ _____.
3. _____ Appropriate medical records of the examination and treatment of the patient are provided at the time of transfer.
4. _____ The patient will be transferred by qualified personnel and transportation equipment as required, including the use of necessary and medically appropriate life support measures.

Provider Certification

I have examined the patient and explained the following risks and benefits of being transferred/refusing transfer to the patient:

_____
_____
_____

Based on these reasonable risks and benefits to the patient and/or newborn child(ren), and based upon the information available at the time of the patient's examination, I certify that the medical benefits reasonably to be expected from the provision of appropriate medical treatment at another medical facility outweigh the increased risks, if any, to the individual's medical condition from effecting the transfer.

_____	_____	_____
Signature of physician or other qualified medical person	**Date**	**Title**

Source: Courtesy of Women & Infants Hospital, Providence, Rhode Island.

Common Allegations Under EMTALA

Fourteen categories have been identified under which EMTALA claims can be brought. They range from failure to screen or physician refusal to evaluate for an emergency condition to inability to pay (the original cause for the law), to inappropriate transfers and refusal to accept transfers. The two that most commonly result in fines or penalties to a hospital are failure to provide screening or stabilization, while issues related to women in labor were less common (Zuabi et al., 2016). Examples of claims that are specific to obstetric cases under EMTALA are transfer of an unstable labor patient and failure to evaluate both mother and fetus (Simpson & Knox, 2003; Zuabi et al., 2016). Delivery en route to a transport facility is regarded as evidence that the woman may have been in active labor and thus unstable at the time of transport (Centers for Medicare and Medicaid Services, 2015).

Record Keeping and Patient Follow-Up

After the emergency is resolved, information needs to flow back to a woman's primary provider. The "long, fragile feedback loops" that come into play whenever multiple institutions or providers are involved in care can lead to failures in diagnosis and timely treatment of complications (Gandhi & Lee, 2010). New or altered medications, referrals, and pending results all can be lost when communication is not ensured. One study found that as many as 41% of discharged patients had pending tests and that neither the ordering provider nor the primary care provider were aware of significant findings (Roy et al., 2005). About 30 times as many outpatient visits as hospital discharges occur each year, and errors in diagnosis, often discovered after discharge, are the primary cause of paid liability claims in outpatient care (Bishop, Ryan, & Casalino, 2011).

EMTALA and Risk Reduction

Facilities can reduce the risk of an EMTALA violation by having the policies and documents in place that reinforce the requirements. Among the recommendations of Glass, Rebstock, and Handberg (2004) are: having a multidisciplinary educational curriculum for all affected areas (ED, obstetric triage); reviewing policies/protocols to ensure that performance of the MSE is performed by appropriately trained personnel; using templates for transfer documentation; and maintaining transfer and discharge records. The development of guidelines and criteria specific to the evaluation of common obstetric events can help ensure that the same level of care is offered for each woman. As Simpson and Knox have noted, the presence of evidence-based guidelines coupled with an approach that prioritizes patient safety over quickly seeing numbers of patients can limit liability, whether pertaining to liability under EMTALA or legal risk in general (Simpson & Knox, 2003). In addition, obstetric triage settings need firm policies and protocols for communication to both patient and provider and tracking logs for pending test results at transfer or discharge. The AWHONN Maternal–Fetal Triage Index is an additional tool.

HEALTH INFORMATION PORTABILITY AND ACCOUNTABILITY ACT

While EMTALA is emergency specific, the HIPAA applies to all clinical encounters. The Act sets a balance between protection of privacy and provision of

quality care (HIPAA, 1996). The Act includes both the Privacy Rule, discussed here, and the Security Rule, which addresses confidentiality of electronic health records. Given the variety of settings in which obstetric triage may occur, and the likelihood that information from a triage visit will be transmitted to others for continued care, the requirements of HIPAA often affect the process.

HIPAA requires that patient privacy be maintained. As Annas (2003) has pointed out, HIPAA is a complex way to apply basic privacy doctrine to modern health care and ensure that only the necessary minimum of information is released to accomplish any purpose. Examples of times when HIPAA can be violated inadvertently include elevator conversations, signing in at reception, or telephone scheduling. Speaking softly or not at all in public areas, keeping records out of casual view, not shouting out information, and moving the central board or monitor with identifying information out of sight are all obvious ways to provide privacy. But triage areas are more likely than most settings to offer minimal protection against overheard discussions. It is important to be conscious of possible listeners when asking the woman or family sensitive questions.

Disclosure of Health Information

Protected health information (PHI) covered under HIPAA includes both medical and financial records. Psychiatric records have separate requirements from general medical care. In the context of emergent care, the ability to obtain records from prior providers and to relay information back to the appropriate primary site directly affects the quality of care. HIPAA specifically permits this exchange of information without written consent to facilitate quality care, such as with specialist consultation or care of a woman arriving at a clinical site different from the location of her usual care (Department of Health and Human Services [DHHS], 2011). However, some facilities may require written consent before they will release records. The decision to require formal consent, but not the choice whether to provide records, is the prerogative of the facility or provider.

There are times when PHI can be disclosed with informal consent or when the woman's consent is not required. Informal consent occurs when a family member, friend, or other individual is present during a conversation, and the patient declines an offer of privacy or does not ask for privacy. When a woman goes to cesarean section emergently and a family member is in the waiting room, the provider can safely give information without violating HIPAA. However, the "friend" who calls to ask if someone has arrived has a limited right to knowledge about the woman, and staff must be careful to limit phone information to that published in the hospital directory (DHHS, 2011). Informal consent to disclosure also covers activities such as a woman requesting that a brother pick up a prescription. By sending him to the pharmacy, she consented to the disclosure of information. Professional judgment is the deciding factor about what information to release in these cases. Individual facilities may decide to have more stringent requirements, such as written consent for disclosure of information to family members.

In addition to the specific concerns of minors who are receiving reproductive care, young adults covered until age 26 on a parental plan and women covered by a partner's plan may find that confidentiality under HIPAA is limited. According to data provided by the Kaiser Family Foundation, 27% of reproductive age women are considered dependents (Gold, 2013). In many cases, explanation of benefits (EOB) forms generated after every insurance-covered encounter is sent only to the policy holder, and PHI may be inadvertently revealed. While the Privacy Rule permits individuals to request that information not be revealed,

this request has to be made of the insurer to cover EOB, and not all may comply. The reason cited is the need to be accountable for deductible limits. Many states are working to clarify and strengthen protections for adolescent and adult women covered as dependents (Andrews, 2016). When women express concerns about the release of information to others, a reminder to speak with their insurer is warranted.

Electronic Media and HIPAA

Communications between providers, or between a provider and a friend or colleague from another setting, can also lead to serious HIPAA violations. Even if e-mail messages are used within an institution as a common method of relaying information about care, consideration must be given to the security of the system and to the specific content of the message. It is the institution's responsibility to set standards to which individuals are required to adhere. For example, using a home e-mail address to send updates to practice partners is inherently less safe than using a hospital system limited to staff. Staying within the facility's firewall does not guarantee confidentiality but lessens the chance of accidentally releasing PHI. Using attachments to send information, password protection, and encrypting documents are ways to decrease the risk of unintended violations of HIPAA (DHHS, 2011).

The proliferation of social media, blogs, electronic discussion lists, and other general access communication forums have led to increased risks of an unconsidered release of PHI. Many factors contribute to violations of patient privacy. These include beliefs that a posting or communication is private, that deleted comments cannot be retrieved, that limited disclosure to an intended recipient is harmless, or that the use of nonspecific identifiers is adequate to maintain confidentiality. Other issues are failure to refrain from sharing information other than for a health care–related need, and the ease of posting combined with the commonplace sharing of personal information on social media (Cronquist & Spector, 2011).

In fact, virtually any posting or e-mail can be forwarded, copied and resent, retrieved by a webmaster, and used as evidence of publication of PHI. Investigations by a state licensing board, workplace discipline/firing, a federal HIPAA investigation, or a liability suit sound like extreme responses to a casual online comment or photo posting, but may be the legitimate response to an electronic disclosure (Hader & Brown, 2010; Spector & Kappel, 2012).

Care of the Adolescent

The care of adolescent women raises confidentiality issues that go beyond the scope of HIPAA. Adolescent women's right to confidentiality is governed by a complex of state and federal laws, Title X, Medicaid, HIPAA, and court cases. HIPAA generally defers to state requirements for parental disclosure, consent to care, access to medical records, and the like (Annas, 2003; English & Ford, 2004). Parents are able to access their minor child's records with three exceptions, which are: the minor has given consent for care, and parental consent is not required by state law; the minor's care is obtained at the direction of the court or someone appointed by the court; or the parent has agreed to a confidential relationship between the child and provider within the limits of that agreement (DHHS, 2011).

Reproductive health care is often considered a special case, again with differing requirements by jurisdiction. Both adolescents and their parents may be unclear on the issues of confidentiality. Minor consent laws are based on either status (e.g., pregnancy) or specific area of care (e.g., mental health; Berlin & Bravender, 2009). Each individual should be aware of jurisdictional requirements relating to adolescent care. Accessing confidential care is difficult enough for teens—knowing what can be promised can prevent later conflicts and loss of trust.

CLINICAL PEARLS

- The EMTALA law was passed to ensure public access to emergency services, including labor and birth care.
- Utilization of evidence-based guidelines, coupled with an approach that prioritizes patient safety over rapid turnaround time, will limit liability.
- In emergency settings, HIPAA specifically permits the exchange of information without written consent to facilitate quality care.

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3 Triage Acuity Tools

Suzanne McMurtry Baird and Nan H. Troiano

Triage, in the context of health care, involves the process of determining the priority of patient care based on urgency of treatment and is associated with emergency and disaster services (Evans, Watts, & Gratton, 2015; McBrien, 2009). Prior to 1986, the concept of obstetric triage was not well defined. At that time, the initial patient contact with a health care provider was often by telephone, resulting in evaluation and management without initial presentation to a health care facility (Sandy, Kaminski, Simhan, & Beigi, 2016). Pregnant women who presented to a health care facility were generally assessed and treated on a "first come, first served" basis. Beginning in 1986, obstetric triage began to develop into a specialized segment of care for both outpatient and eventual inpatient care.

Since that time, there has been an evolution in triage services within obstetrics. In 2014, Angelini and Howard published the results of a systematic review of the literature on obstetric triage over a 15-year period (Angelini & Howard, 2014). From their review, seven key categories were identified, and best practices were developed for obstetric triage that can be used to guide clinical practice as well as further research. One of these categories involves the use of a triage acuity tool to determine risk stratification. Not only is determination of acuity essential for safe, effective prioritization of patient care, but it is also used to allocate resources.

Prior to 2007, there were no published obstetric triage acuity tools. For this reason, standard emergency department (ED) acuity tools were utilized in some obstetric triage settings (Angelini & Howard, 2014; Paisley, Wallace, & DuRant, 2011; Zocco, Williams, Longobucco, & Bernstein, 2007). Recently developed and validated obstetric triage acuity tools may improve the quality and efficiency of care, guide resource allocation, and serve as a template for use in individual hospital obstetric units (American College of Obstetricians and Gynecologists [ACOG], 2016). Acuity tools commonly used in an ED setting as well as tools specific to obstetrics are described and compared in this chapter. General goals of acuity tools are (a) prioritized care for higher acuity patients, (b) expedited assessment and management of the unstable woman, (c) efficient utilization of resources, and (d) improved communication of the health care team.

EMERGENCY DEPARTMENT ACUITY TOOLS

Triage acuity tools frequently used in the ED setting include the Emergency Severity Index (ESI) and the Canadian Triage and Acuity Scale (CTAS). A brief review of ED acuity tools follows.

The purpose of triage in the ED is to prioritize incoming patients and to identify those who cannot wait to be seen. The process involves a brief, focused assessment and assigns the patient a triage acuity level, which is a proxy measure of how long an individual patient can safely wait for a medical screening examination (MSE) and treatment. In 2009, the Centers for Disease Control and Prevention (CDC) reported 136.1 million visits to EDs in the United States (Hing & Bhuiya, 2012). Mean wait time to see a health care provider in EDs increased compared to data from the previous year. The Institute of Medicine (IOM) published a landmark report that described the worsening crisis of crowding that occurs daily in most EDs (Institute of Medicine of the National Academies [IMNA], 2006). With more patients waiting longer in the ED waiting room, development and use of an accurate triage acuity level was determined to be a critical process improvement strategy.

Based on expert consensus of available evidence at the time, the Board of Directors of the American College of Emergency Physicians (ACEP) and the Emergency Nurses Association (ENA) drafted an initial position statement that asserted the belief that the quality of patient care would benefit from implementation of a standardized ED triage scale and acuity categorization process (ENA, 2003). Subsequent recommendations included the use by EDs of either the ESI or the CTAS, both of which had established reliability and validity (Fernandes et al., 2005). In 2010, the ACEP and ENA supported the adoption of a reliable, valid five-level triage scale such as the ESI (ACEP, 2010). Since the adoption of this position statement, the number of EDs using other three-level triage systems has decreased, and the number of EDs using the five-level ESI triage system has increased significantly (McHugh & Tanabe, 2011).

The ESI is a five-level triage scale developed by ED physicians Richard Wuerz and David Eitel (Wuerz, Milne, Eitel, Travers, & Gilboy, 2000). The ESI was developed around a new conceptual model of ED triage. In addition to asking which patient is seen first, triage nurses use the ESI to consider what resources are necessary to move the patient to a final disposition (admission, discharge, or transfer). The tool retains the traditional foundation of initially evaluating patient urgency and then seeks to maximize patient streaming: getting the right patient to the right resources at the right place and the right time. Initially implemented in 1999, the tool is now in its fourth version and continues to be endorsed by the Agency for Healthcare Research and Quality for use in ED settings (Gilboy, Tanabe, Travers, & Rosenau, 2012).

As previously described, five ESI levels are specified, with level one indicating the greatest urgency. The levels are:

1. Resuscitation
2. Emergent
3. Urgent
4. Less Urgent
5. Nonurgent

The ESI algorithm identifies four decision points to sort patients into one of the five triage levels. The decision points address the following questions (Gilboy et al., 2012): (a) Does the patient require immediate life-saving intervention? (b) Can the patient wait? (c) How many resources will the patient need? and (d) What are the patient's vital signs? Triage with the ESI algorithm requires an experienced ED nurse. With practice, the triage nurse can rapidly move from

one ESI decision point to the next. The ESI has been translated into several languages and evaluated for reliability and validity. The most current version includes recommendations for the triage of pediatric patients.

The ESI has been implemented by hospitals in different regions of the country, by university and community hospitals, and by teaching and nonteaching facilities. One benefit of the ESI is the rapid identification of patients that need immediate attention. Other benefits include determination of those patients that do not need to be seen in the main ED and those who can safely and more efficiently be seen in a fast-track or urgent care area. It has also been used as the foundation for ED policies that address specific populations. The ESI does not address obstetrics and has not been studied with respect to the pregnant population.

Canadian Triage and Acuity Scale

The CTAS, developed by a group of Canadian emergency physicians, has been endorsed by the National Emergency Nurses' Affiliation, Inc. (NENA) and the Canadian Association for Emergency Physicians (CAEP) as the national standard for ED triage (Beveridge & Ducharme, 1997; CAEP, 2002). Like the ESI, it is a five-level triage acuity tool. The levels are numbered one through five, with level one indicating the greatest urgency (1. Resuscitation, 2. Emergent, 3. Urgent, 4. Less Urgent, and 5. Nonurgent). Unlike the ESI, the underlying assumption of the CTAS is that the purpose of triage is to determine how long the patient can wait for care in the ED. Clear definitions of time to physician evaluation are an integral component of the CTAS algorithm. The ESI does not define expected time intervals to physician evaluation.

Canadian and American researchers directly compared the interrater reliability of the CTAS and the ESI in a randomized trial (Worster et al., 2004). Excellent interrater reliability was demonstrated by both groups.

HEALTH ACUITY TOOLS IN OBSTETRIC/WOMEN'S HEALTH

With the expansion of obstetric triage practice in many institutions and inconsistencies in clinical practice, there is a need for specific acuity tools that address the most common emergent and nonemergent complaints in pregnancy (Scheich & Bingham, 2015). Currently, three obstetric-specific triage acuity tools have been described in the literature, each of which is outlined here. Owing to the diversity of obstetric presentation, differences in scope of practice in obstetric triage units, variations in clinical processes for MSE, contrasts in qualified medical provider (QMP) skill set, and the specialized needs of the obstetric patient, any tool requires individualization and adaptation for use in each clinical agency based on identified scope of service.

Florida Hospital System

An interprofessional team at the Florida Hospital System (FHS) developed and published the first obstetric-specific acuity tool after identifying variations in triage practices across a multicampus hospital system (Paisley et al., 2011). Inconsistent practices surveyed included nursing assessments on a "first come, first served" basis, assignment of the CTAS acuity score after the MSE instead of after initial brief assessment, inconsistent assignment of acuity in women

with similar complaints, and determination that the existing acuity tool (CTAS) was nonspecific for obstetrics. During the team's initial step of the quality improvement (QI) project, the literature search revealed no obstetric-specific acuity tools. The literature focused on MSE requirements, provider roles and qualifications, regulatory requirements, review articles, and individual hospital practices (Paisley et al., 2011).

This obstetric acuity tool, by Paisley et al., was developed with a format similar to the five-tiered, "complaint-oriented" CTAS. The five categories of acuity were color coded with an operational timed goal from acuity assignment to MSE. The categories were (1) Immediate (red), (2) Urgent–within 15 minutes (purple), (3) Semiurgent–within 30 minutes (yellow), (4) Less Urgent–within 60 minutes (green), and (5) Procedure/Testing–less than or equal to 120 minutes (gray). In addition to the acuity tool, the team developed a standardized process to improve consistency in practice. The primary goals included an obstetric nurse initial assessment within 10 minutes of arrival and acuity score assignment to determine priority of care. Data collected after the initial education and implementation focused on time parameters for arrival to unit, acuity assignment, and time of MSE. After reviewing the recorded data and observing the obstetric nurses in the clinical area, several conclusions were drawn. First, it was determined that nurses were not assigning the acuity score until after the MSE and not differentiating the timing of arrival and acuity assignment. Second, time of the MSE was documented as the time when the electronic fetal monitor (EFM) was applied. In addition, interrater reliability of the tool was lacking. Once these determinations were made, additional education and changes to the hospital system electronic medical record (EMR) were completed to enhance the process. These changes allowed for data collection to include time interval from arrival to interview with a triage nurse (to measure the less-than-10-minute requirement), reliability of acuity assignment, and time of MSE initiation.

In the four FHS obstetric triage units, there were 18,936 triage visits in the 17 months of the project. The majority of acuity levels utilizing the FHS tool were assigned at levels 2 and 3 (83%). In addition, 96% of the women had initial screening by a RN and acuity assignment within 10 minutes. However, time to assessment by a QMP for women assigned an acuity level of 2 or 3 did not decrease. Barriers to compliance for the FHS tool included staffing levels and delayed test results that impacted patient flow out of triage (Paisley et al., 2011).

Limitations of this tool included the lack of described interrater reliability, the number of hospitals for implementation (four) within the same hospital system, absence of implementation within a teaching or tertiary care environment, and lack of variation in systems and processes for QMP assessment (staff RN only). In addition, there were no data regarding patient flow from triage. Therefore, the authors concluded that even though the process worked well in this hospital system, it was not known whether this tool would be successful in other hospital settings (Paisley et al., 2011).

Obstetrical Triage Acuity Scale (OTAS)

The OTAS is a color-coded, five-category acuity tool (1. Resuscitative, 2. Emergent, 3. Urgent, 4. Less Urgent, 5. Nonurgent) developed by an interprofessional team and implemented at the London Health Sciences Center. It was the first obstetric triage acuity tool with demonstrated reliability and validity. London Sciences Center is a tertiary care center in Southwestern Ontario and

averages over 11,500 triage visits and 5,800 births per year with a referral catchment from the southwest region of Ontario. The obstetric triage scope of service includes urgent and emergent care after 20 weeks gestation. The first OTAS was modeled after the CTAS and included a comprehensive list of obstetric-specific complaints organized into categories of patient signs and symptoms, such as labor/fluid loss, hypertensive, neurologic, and respiratory. The tool also embeds suggested response of time to initial assessment and provider attendance for each acuity level. The OTAS was first implemented in 2012 by a group of triage nurses designated as "OTAS Champions." Compliance with utilization was greater than 90% and the tool evaluated with excellent interrater reliability. In addition, the study showed a correlation between higher acuity and hospital admission to the antepartum or birthing unit (Smithson et al., 2013).

In a follow-up study of the OTAS, interrater reliability at London Health Sciences Center was compared to that in two community hospital settings and showed no significant differences. Intrarater reliability was determined with retesting at 9 months. To test the validity of the OTAS, the study also examined correlation of acuity with hospital resource utilization of laboratory investigations (routine and second-order labs) and performance of point-of-care ultrasound. Data indicated a significant correlation between acuity level and laboratory evaluations, both routine and second-order labs, and point-of-care ultrasound. Additional findings showed acuity level correlation with nursing workload of intensive observation and assessment, as well as health care provider attendance, which may be utilized for resource allocation (Gratton et al., 2016).

The 2016 publication also included revisions to the OTAS based on feedback and consensus from the National Obstetric Triage Working Group in Canada. The revised tool aligned the color-coding system with changes made to the CTAS, clarified respiratory complaints (mild, moderate, and severe), with additional categories of pain, abdominal trauma, infection, substance use, mental health, and hemodynamic acuity modifiers. Included in the hemodynamic stability category were vital sign parameters adapted from the Maternal Early Warning Criteria (Mhyre et al., 2014) and Modified Early Obstetric Warning System (Singh, McGlennan, England, & Simons, 2012) that would influence determination of acuity (Gratton et al., 2016).

Even though utilization of the OTAS decreased the overall length of stay by 3.9%, additional data analysis was completed to determine whether there was a relationship between acuity level assignment and length of stay. It was determined that the longest length of stay was OTAS 2, followed by OTAS 4 and 5. The shortest length of stay was OTAS 3, indicating poor correlation between OTAS 2 through 5. To improve efficiency of patient flow, a fast-track area within the triage unit was proposed on the basis of data from a simulation modeling computer program. Following conversion of space and implementation of a fast-track area for lower acuity women, overall length of stay dropped another 3% and improved the correlation between acuity and length of stay (Smithson, Twohey, Watts, & Gratton, 2016).

Maternal Fetal Triage Index (MFTI)

The MFTI was developed by an expert task force for the Association of Women's Health, Obstetric, and Neonatal Nursing (AWHONN) organization with an overall objective of creating a standardized tool for obstetric triage. The tool was published in 2015 after extensive interprofessional content validation and interrater reliability. Content validity was performed in two rounds by practicing

clinicians from across the United States, including 15 registered nurses, 15 certified nurse midwives, and 15 physicians (Ruhl, Scheich, Onokpise, & Bingham, 2015a). An observational study provided data for interrater reliability in a large suburban hospital (Ruhl, Scheich, Onokpise, & Bingham, 2015b). The overall goals of the MFTI program were improvement in the quality and efficiency of nursing care with utilization of a standardized tool, increased nursing knowledge and awareness of triage, and improvement in communication among the obstetric team (Ruhl et al., 2015a).

The MFTI is a five-tiered acuity index based on a brief nursing assessment of vital signs, gestational age, pain, fetal movement, and patient complaint. Key nursing questions are then applied to determine the priority level: (1) Stat, (2) Urgent, (3) Prompt, (4) Nonurgent, and (5) Scheduled or Requesting a Service. Examples of clinical conditions that correspond to each level are provided in the algorithm. The MFTI includes abnormal maternal vital signs and fetal heart rate parameters in levels 1, 2, and 3. If the woman presents with complaints of labor, pain is evaluated by "coping/not coping" to facilitate management of the woman who is not coping with labor. Otherwise, pain is assessed using the 0 to 10 scale (Ruhl et al., 2015a).

The MFTI is unique in providing key prompt questions for the triage RN. For example, when the triage RN makes a determination of acuity level 2 (Urgent), the RN is prompted to question the need for transfer of the woman to a higher level of care than the current institution can provide. Another prompt included is when a woman presents for a scheduled procedure/testing, the nurse asks a key question to determine whether the woman's condition has changed or whether she has a new complaint in order to expedite evaluation. Suggested timelines for evaluation are not included in the MFTI to encourage each institution to determine its process goals. Currently, the MFTI is being piloted by numerous hospitals throughout the United States in order to identify barriers to implementation in clinical practice and the EMR and to provide feedback for systems support strategies and education tools (Ruhl et al., 2015a).

COMPARISION OF OBSTETRIC-SPECIFIC TOOLS

The obstetric-specific acuity tools have similar processes from patient presentation to MSE by a QMP. Figure 3.1 illustrates the general process.

Factors that may consistently affect compliance with triage acuity tools include adequate staffing, nursing skill sets, clear guidelines, protocols, medical

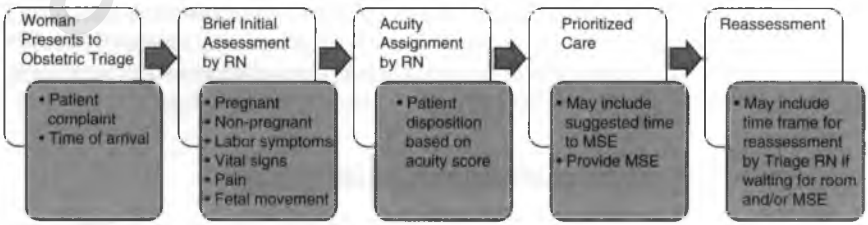

Figure 3.1 Triage acuity process

MSE, medical screening examination.

Sources: Adapted from Gratton et al. (2016); Paisley et al. (2011); Ruhl et al. (2015a, 2015b), Smithson et al. (2013).

bylaw designation regarding QMP examination, training, education, environment, bed availability, EMR, and patient disposition off the unit. Compliance in utilization of the tool may be driven by a low census. For example, some nurses may not see the need for acuity assignment if there is bed availability and only one patient in triage. However, consistent assignment allows for data tracking of patient complaints, assigned acuity trends, patient assessment and flow, and processes in triage that may be utilized to plan staffing (e.g., number, days of week, hours of day) and improve resource utilization. In addition, consistent use may facilitate nurse-to-provider communication (Ruhl et al., 2015a).

In general, there is an increasing complexity of the obstetric-specific tools. None of the tools encompassed gynecology or women's health general complaints, which may require adaptation for triage units in a dedicated women's hospital or women's ED setting. All of the current obstetric-specific triage tools utilize "complaint-oriented triage" and have five levels of priority, with color representation for each level. However, there are differences in terminology and level color coding that is determined on the basis of hospital ED system and/or national color code recommendations. Implementation of each triage acuity tool began with extensive education based on case scenario presentation and acuity assignment.

The OTAS and MFTI use acuity modifiers such as abnormal vital signs or fetal parameters as determinants of priority of acuity level. In regard to suggested assessment time frames (e.g., time from arrival, acuity assignment, and MSE), OTAS and Florida Hospital have identically defined time parameters. However, the time frame for required reassessment by the triage RN occurs less often with decreased acuity in the OTAS tool. Both tools noted that the time frames were suggested operational parameters and were not dictating standard of care. The MFTI tool did not define time to MSE, but instead urged hospitals to define it.

Reliability and validity are two fundamental principles of the scientific method. Interrater reliability was shown in the OTAS and MFTI tools by having different nurses rate the same patient scenarios and generate the same results. Intrarater reliability was reported in the OTAS study by retesting the same nurses at a later date and labeling the patient scenarios with the same acuity levels. Validity, the accuracy of the rating system, was demonstrated in the OTAS and MFTI tools. These findings reinforce acceptance of these tools for use in other facilities.

Even with utilization of an acuity tool to facilitate timely assessment, it is important to consider patient-centered care concepts. These include keeping the woman informed of progress or delays, completing a follow-up assessment to make sure the woman's status has not changed, and reassurance to calm/alleviate fear and anxiety (Gilboy et al., 2012). All of the obstetric-specific acuity tools have recommendations for reassessment, but differ on time frames. Table 3.1 provides a comparison of each obstetric acuity tool.

CONCLUSIONS

An obstetric-specific triage acuity tool is recommended to standardize and prioritize care for women with urgent needs. Even though the pregnant woman presents with unique needs, terminology and color codes for triage prioritization are coordinated within each hospital for similar processes in all units. With the evolution and complexity of triage in the obstetric population, it is recommended that all obstetric services implement an acuity tool for triage of pregnant women.

Table 3.1 Comparison of Obstetric Acuity Tools

OBSTETRIC ACUITY TOOL	SETTING	METHODOLOGY	KEY FINDINGS/HIGHLIGHTS
FHS	Four community hospitals within a U.S. health system	QI project	• Process improvement for initial assessment by a RN and acuity score assignment for prioritized triage within 10 minutes • First published obstetric-specific acuity tool • Validity and reliability not reported
National Obstetric Triage Working Group in Canada OTAS	London Health Sciences Center; tertiary care center in Ontario, Canada	Scale development; content validity, interrater reliability, and intrarater reliability demonstrated	• Modeled after the Canadian Triage Acuity Scale • Correlation between higher acuity scores and hospital admission, lab, and ultrasound testing • Higher acuity scores associated with increased resource allocation (nursing, providers) • Utilization decreased length of stay
AWHONN MFTI	Community hospital in United States	Content validation and interrater reliability demonstrated	• Triage algorithm based on vital signs and presenting complaint • Utilizes nursing prompt questions, including need for transfer to a higher level of care

AWHONN, Association of Women's Health, Obstetric, and Neonatal Nursing; FHS, Florida Hospital System; MFTI, Maternal Fetal Triage Index; OTAS, Obstetrical Triage Acuity Scale; QI, quality improvement.

Sources: Gratton et al. (2016); Paisley et al. (2011); Ruhl et al. (2015a, 2015b); Smithson et al. (2013).

CLINICAL PEARLS

- Recommendations for a best-practices model include use of an acuity scale specific to obstetric triage.
- Owing to the diversity of obstetric presentation, variations in clinical processes for MSE, and contrasts in QMP skill set, any obstetric triage acuity tool requires adaptation for use in each clinical agency.
- Factors that may consistently affect compliance with triage acuity tools include adequate staffing, nursing skill set, clear guidelines, protocols, medical bylaw designation regarding QMP examination, training, education, environment, bed availability, EMR, and patient disposition off the unit.

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Ectopic Pregnancy

Roxanne Vrees

Ectopic pregnancy, which refers to the implantation of a fertilized ovum outside the endometrial cavity, is a potentially life-threatening condition affecting women worldwide. The true incidence of ectopic pregnancy is difficult to estimate because the majority of patients are treated in an ambulatory setting. Available data in the United States classify approximately 1% to 2% of pregnancies as ectopic, with an attributed 3% to 4% rate of pregnancy-related death (Centers for Disease Control and Prevention [CDC], 2003). Ectopic pregnancy mortality rates steadily declined during the latter portion of the 20th century and remained stable through 2008 at 0.5 deaths per 1,000 pregnancies (Creanga et al., 2011). These improved survival outcomes were due largely to earlier diagnosis alongside improved treatment modalities. However, despite earlier detection in conjunction with successful outpatient medical management, ectopic pregnancy continues to remain the leading cause of maternal death in the first trimester of pregnancy (Creanga et al., 2011). Furthermore, recent estimates based on data in certain regions of the United States suggest an abrupt increase in ectopic-related mortality rates among women with limited access to care and those who use illicit substances (CDC, 2012). Public health efforts to promote awareness about early pregnancy testing, risk factors for ectopic pregnancy, improved access to health care, and the risks associated with substance abuse during pregnancy are critical to reducing maternal morbidity and mortality, preserving future fertility, and decreasing medical expenses that would otherwise be incurred with hospitalization and surgery (Barnhart, 2006).

VARIANTS OF ECTOPIC PREGNANCIES

The vast majority of ectopic pregnancies (97%) implant within the fallopian tube. The most common risk factor for developing an ectopic pregnancy is underlying tubal pathology. One third of pregnancies occurring after sterilization failure are ectopic pregnancies, accounting for 10% of all ectopic implantations (American College of Obstetricians and Gynecologists [ACOG], 2014). However, any condition that alters either tubal integrity or function, such as prior tubal surgery, genital tract infections, and prior ectopic pregnancy, are all significant contributing factors. Additional risk factors include infertility, assisted reproductive technologies, prior pelvic or intra-abdominal surgery, and smoking. It is critical to note that half of all women who present with an ectopic pregnancy have no known risk factors. This poses a diagnostic challenge when evaluating

pregnant women who present with seemingly common symptoms such as lower abdominal cramping or vaginal spotting. Hence, maintaining a high index of suspicion ultimately aids in early diagnosis.

As previously noted, most ectopic pregnancies occur in the fallopian tube. However, several nontubal implantation locations are possible, accounting for up to 10% of ectopic pregnancies (Dilbaz, Katas, & Demir, 2005). These include the interstitial portion ("cornua") of the fallopian tube, ovary, cervix, cesarean scar tissue, broad ligament, peritoneum, and abdominal cavity. Although less common, nontubal ectopic pregnancies are associated with higher rates of maternal morbidity and mortality due to the difficulties in diagnosing these types of ectopics and clinical presentation at more advanced gestations.

The terms *interstitial pregnancy* and *cornual pregnancy* are commonly used interchangeably; however, a distinction should be made. The term *interstitial* specifically refers to the interstitial portion of the fallopian tube, which is the proximal segment of the tube that is embedded within the muscular wall of the uterus. True interstitial pregnancies comprise approximately 3% of ectopic pregnancies (Dilbaz et al., 2005). These pregnancies are at particularly increased risk for rupture and subsequent hemorrhage given the tendency to present late in gestation. Typical ultrasound findings of an interstitial ectopic pregnancy, as noted in Figure 4.1, include an empty uterus and an eccentrically located gestational sac greater than 1 cm from the endometrial stripe with a continuous rim of myometrium measuring less than 5 to 8 mm (Jurkovic & Marvelos, 2007). In contrast, true cornual ectopic pregnancies implant within the "horn" of a bicornuate uterus or the rudimentary horn of a unicornuate uterus. These pregnancies are exceedingly rare and account for 0.27% of ectopic pregnancies

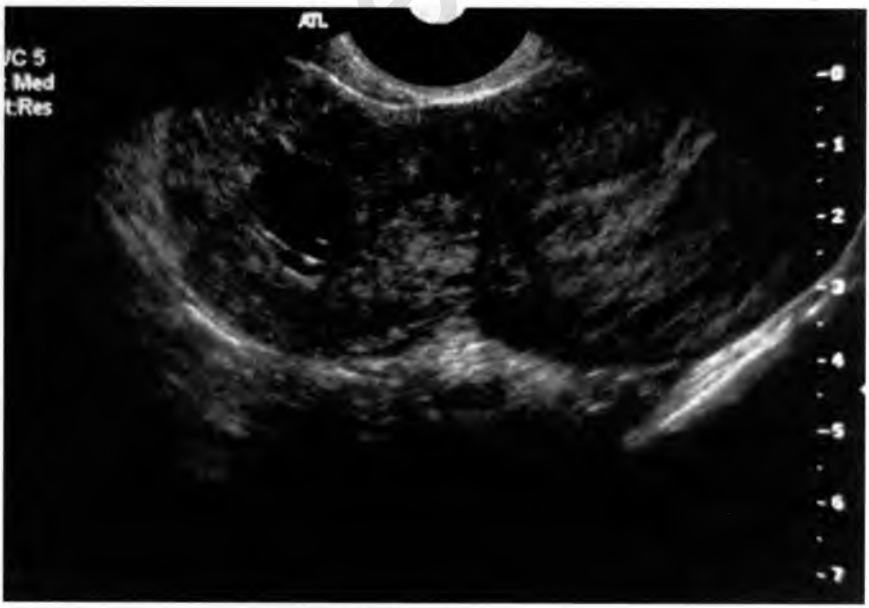

Figure 4.1 Interstitial ectopic pregnancy in patient presenting with abdominal pain at 7 weeks gestation

Source: Courtesy of Radiology Department, Women & Infants Hospital, Providence, RI.

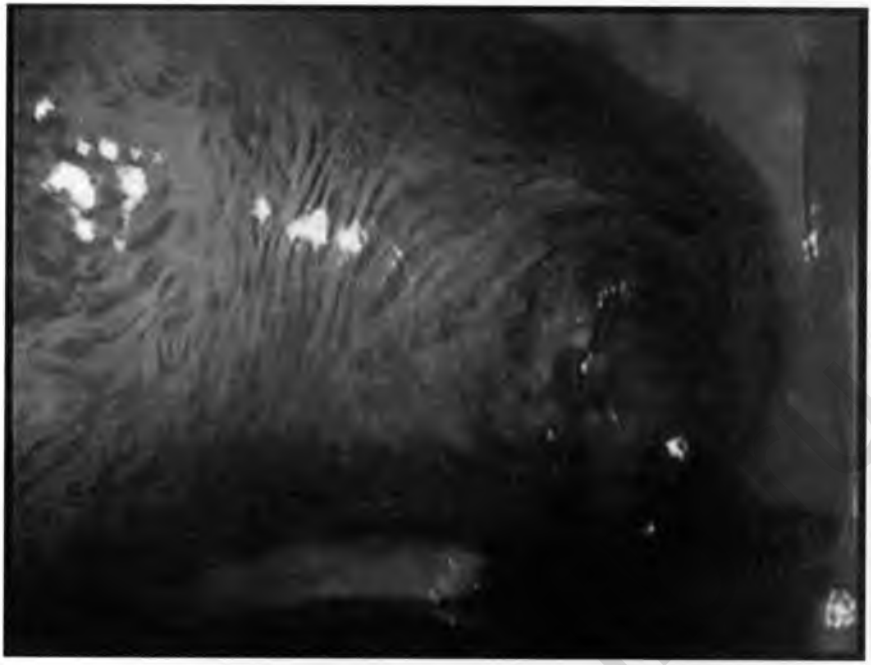

Figure 4.2 Cornual ectopic pregnancy

Source: Courtesy of Division of Reproductive Endocrinology and Infertility, Women & Infants Hospital, Providence, RI.

(Nahum, 2002). Ultrasound findings of a cornual pregnancy, depicted in Figure 4.2, include a gestational sac that is mobile and surrounded by myometrium and is separate from the main body of the uterus (Jurkovic & Marvelos, 2007).

Ovarian pregnancies comprise approximately 1% to 3% of ectopic pregnancies, with an incidence ranging from 1 in 2,100 to 1 in 60,000 pregnancies. These occur when a fertilized ovum remains in the peritoneal cavity and subsequently implants on the surface of the ovary (Molinaro & Barnhart, 2007). This form of ectopic pregnancy is particularly difficult to diagnose and is often misdiagnosed as a corpus luteal cyst (Figure 4.3).

Heterotopic pregnancies occur when there is simultaneously an intrauterine and an extrauterine pregnancy. These account for 1 in 4,000 pregnancies in the general population and 1 in 100 cases for women undergoing assisted reproductive technology treatments (Barnhart, 2009).

Cervical pregnancies are an extremely rare form of ectopic pregnancy and occur in less than 1% of all pregnancies, with an estimated incidence of 1 in 2,500 to 1 in 18,000 pregnancies (Molinaro & Barnhart, 2007; Vela & Tulandi, 2007). A cervical pregnancy as shown in Figure 4.4 is one in which the pregnancy implants within the mucosa of the endocervical canal, resulting in a "barrel-shaped" cervix and a gestational sac below the level of the internal os (Kirk & Bourne, 2009). Patients with a cervical ectopic pregnancy typically present with heavy vaginal bleeding that is often painless and, less commonly, with lower abdominal pain.

With rising rates of cesarean births, a recently described form of nontubal ectopic pregnancy is one in which there is implantation of a pregnancy within

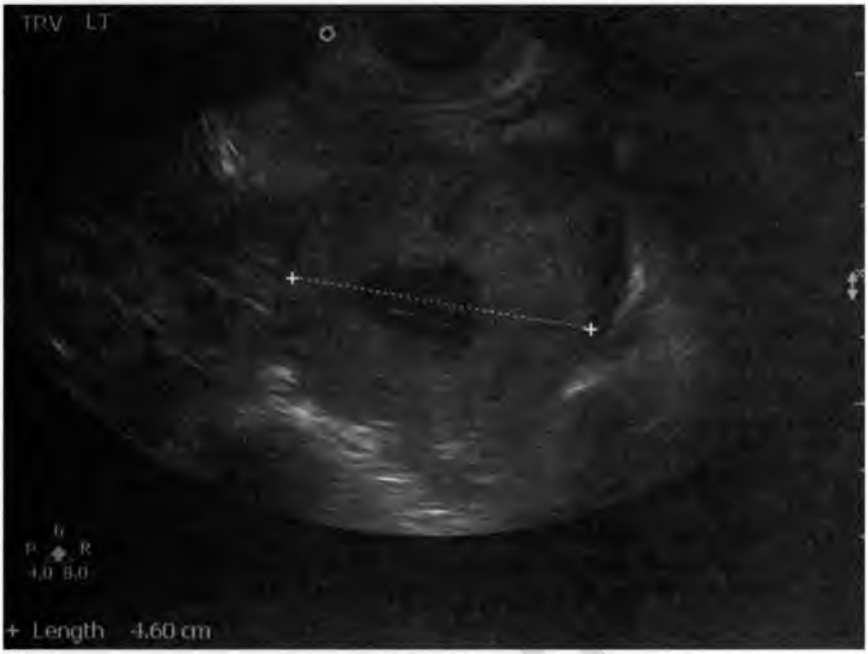

Figure 4.3 Ovarian ectopic pregnancy located on 2D ultrasound

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

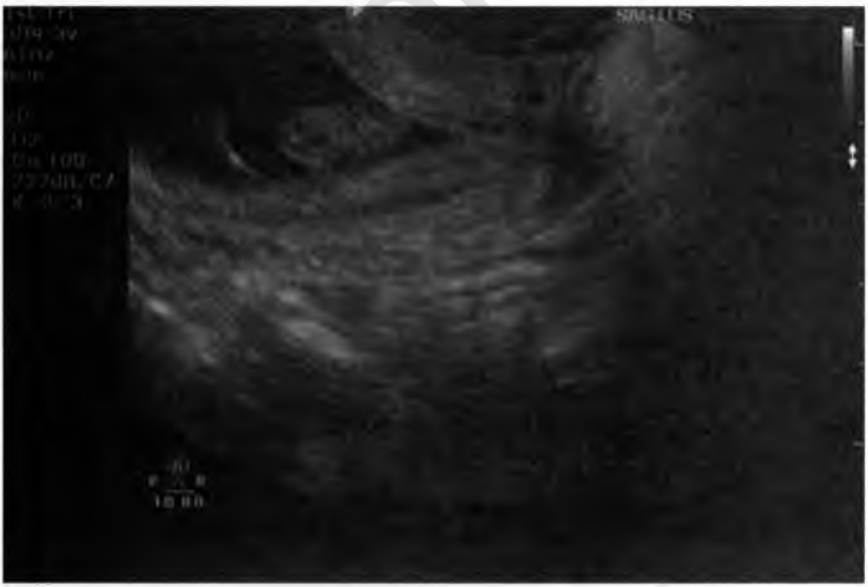

Figure 4.4 Cervical ectopic pregnancy

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

a prior cesarean section scar. Common ultrasound findings of a cesarean scar pregnancy seen in Figure 4.5 include an empty uterus with a gestational sac located anteriorly at the level of the internal os covering the site of the previous lower uterine segment cesarean section scar (Kirk & Bourne, 2009).

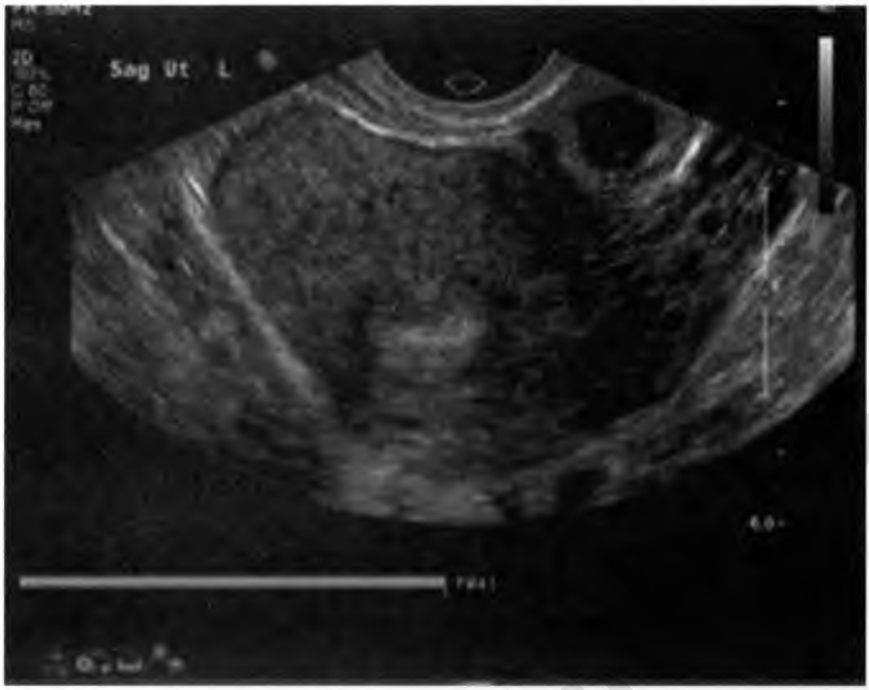

Figure 4.5 Cesarean scar ectopic pregnancy

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

One final consideration is that of an abdominal pregnancy. Although exceptionally rare, the potential sequelae from this particular form of ectopic pregnancy can be devastating. Providers need to consider this in their diagnostic evaluation of all women with a pregnancy of unknown location. Abdominal pregnancies can be a result of the direct implantation of the developing embryo on the abdominal viscera or peritoneal surface (Figure 4.6). Also, they may be due to the expulsion of an embryo from the fallopian tube. As a result of these variable locations, abdominal pregnancies are associated with a wide range of signs and symptoms. Unlike tubal pregnancies, they may go undetected until a very advanced gestational age. Thus, it is imperative to maintain a high index of suspicion when making the diagnosis.

PRESENTING SYMPTOMATOLOGY

Ectopic pregnancies can be fatal when misdiagnosed. Even the most conservative and vigilant approaches can fail to make a correct and timely diagnosis. Several factors that contribute to missed or delayed diagnosis include poor patient reliability with respect to presenting symptoms, limited access to health care, substance abuse, absent or nonspecific findings on physical exam, and the fact that almost 50% of women with an ectopic pregnancy have no apparent risk factors (ACOG, 2014; CDC, 2012). The presentation of an ectopic pregnancy is quite variable, and diagnosis relies on a combination of clinical, biochemical, and imaging findings. Ultimately, early diagnosis is facilitated by maintaining

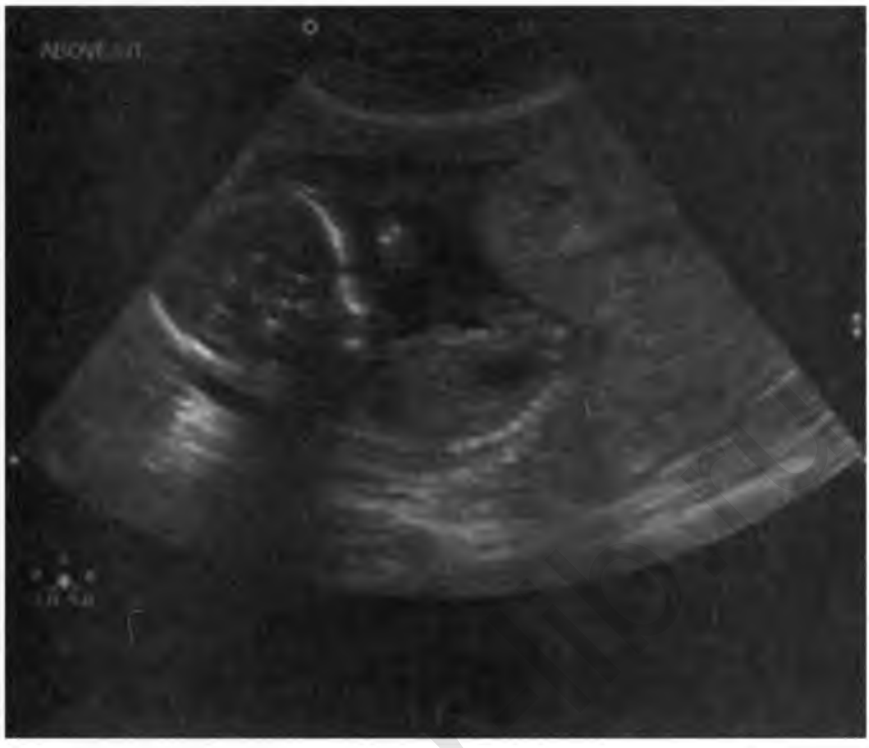

Figure 4.6 Abdominal pregnancy post rupture of an interstitial pregnancy

Source: Courtesy of Radiology Department, Women & Infants Hospital, Providence, RI.

clinical vigilance in conjunction with a comprehensive approach to patient evaluation.

Abdominal pain and vaginal bleeding are common reasons for women to seek medical care during the first trimester of pregnancy, and as many as 18% of emergency department visits for these symptoms are due to ectopic pregnancies (ACOG, 2014). Accordingly, all reproductive-aged women who present with these symptoms should be screened for pregnancy. Historically, the diagnosis of ectopic pregnancy was often made in the setting of rupture, which made this condition primarily a surgical issue. For women presenting with signs and symptoms of a ruptured ectopic pregnancy, this then becomes a surgical emergency. Symptoms suggestive of tubal rupture include hemodynamic instability (hypotension, tachycardia), rebound tenderness due to hemoperitoneum, a large amount of free fluid on ultrasound, and referred shoulder pain. Symptoms of an abdominal pregnancy range from nausea and vomiting from a pregnancy implanted on the bowel to an acute abdomen with subsequent shock due to massive intra-abdominal hemorrhage. The differential diagnoses include any other form of extrauterine pregnancy, placental abruption, a true cornual pregnancy, and uterine rupture. Regardless of the gestational age at presentation, the primary treatment option is surgical for a ruptured ectopic. Ideally, the treatment of these women is managed by an obstetrician/gynecologist and, in more remote areas, a general surgeon. Fortunately, with the advent of increased accuracy and sensitivity of pregnancy testing, improved ultrasonography, and improved treatment options, the vast majority of ectopic pregnancies are now being diagnosed well in advance of rupture, allowing for less invasive treatment

options. Hence, ectopic pregnancy remains a predominantly nonsurgical entity with respect to both the diagnosis and subsequent management.

PHYSICAL EXAMINATION

Vaginal bleeding is a common occurrence in early pregnancy. Approximately half of these pregnancies will go on to miscarry, and the remainder will be either viable intrauterine pregnancies or ectopic pregnancies. Thus, the diagnosis of an ectopic pregnancy must be considered in any woman presenting with nonspecific symptoms such as lower abdominal cramping and vaginal bleeding. Unfortunately, the classic triad of pain, vaginal bleeding, and a palpable adnexal mass is present in less than half of ectopic cases.

LABORATORY AND IMAGING STUDIES

The first step in evaluating any woman who presents with a pregnancy of unknown location is to determine whether it is a normal pregnancy, a failed pregnancy, or an extrauterine pregnancy. This can be accomplished by utilizing sensitive serum quantitative human chorionic gonadotropin (hCG) assays in conjunction with high-resolution transvaginal sonography. Regardless of pregnancy location or viability, all women presenting with vaginal bleeding in early pregnancy must have a blood type and screen obtained. In Rh-negative women who have no evidence of sensitization, anti-D immune globulin should be administered.

Ultrasonographic Evaluation

Absolute criteria for a failed intrauterine pregnancy include a crown–rump length greater than or equal to 7 mm with no fetal heart rate, a mean sac diameter greater than or equal to 25 mm with no embryo, absence of an embryo with fetal heart for 2 weeks and above following an ultrasound with a prior gestational sac without a yolk sac, and absence of an embryo with a fetal heart rate for 11 days or more after a scan demonstrating a gestational sac with a yolk sac (Doubilet, Benson, Bourne, & Blaivas, 2013). When any of the previous criteria are met, a patient can safely be diagnosed with a nonviable intrauterine pregnancy. If the diagnosis of a failed intrauterine pregnancy cannot be definitively made on the basis of these absolute criteria, then an ectopic pregnancy must be a consideration. The sensitivity of transvaginal ultrasound for diagnosing an ectopic pregnancy ranges from 73% to 93% (Barnhart, 2009). This range in sensitivity is dependent on several factors including gestational age, ultrasound equipment, and technical abilities of the ultrasonographer.

Ultrasound alone can be diagnostic of an ectopic pregnancy if an embryo with fetal cardiac activity is visualized in an extrauterine location. Unfortunately, this is often not the case. The most common finding for an ectopic pregnancy on transvaginal ultrasound is an adnexal mass, usually located between the uterus and ovary. However, not all adnexal masses are ectopic pregnancies. In fact, most represent hemorrhagic corpus luteum. A mass in the setting of an ectopic pregnancy may be a solid, complex, ring-like structure; but it can also be subtle and appear as a mere asymmetry of ovarian size. Alternatively, a mass representing an ectopic pregnancy may be mistaken for another benign structure such as adjacent bowel, a simple or paratubal cyst, or an endometrioma.

Ultimately, the location of a corpus luteum is not helpful because contralateral implantation occurs in up to a third of cases. An additional aspect to consider is the echotexture of the mass. For example, the relative echogenicity of a "tubal ring," as shown in Figure 4.1, is a useful characteristic that can differentiate an ectopic pregnancy from a corpus luteum (Frates, Visweswaran, & Laing, 2001). Real-time ultrasound imaging with utilization of the probe and gentle pressure on the abdominal wall is also a useful diagnostic tool because it can facilitate movement of a mass to separate from the ovary. Lack of independent motion of an adjacent mass and ovary is strongly suggestive of a nonectopic mass (Blaivas & Lyon, 2005). Of note, if a transvaginal ultrasound alone is performed to rule out an ectopic pregnancy, to be completely thorough, an abdominal ultrasound is also recommended in order to evaluate for the rare circumstance of an abdominally implanted pregnancy.

Small amounts of free fluid can be seen on ultrasound in both ectopic and intrauterine pregnancies; however, moderate to large amounts of fluid increase the suspicion for an ectopic pregnancy. The presence of heterogeneous, echogenic fluid detected by transvaginal ultrasonography closely correlates with hemoperitoneum detected at the time of surgery in women with suspected ectopic pregnancies.

Quantitative Beta-hCG Trends

Beta-hCG levels play a critical adjunctive role in the early diagnosis of ectopic pregnancies. Although there is no single level of serum beta-hCG that is diagnostic in distinguishing between an intrauterine and an ectopic pregnancy, serial values can be used to demonstrate how the beta-hCG values trend. When serial hCG levels performed at 48-hour intervals demonstrate either a suboptimal rise for a normal intrauterine pregnancy or a decline not consistent with a spontaneous miscarriage, two thirds of the time the ultimate diagnosis is an ectopic pregnancy (Surampudi & Gundabattula, 2016). Although nondiagnostic, the "discriminatory zone," which is the lowest level at which an intrauterine gestational sac can be reliably visualized on ultrasound, is also helpful in determining index of suspicion for a nonviable or extrauterine pregnancy. The discriminatory zone for beta-hCG has been reported to range between 1,500 and 2,000 mIU/mL for transvaginal ultrasound and 6,500 mIU/mL for transabdominal approaches (Seeber & Barnhart, 2006). However, this hCG level is institutionally dependent and varies on the basis of multiple factors. These factors include the particular hCG assay utilized by the laboratory, the quality of the ultrasound equipment, the skill of the ultrasonographer, and the presence of physical factors (e.g., patient habitus, fibroids).

The minimal rise in beta-hCG for a normal viable pregnancy is 24% at 1 day and 53% at 2 days (Barnhart et al., 2004). However, whereas 99% of viable intrauterine pregnancies will demonstrate this trend, 21% of ectopic pregnancies will also demonstrate a similar rise (Silva et al., 2006). Conversely, 8% of ectopic pregnancies will demonstrate declining beta-hCG levels at the same rate as a spontaneous miscarriage (Silva et al., 2006). In addition, some normal pregnancies will not have a gestational sac on initial ultrasound despite either normally rising hormone levels or levels above the discriminatory zone. In such cases, it is prudent to perform serial ultrasound, particularly in women with a desired pregnancy, in order to definitively establish the location of the pregnancy. Regardless of an institution's particular discriminatory zone, clinical management is best guided by serial beta-hCG levels, which are more accurate than any single measurement. Furthermore, it is critical that institutions adopt a comprehensive process to maximize the sensitivity for diagnosing an ectopic

pregnancy while minimizing the possibility of disrupting a normal intrauterine pregnancy.

The previously mentioned beta-hCG levels are useful in determining abnormal trends; however, abnormal trends do not establish pregnancy location. Once the possibility of a viable pregnancy has been excluded, uterine curettage plays an important role in distinguishing a nonviable intrauterine pregnancy from an extrauterine pregnancy. When ultrasound cannot definitively locate the abnormal pregnancy and the presumptive diagnosis of an ectopic pregnancy is made, a uterine curettage determines the presumptive diagnosis is inaccurate in almost half of cases (Frates et al., 2001). Thus, once a pregnancy has been deemed to be nonviable through serial ultrasounds and abnormal beta-hCG trends, a reasonable diagnostic, as well as potentially therapeutic, option is to perform a uterine curettage (Rivera, Nguyen, & Sit, 2009). Intrauterine confirmation can be made by either the presence of chorionic villi detected by histopathology or by a 20% decline in follow-up beta-hCG levels 12 to 24 hours following uterine aspiration (Barnhart, Katz, Hummel, & Garcia, 2002). Uterine evacuation, however, is also limited in its clinical applicability based on provider skill and experience, availability of the necessary equipment, and the potential for disruption of a potentially viable pregnancy. Figure 4.7 provides an algorithm for the management of a pregnancy of unknown location.

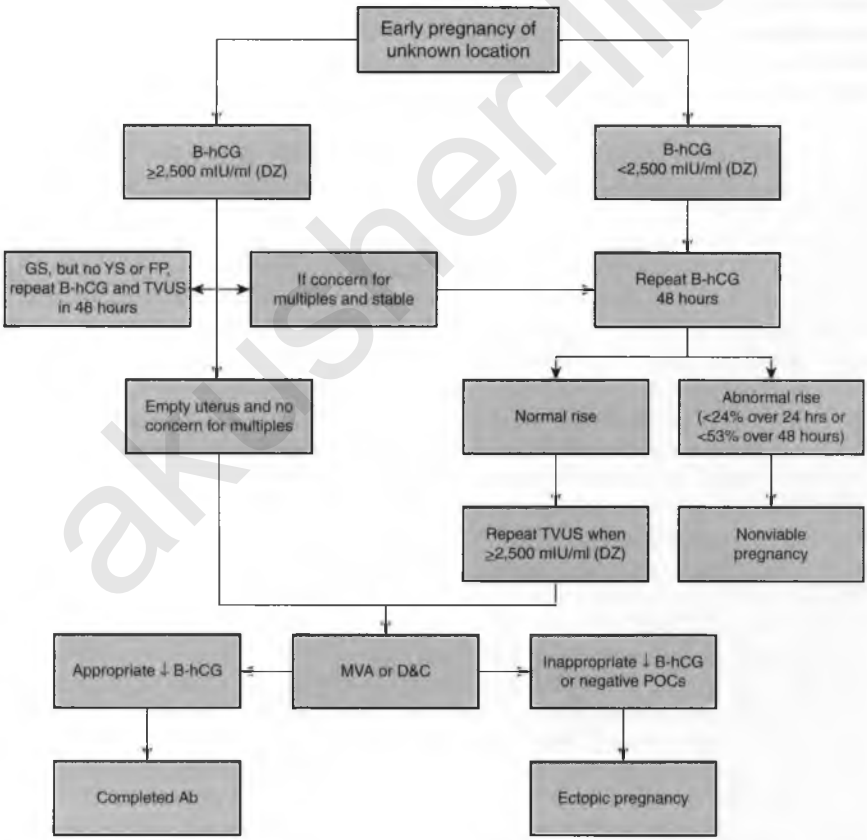

Figure 4.7 Management of the early pregnancy of unknown location.

B-hCG, beta–human chorionic gonadotropin

Source: Courtesy of Emergency Obstetrics and Gynecology Division, Women & Infants Hospital, Providence, RI.

CLINICAL MANAGEMENT AND FOLLOW-UP

Treatment options for ectopic pregnancies include expectant management, medical therapy, and surgical intervention. Expectant management involves serial beta-hCG monitoring in conjunction with close outpatient follow-up to ensure complete resolution of the ectopic pregnancy. Criteria for this management option include hemodynamic stability, absence of symptoms, beta-hCG levels greater than 200 mIU/mL, a reliable patient, informed consent, and ability to comply with ongoing close observation. The ultimate decision regarding appropriate treatment is largely dependent on both characteristics of the patient and clinical expertise of the provider.

Medical Management

As the earlier detection of ectopic pregnancies has increased over the past decade, minimally invasive therapy has become the standard of care. The key to successful conservative medical management lies in early diagnosis. Today, providers are far more likely to treat appropriate candidates in an outpatient setting with the use of methotrexate as described in Exhibit 4.1.

Methotrexate is an antineoplastic agent, which binds to dihydrofolate reductase, thus inhibiting DNA synthesis. It primarily affects actively proliferating cells such as malignant cells, bone marrow, buccal and intestinal mucosa, respiratory epithelial cells, and trophoblastic tissue. In addition to its clinical utility, its mechanism of action and impact on rapidly dividing cells

EXHIBIT 4.1

Methotrexate (MTX) Treatment Regimens

- **Pretreatment evaluation:** Rule out failed intrauterine pregnancy.
- **Baseline labs:** Beta-hCG, creatinine, liver function tests, complete blood count, blood type, and screen
- **Single-dose protocol:** MTX 50 mg/m^2 IM on day 1, with hCG measurements on days 4 and 7. Expect 15% decline in hCG levels from day 4 to 7. Then follow weekly to nonpregnant levels. If inappropriate decline or levels plateau/increase, redose MTX.
- **Sequential or two dose:** MTX 50 mg/m^2 IM on day 0 and day 4, with hCG measurements on days 4 and 7. Monitor decline as previously noted. If inappropriate decline or levels plateau/increase, redose on days 7 and 11 and monitor for 15% decline.
- **Fixed multidose:** MTX 1 mg/kg IM on days 1, 3, 5, and 7, with leucovorin rescue at 0.1 mg/kg IM on days 2, 4, 6, and 8. Measure hCG levels on MTX dose days and continue to monitor until 15% decline from initial level and then weekly until nonpregnant levels. Redose as per the previous protocol if inappropriate decline or levels plateau/increase.

hCG, human chorionic gonadotropin; IM, intramuscular.

Source: Adapted from ACOG (2014).

EXHIBIT 4.2

Side Effects of Methotrexate

- Gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea)
- Stomatitis
- Macular rash
- Central nervous system symptoms (e.g., headache, dizziness, fatigue, difficulty concentrating)
- Blood dyscrasias (e.g., anemia, macrocytosis)
- Alopecia
- Fever
- Hepatic, pulmonary, and renal toxicity

Source: Adapted from ACOG (2014).

also accounts for many of the potential side effects of methotrexate as noted in Exhibit 4.2. Its use by experienced providers is both a safe and appropriate alternative to surgical management in the carefully selected patient. There are various regimens for methotrexate therapy, with the overall success rates ranging between 71.2% and 94.2% (Barnhart, 2006). The single-dose regimen is most frequently used in clinical practice and has been shown to be safe and cost-effective when utilized in appropriately selected women (Stovall, Ling, & Gray, 1991). However, the "two-dose" protocol offers the additional benefits of both convenience and efficacy (Hajenius et al., 2007). Specifically, this regimen can be utilized in women with beta-hCG levels above 5,000 mIU/mL, but allows for fewer injections and surveillance visits than the "fixed multidose" regimen.

Ultrasound indicators for ectopic pregnancies that can be treated with methotrexate include lack of free fluid, adnexal mass less than 3.5 to 4.0 cm, and absent embryonic cardiac activity. Although the adnexal mass may increase in size after administration of methotrexate, the pregnancy will not demonstrate any signs of further development. Treatment success is monitored by both clinical symptoms and ongoing beta-hCG levels. One caveat is that individuals who have none of the contraindications for methotrexate listed in Exhibit 4.3 but otherwise have a poor social situation (e.g., homeless, substance abuse) are not candidates for medical management unless appropriate follow-up can be assured.

Factors associated with failed medical management include initial beta-hCG levels above 5,000 mIU/mL, ultrasonographic evidence of significant free fluid, presence of fetal cardiac activity, and a pretreatment beta-hCG level that has increased more than 50% over a 48-hour period (Barnhart, 2009). In addition to a pretreatment laboratory evaluation, women opting for medical management require prolonged follow-up regardless of the particular methotrexate dosing regimen chosen. Women who have failed both expectant and medical management for an ectopic pregnancy ultimately require surgical intervention. Of note, nontubal ectopic pregnancies have historically been treated surgically with open procedures. However, with technological advances in ultrasound equipment, clearly defined algorithms for early pregnancy identification, and growing clinical experience, these rare types of ectopic pregnancies are also being treated more conservatively with medical management and/or minimally invasive surgical approaches. Provider experience and availability of resources are rate-limiting factors in these cases.

EXHIBIT 4.3

Contraindications to Methotrexate Therapy

- Absolute contraindications: known intrauterine pregnancy, blood dyscrasias (e.g., severe anemia, thrombocytopenia), immunodeficiency (i.e., dysfunction of the immune system) current breastfeeding, prior sensitivity to methotrexate, active pulmonary disease, active peptic ulcer disease, liver disease (alcoholic or other chronic disease), and kidney disease
- Relative contraindications: embryonic cardiac activity detected by transvaginal ultrasonography, patient declines blood transfusion, high initial hCG concentration (>5,000 mIU/mL), ectopic pregnancy greater than 3.5 to 4.0 cm in size as imaged by transvaginal ultrasound, refusal to accept blood products, and inability to participate in follow-up

hCG, human chorionic gonadotropin.

Sources: Adapted from ACOG (2014) and Practice Committee of the American Society for Reproductive Medicine (ASRM; 2008).

Surgical Management

Although the management approach for ectopic pregnancies has largely moved away from surgery, there are still women for whom surgery is indicated. Appropriate indications for surgical management include hemodynamic instability or ruptured ectopic pregnancy, coexisting intrauterine pregnancy, contraindications to methotrexate, desire for permanent sterilization, and those patients who have failed medical management.

The primary surgical approaches involve removing the entire tube via a salpingectomy versus a salpingostomy, in which the ectopic is removed from the affected tube while preserving the fallopian tube. Although no studies to date have directly compared the two procedures, there are similar outcomes with respect to operative morbidity and subsequent fertility rates. However, the obvious disadvantage of a salpingostomy is that it is less successful than either a salpingectomy or an open surgical approach because of the increased risk for a persistent or recurrent ectopic pregnancy in an already damaged fallopian tube (Hajenius et al., 2007). If a salpingostomy is performed, it is critical to follow beta-hCG levels to nonpregnant levels in order to detect a persistent ectopic. In these cases, postoperative prophylactic single-dose methotrexate can be administered to reduce this risk (Practice Committee of the American Society for Reproductive Medicine [ASRM], 2008). Either procedure can be performed laparoscopically, which is the current standard and preferred surgical approach for ectopic pregnancy. However, conversion to an open laparotomy is appropriate under certain circumstances. The final decision to move toward an open surgical approach is based on the clinical status of the patient in conjunction with the clinical expertise and judgment of the surgeon and anesthesiologist. Regardless of the surgical approach chosen, there are similar recurrence and tubal patency rates following both medical and surgical intervention (Buster & Krotz, 2007).

CLINICAL PEARLS

- Ectopic pregnancy represents a leading cause of maternal mortality in the first trimester, and prompt diagnosis is critical to minimize complications.
- Early diagnosis is typically made through trending serial quantitative beta-hCGs, in combination with ultrasound.
- Early diagnosis facilitates nonsurgical management options, including medical management with methotrexate.

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5 *Vaginal Bleeding in Early Pregnancy*

Beth Cronin

Vaginal bleeding in the first trimester of pregnancy is a common complaint among women who present to an emergency room. Approximately 25% of clinically relevant pregnancies have vaginal bleeding in the first trimester and half of these will eventually miscarry (Paspulati, Bhatt, & Nour, 2004). Vaginal bleeding may be caused by implantation of the embryo, subchorionic hematoma, miscarriage, gestational trophoblastic disease, or ectopic pregnancy. It is crucial for the clinician to initially assess for the most dangerous causes, especially ectopic pregnancy. Ectopic pregnancy, the implantation of the embryo outside the uterine cavity, is a potentially life-threatening complication, with an incidence of approximately 1.5% to 2% of all pregnancies. The morbidity and mortality from ruptured ectopic pregnancies have decreased due to early detection and effective management strategies. However, 6% of maternal deaths are still caused from ruptured ectopic pregnancies, often due to failure to recognize the early signs and symptoms (Barnhart, 2009).

PRESENTING SYMPTOMATOLOGY

The amount of vaginal bleeding can range from spotting to severe hemorrhage; however, the amount of bleeding is not necessarily indicative of the cause of bleeding. The pace of a woman's evaluation will depend on the presenting history and symptomatology. It is critical to initially quantify the amount of blood loss because if there has been heavy bleeding, anemia and even hemodynamic instability may ensue.

Vaginal bleeding may or may not be associated with abdominal pain. In a woman presenting with vaginal bleeding and abdominal pain, ectopic pregnancy is at the top of the differential diagnosis until proven otherwise. Additional symptoms of hemoperitoneum from a ruptured ectopic pregnancy include right shoulder pain, dizziness, and abdominal distension.

Along with the bleeding, the woman may have noticed the passing of tissue, or even a fetus, which, if available, can be examined for chorionic villi or fetal parts. Temporal associations are also relevant. For example, if the bleeding only occurs when passing urine, it could be that the bleeding is from a urinary tract infection.

HISTORY AND DATA COLLECTION

Many women presenting with vaginal bleeding may be unaware that they are pregnant. Every sexually active, reproductive-age woman who presents with irregular vaginal bleeding or abdominal pain needs a pregnancy test.

If known, the woman's last menstrual period (LMP) can be used to estimate gestational age. If the woman has irregular menses or an unsure LMP, basing gestational age on LMP may be inaccurate. A previous ultrasound in this pregnancy that documents an intrauterine pregnancy, in conjunction with the LMP, is the most accurate assessment of gestational age. A previous ultrasound documenting an intrauterine pregnancy almost 100% negates concern for ectopic pregnancy. The risk of heterotopic pregnancy, a concurrent pregnancy in the uterus and ectopic pregnancy, is extremely low in patients that have not used assisted reproductive techniques, estimated at approximately 1/4,000 (Deutchman, Tubay, & Turok, 2009).

If the location of the pregnancy is unknown, it is important to assess for risk factors for an ectopic, including previous ectopic pregnancy, tubal surgery, current intrauterine device, infertility treatments, history of pelvic inflammatory disease, age over 35 years, and smoking (Barnhart, 2009; Deutchman et al., 2009). Although conception after tubal ligation or with an intrauterine device in place is rare, if pregnancy does occur, there is an extremely high rate (25%–50%) of ectopic pregnancy (Barnhart, 2009).

Ectopic pregnancies most commonly implant in the fallopian tubes, accounting for over 95% of all ectopic pregnancies (Bouyer, Coste, Fernandez, Pouly, & Job-Spira, 2002). However, those ectopic pregnancies that implant in the cervix, uterine cornua, cesarean section scar, ovaries, or abdominal cavity are more difficult to diagnose and manage, leading to higher morbidity. Timely diagnosis of an ectopic pregnancy arising in one of the more rare locations requires a high level of suspicion, radiologic expertise, and at times magnetic resonance imaging (MRI) in addition to ultrasound.

PHYSICAL EXAMINATION

In addition to the history, vital signs and clinical appearance are crucial to determine the pace and breadth of the clinical workup. It is crucial to remember that a woman may lose between 15% and 25% of her blood volume before developing hypotension and tachycardia (Roberts, 2003). Acute blood loss leading to hemorrhagic shock can develop from a ruptured ectopic pregnancy or hemorrhage from a spontaneous abortion.

The physical examination initially includes a careful abdominal examination in order to palpate for uterine enlargement, tenderness, abdominal distension, and peritoneal signs. A pelvic examination is then performed in all women complaining of vaginal bleeding. A visual inspection of external genitalia can identify nonobstetric causes of bleeding, such as hemorrhoids or trauma. A speculum examination is helpful in assessing the amount of blood in the vagina as well as evidence of active bleeding. The cervix is visualized to elicit other nonobstetric causes of bleeding, such as sexually transmitted infections, polyps, or other cervical masses. Significant cervical dilation or visible products of conception are indicative of an inevitable abortion. Often removing these products of conception from the cervical os provides immediate relief of a woman's pain and can limit the amount of bleeding. Uterine size and position should be evaluated by bimanual examination.

The adnexae are palpated for masses and tenderness, which may indicate an ectopic pregnancy or other etiology, such as an ovarian cyst.

LABORATORY AND IMAGING STUDIES

The first measurable finding of a pregnancy is an elevated human chorionic gonadotropin (hCG) test. HCG is detectable in the plasma of pregnant women 8 days after ovulation, at the time of implantation of the blastocyst. Home pregnancy tests can detect hCG as low as 25 mIU/mL (Deutchman et al., 2009). Therefore, it is currently possible to detect a pregnancy even before a woman misses a menses.

A single hCG value does not identify the location or viability of a pregnancy but can serve as an estimate for gestational age. The discriminatory zone is most commonly defined as the hCG above which one expects to see a gestational sac (GS) on transvaginal ultrasound (TVUS). Failure to see a GS above this level suggests either an ectopic pregnancy or an abnormal intrauterine pregnancy. The discriminatory zone has been reported between 1,500 and 3,000 mIU (Barnhart, 2009), but is not absolute and may vary, depending on the testing results of an individual institution. If a smaller number is used (e.g., 1,500 mIU), the sensitivity for diagnosing an ectopic pregnancy increases, but the risk of mistaking a normal pregnancy as abnormal and interrupting the pregnancy also increases. If a higher number is used (e.g., 3,000 mIU), the diagnosis of an ectopic pregnancy may be delayed. A small collection of fluid in the uterus, or pseudosac, may appear as an anechoic structure similar to the GS. Due to this possible confusion, a GS is suggestive of an intrauterine pregnancy, but the presence of a yolk sac (YS) is necessary to definitively diagnose and confirm an intrauterine pregnancy.

TVUS is critical in the evaluation of women with early gestational bleeding in order to determine the viability and location of the pregnancy. If a pregnancy is not visualized, then the ultrasound findings need to be correlated to hCG measurement. The determination of viability and location of a pregnancy is not always possible in one emergency room or obstetric triage visit. TVUS is preferred to transabdominal in the first trimester because it can more clearly identify fetal structures at an earlier gestational age.

There are various presentations and ultrasound findings of spontaneous abortions, depending on the gestational age of the pregnancy. One must be familiar with normal pregnancy development in order to recognize a failing pregnancy. A GS is first seen around 5 weeks; the traditional "double sac sign" was described using transabdominal ultrasound, but this is a subjective measure with poor interobserver agreement (Doubilet & Benson, 2013). A YS (Figure 5.1) then appears around 5.5 weeks with the embryo first being present around 6 weeks. The preferred method to assess cardiac activity in early pregnancy is M mode, which has significantly lower energy output than Doppler (Abramowicz, Kossoff, Marsal, & ter Haar, 2003; Figure 5.2).

DIFFERENTIAL DIAGNOSIS

The differential for first trimester bleeding includes ectopic pregnancy, spontaneous abortion, threatened abortion, laceration, cervical mass, and gestational trophoblastic disease. Normal pregnancies may also have bleeding in the first trimester, often from a subchorionic hematoma, as pictured in Figure 5.3.

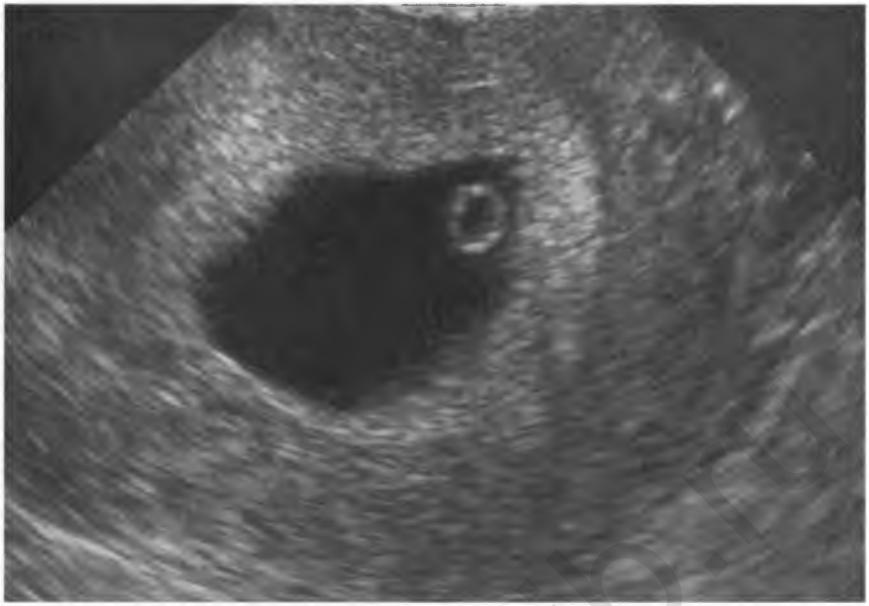

Figure 5.1 Yolk sac

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

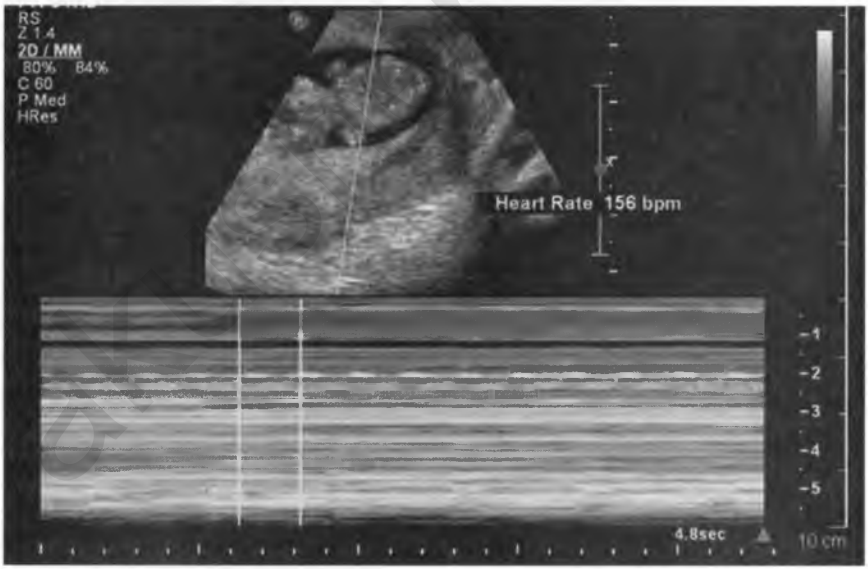

Figure 5.2 Fetal cardiac activity, M mode

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

Subchorionic hematomas may occur in up to 20% of women with threatened abortions (Paspulati et al., 2004). When the hematoma is small, it may be physiologic; however, there may be a correlation between a large subchorionic hematoma and early pregnancy loss. Awareness that an unfused amnion and

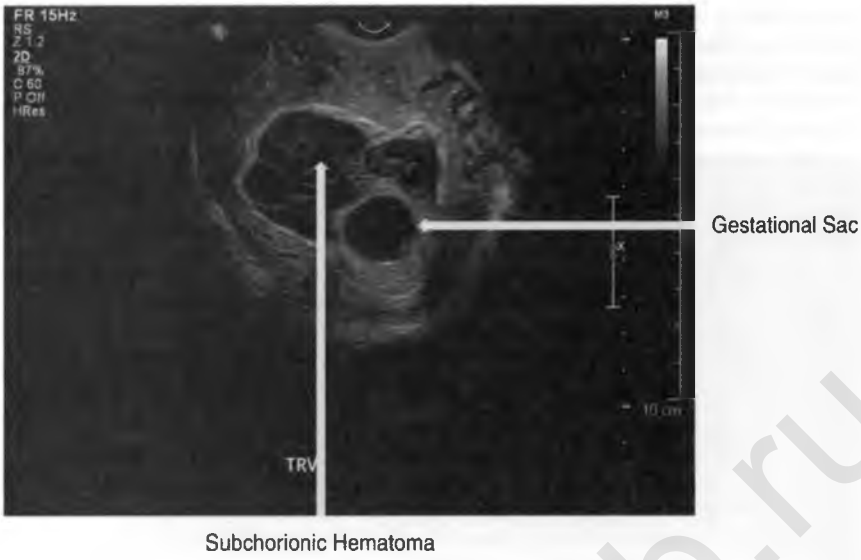

Figure 5.3 Subchorionic hematoma

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

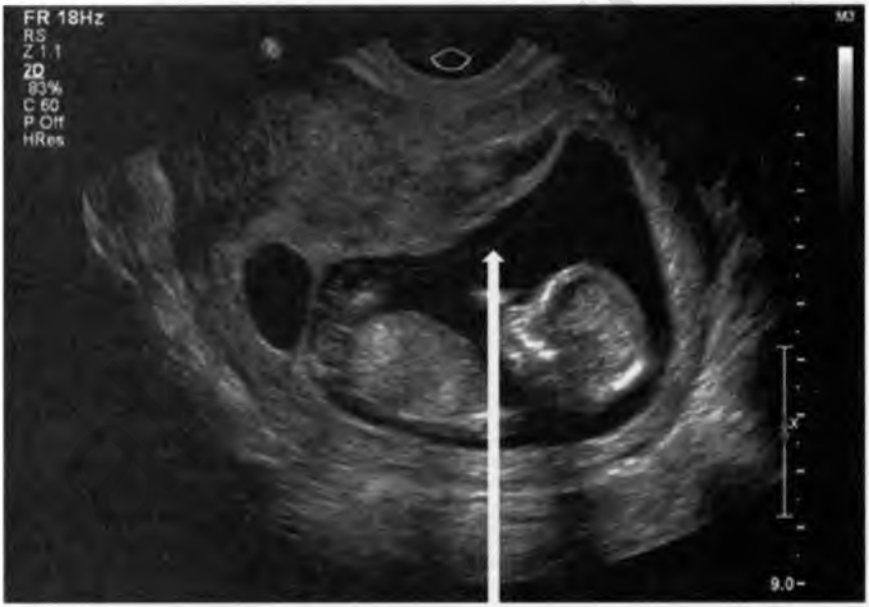

Figure 5.4 Unfused amnion and chorion

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

chorion, as shown in Figure 5.4, can be mistaken for a subchorionic hematoma is important.

An embryonic demise is defined as a visible embryo without a heartbeat. Cardiac activity may not be visible in an early normal embryo, but once crown-rump length (CRL) is 7 mm or greater, lack of heartbeat is diagnostic

of pregnancy failure (Abdallah et al., 2011). Traditional teaching was "5 alive," meaning a heartbeat should be visible by the time CRL is 5 mm. Further evaluation of these data demonstrated a specificity of 90% to 100%, indicating an increased chance of false-positive diagnosis of pregnancy failure (Doubilet, Benson, Bourne & Blaivas, 2013), leading to the adoption of a 7 mm CRL cutoff. A heart rate less than 100 beats per minute can be a worrisome finding at 6 weeks, but its prognosis is nonspecific. Because it is possible for the rate to increase quickly over the next week, such findings should prompt a repeat ultrasound in 7 to 10 days to assess for viability (Arleo & Troiano, 2011).

An anembryonic gestation is present when the GS forms, but the embryo fails to develop. This has historically been characterized on TVUS as a GS with a mean diameter greater than 16 mm without a YS or embryo (Paspulati et al., 2004). However, the larger the sac size used, the greater the positive predictive value, and the lower the chance of interrupting a potentially viable pregnancy. Recent studies advocate using 25 mm as the cutoff for mean sac diameter (Doubilet & Benson, 2013; Pexsters et al., 2011). In addition, not all pregnancies result in a GS this large, or an embryo, so additional criteria that can be used include absence of embryo with heartbeat 2 weeks or more after a scan that showed a GS or absence of embryo with heartbeat 11 days or more after a TVUS that showed GS and YS (Table 5.1).

With both anembryonic and failed embryonic pregnancies, correlation with expected gestational age and follow-up ultrasound may be useful in determining fetal viability. Not immediately knowing the viability of the pregnancy may represent an emotionally difficult situation for the patient, but this inconvenient situation needs to be balanced against the potential inadvertent termination of a normal pregnancy. Waiting to repeat an ultrasound in 7 to 10 days is not likely to lead to any physical harm, but the woman may need emotional support.

Gestational trophoblastic disease, or molar pregnancy, is characterized by markedly elevated hCG levels and ultrasound findings of a diffuse mixed echogenic pattern or "snowstorm" appearance, as seen in Figure 5.5. Cystic enlargement of the ovaries, including theca lutein cysts, may also be present. Early or partial moles may have subtle or no ultrasound findings.

Table 5.1 Transvaginal Ultrasound Diagnosis of Pregnancy Failure

	DIAGNOSTIC CRITERIA
Diagnostic of pregnancy failure	• CRL ≥ 7 mm, no FH • MSD ≥ 25 mm, no embryo • No embryo with FH ≥ 2 weeks after US with GS • No embryo with FH ≥ 11 days after US with GS and YS
Suspicious for pregnancy failure	• CRL < 7 mm, no FH • MSD 16–24 mm, no embryo • No embryo with FH ≥ 7–13 days after US with GS • No embryo with FH ≥ 7–10 days after US with GS and YS • No embryo ≥ 6 weeks after LMP • Empty amnion • YS > 7 mm • Small GS in relation to embryo size (<5 mm between MSD and CRL)

CRL, crown-rump length; FH, fetal heart beat; GS, gestational sac; MSD, mean sac diameter; US, ultrasound; YS, yolk sac.

Adapted from Doubilet et al. (2013).

Ectopic pregnancy is always in the differential until the pregnancy is located. An embryo with cardiac activity outside of the uterus confirms ectopic pregnancy, as shown in Figure 5.6. An adnexal mass without an embryo, as seen

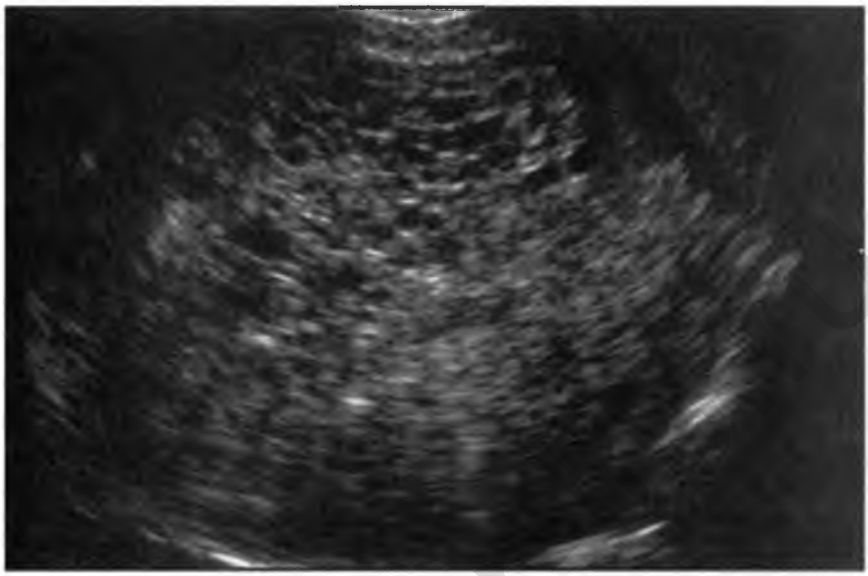

Figure 5.5 Gestational trophoblastic disease

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

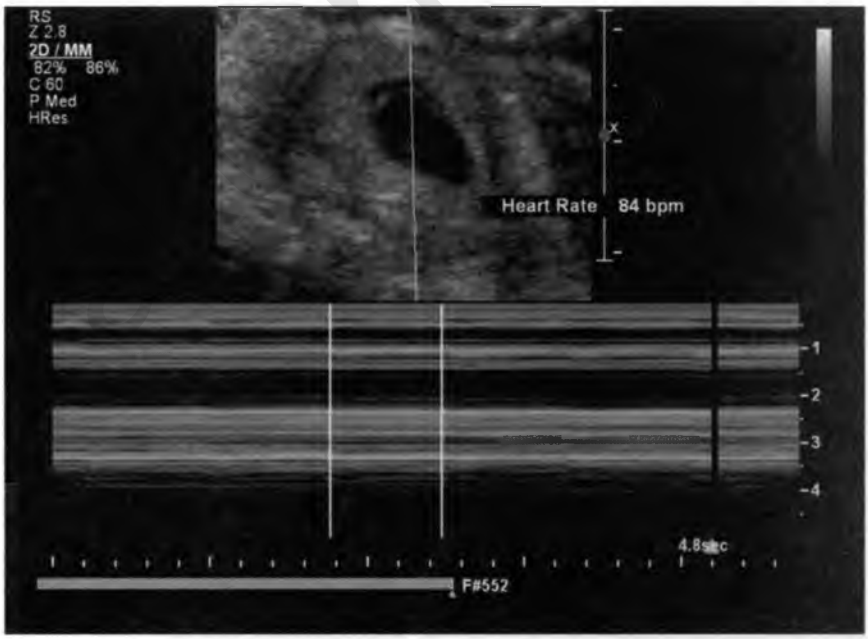

Figure 5.6 Adnexal mass with fetal cardiac activity

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

in Figure 5.7, or hemoperitoneum, shown in Figure 5.8, are highly concerning for an ectopic pregnancy.

The clinical scenario often arises when there is no definitive GS or ectopic pregnancy visible on ultrasound. This could potentially be a viable pregnancy,

Figure 5.7 Right adnexal mass without an embryo

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

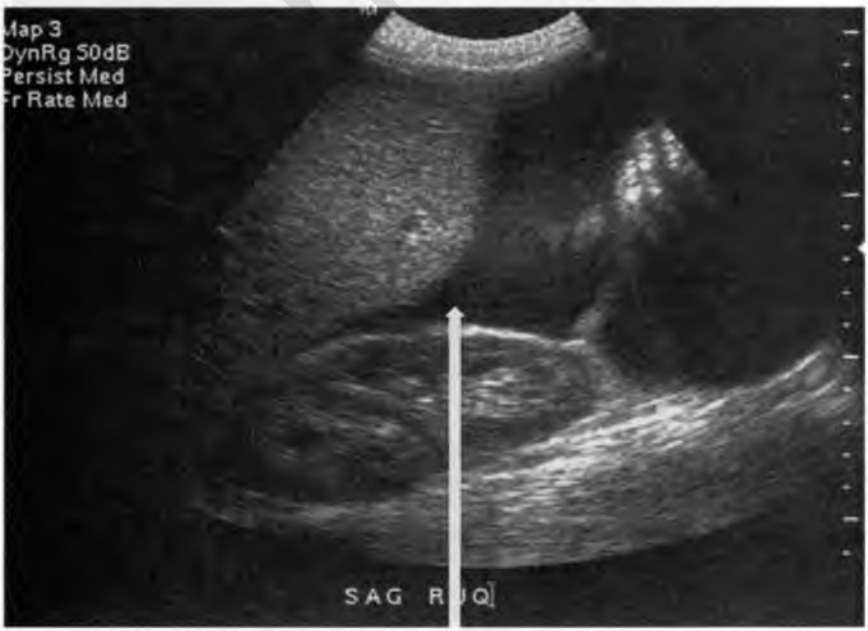

Figure 5.8 Hemoperitoneum

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

failed intrauterine pregnancy, or ectopic pregnancy. Detailed counseling of the patient and close follow-up with hCG and TVUS are required until a definitive diagnosis can be made.

CLINICAL MANAGEMENT AND FOLLOW-UP

If the previous evaluation has not confirmed the pregnancy location, then serial measurements of hCG are often helpful. In a normal pregnancy, hCG rises in a predictable fashion during the first 8 weeks or so. Approximately 99% of viable intrauterine pregnancies will have a minimal rise of 53% in 2 days (Barnhart, 2009). A rise less than this or a decrease in hCG either reflects an ectopic pregnancy or a failed intrauterine pregnancy. Multiple gestations have a similar rise in hCG, but the absolute values are higher than singleton pregnancies. Therefore, multiple gestation pregnancies do not have the same discriminatory zone as singleton pregnancies, but a separate discriminatory zone has not yet been established.

In women with a miscarriage, hCG generally declines between 20% and 35% in 48 hours (Barnhart et al., 2004). However, lower initial hCG values decline at a slower rate. For example, a hCG of 50 mIU has a mean decline of 12% in 48 hours (Chung et al., 2006). When hCG values are declining at a rate that is at least as high as expected, outpatient monitoring with serial hCG levels is appropriate until levels are undetectable.

Approximately half of ectopic pregnancies have rising hCG levels and the other half have declining levels. However, in 71% of ectopic pregnancies, the change in hCG is outside the normal range for normal pregnancies or spontaneous abortion (Silva et al., 2006). The other 30% of ectopic pregnancies have hCG curves that mimic normal gestations or miscarriages.

There are times in early pregnancy when the pregnancy location is unknown. This can happen when the hCG is above the discriminatory zone without evidence of an intrauterine pregnancy or if hCGs are declining very slowly or rising less than the expected 53% in 48 hours. Tissue sampling with uterine evacuation is useful in these situations. If products of conception, specifically chorionic villi, are identified on pathology, then the nonviable intrauterine pregnancy has been diagnosed and treated. Alternatively, a quantitative hCG obtained prior to the uterine evacuation can be compared to a repeat hCG obtained 12 to 24 hours after the procedure. If the hCG declines 20% or more in this time frame, then the trophoblastic cells were likely removed from the uterus, and there was a nonviable intrauterine pregnancy (Barnhart, 2009). The hCG level can then be monitored with serial measurements until it is undetectable. If the hCG fails to decline 20% after uterine evacuation, it strongly suggests that the trophoblasts are still present and an ectopic pregnancy exists. The woman then needs appropriate treatment of the ectopic pregnancy.

Women diagnosed with a miscarriage have a variety of options for clinical management. Often, these pregnancies are highly desired, and the provider needs to recognize the grief the woman and family may be experiencing. Most miscarriages occur spontaneously and completely and do not require any intervention. Historically, dilation and curettage was the treatment of choice for miscarriages. Under stable clinical circumstances, if the woman has not completed the miscarriage, either expectant management or medical management with misoprostol may represent a safe, effective, and preferable form of treatment. Incomplete abortions have a high treatment success rate, defined as complete expulsion of the pregnancy, with either expectant management

(86%) or medical management (100%) (Bagratee, Khullar, Regan, Moodley, & Kagoro, 2004). However, expectant management has drastically lower success rates with embryonic demise or anembryonic pregnancies. By day 7, expectant management only has a 29% success rate compared with 87% for medical management (Bagratee et al., 2004).

Although misoprostol is not approved by the United States Food and Drug Administration for use in treating miscarriage, studies have shown its safety and efficacy (Winikoff, 2005; Zhang et al., 2005). Misoprostol has fewer gastrointestinal side effects when administered vaginally instead of orally. Recommendations from the American College of Obstetricians and Gynecologists (ACOG) include 800 mcg of misoprostol to be placed vaginally, and if the woman does not have complete expulsion by day 3, then this dose is repeated. Complete expulsion is defined as no GS and endometrial thickness less than 3 cm on TVUS in a clinically stable woman. On day 8, if there is not complete expulsion, then uterine evacuation is performed (Zhang et al., 2005).

Thorough counseling and clearly defined expectations must be provided to the patient in order to prevent unnecessary revisits and to ensure satisfaction with a nonsurgical option to incomplete miscarriage. Antibiotic prophylaxis is not necessary for expectant management or medical management (Achilles & Reeves, 2011). Because there is a known intrauterine pregnancy, following hCG levels has no role in the management of these women.

Uterine evacuation of an incomplete, missed, or inevitable abortion can be performed with either a manual vacuum aspiration or dilation and curettage. Manual vacuum aspiration has been shown to be as efficacious, safe, and tolerable as dilation and curettage for evacuating the uterus in the first trimester (Wen, Cai, Deng, & Li, 2008). Antibiotic prophylaxis with doxycycline prior to surgical intervention is recommended (Achilles & Reeves, 2011).

Women who present with vaginal bleeding in pregnancy must have a blood type and antibody screen. Women who do not carry the RhD antigen are identified as RhD negative and may become alloimmunized if exposed to RhD-positive blood from a fetomaternal hemorrhage. The administration of anti-D immune globulin drastically decreases the rate of alloimmunization. In the first trimester, the red cell mass of the fetus is small. The dose of anti-D immune globulin necessary to protect against sensitization by 2.5 mL of red blood cells is 50 mcg (ACOG Committee on Practice Bulletins—Obstetrics, 1999).

CLINICAL PEARLS

- Vaginal bleeding in early pregnancy is very common. Its cause should be investigated to rule out potentially life-threatening complications.
- Recent updates for diagnosis of pregnancy failure include CRL of 7 mm or greater with no fetal heart rate, a mean sac diameter of 25 mm or greater with no embryo, no embryo with fetal heart beat (FH) 2 or more weeks after ultrasound with GS, or no embryo with FH 11 or more days after ultrasound with GS and YS.
- Although subsequent isoimmunization may be a rare complication in the first trimester, a blood type should be obtained, if not already known in every case of bleeding. Anti-D immunoglobulin must be administered when clinically indicated.

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6

Recognition and Treatment of Postabortion Complications

Janet Singer

Just under 1 million pregnancies are terminated each year in the United States (Jones & Jerman, 2017). Less than 1% of women terminating a pregnancy will experience a major complication, and most complications will be recognized in the immediate postabortion period and treated by the provider onsite (Cappiello, Beal, & Simmonds, 2011). Still, some abortion complications will emerge after the woman is discharged home, and clinicians working in an emergency department or obstetric triage unit need to be able to recognize these complications.

This chapter will cover symptomatology, physical assessment, and clinical management of the most common complications of abortion, including infection and bleeding. Other rare complications, including uterine perforation, cervical lacerations, sepsis, and a discussion of postabortion emotional issues, will also be included.

TYPES OF ABORTIONS

Early abortions can be accomplished with either aspiration or medication. Early aspiration abortion, sometimes called surgical abortion, is completed with dilation and suction curettage. The incidence of complications from aspiration abortion is outlined in Exhibit 6.1. In medication abortion, mifepristone and

EXHIBIT 6.1

Types and Incidences of Complications From Aspiration Abortion

- Incomplete abortion (0.3%–2.0%)
- Infection (0.1%–2.0%)
- Cervical laceration (0.6%–1.2%)
- Uterine perforation (<0.4%)
- Blood clots (<0.2%)
- Excessive bleeding (0.02%–0.3%)
- Death (0.0006%, 1 in 160,000 cases)

Sources: Achilles & Reeves (2011); National Abortion Federation (2006); Paul and Stein (2011).

EXHIBIT 6.2

Types and Incidences of Complications From Medication Abortion

- Incomplete abortion (<3%)
- Continuing pregnancy (<1%)
- Excessive bleeding (<1%)
- Infections (0.09%–0.6%)
- Death from *Clostridium sordellii*-related toxic shock (<0.001%)

Sources: American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 143 (2014); National Abortion Federation (2006, 2014); Paul and Stein (2011).

misoprostol are the medications of choice, though sometimes misoprostol alone or methotrexate is used. Exhibit 6.2 lists the incidence of complications from medication abortion. Later abortions involve performing dilation and evacuation of the pregnancy, or labor induction.

PRESENTING SYMPTOMATOLOGY

Women with complications from abortion will most often present with bleeding, pain, or both. While bleeding and crampy pain are normal after an abortion, symptoms, such as uterine tenderness, heavy bleeding, and fever, suggest a postabortion complication.

Nearly all women experience bleeding postabortion, typically for several days, followed by spotting for up to 4 weeks or longer (Davis, Westhoff, & DeNonno, 2000; Paul & Stein, 2011). Bleeding with a medication abortion is often heavier than a normal period (ACOG Practice Bulletin No. 143, 2014). However, comparative studies of aspiration and medication abortion show total blood loss to be similar in the two methods, with bleeding after a medication abortion having a longer duration (Jensen, Astley, Morgan, & Nichols, 1999; National Abortion Federation, 2014). Most women experience cramping after an abortion. With medication abortion, pain can range from mild to severe, usually resolving shortly after the abortion is complete (National Abortion Federation, 2014; Spitz, Bardin, Benton, & Robins, 1998). With aspiration abortion, most women experience only mild uterine cramping and this usually resolves within a few days.

HISTORY AND DATA COLLECTION

For any woman presenting postabortion, it is crucial to determine when the abortion occurred, what type was performed, and at what gestational age. The later in gestation that a woman has an abortion, the more likely she is to experience a complication. It is critical to obtain a description of any bleeding the woman is experiencing, the rate at which the woman is saturating pads, and whether any clots or tissue have been passed. In assessing pain, it is important to distinguish between cramping, which can be associated with retained products of conception (POCs), and fundal tenderness, which can

be associated with infection. Additional history includes whether the woman experienced any fevers, chills, lightheadedness, or any persistent pregnancy symptoms like breast tenderness, nausea, and vomiting. It is important to take a careful medication history. After an abortion, it is usual for women to receive antibiotics, commonly doxycycline, and uterotonics such as methergine. In gathering the history, it may be helpful to speak with the abortion provider to obtain details of the procedure and any immediate complications. Complete and compassionate care requires assessing each woman's emotional status, as the life situation that leads a woman to terminate a pregnancy can be complex and stressful. Careful assessment will identify those women most likely to need postabortion emotional support.

In addition, some women who have attempted a self-induced abortion may present for care. One study reported more than 2% of abortion patients had ingested something in an attempt to end a pregnancy. They most commonly used misoprostol, but also reported using herbs, teas, and vitamin C (Jones, 2011; Texas Policy Evaluation Project, 2015).

PHYSICAL EXAMINATION

Vital signs are obtained to assess for fever, tachycardia, and/or hypotension. If the uterus is enlarged above the pubic symphysis an abdominal examination is performed to assess for tenderness, uterine tone/consistency, and size. A speculum examination is an essential part of the physical assessment. During the speculum examination, inspect for bleeding and determine whether the bleeding is coming from the cervical os and whether there are any cervical or vaginal lacerations. The amount of bleeding in terms of number of scopettes used to wipe away the blood and the color of the blood is described. Any mucopurulent discharge and any POCs in the vagina or protruding from the cervical os should be identified. Gonorrhea and chlamydia cultures are collected, if these have not already been collected near the time of the abortion. After the speculum examination, a bimanual examination to assess the uterus for enlargement, tone, and tenderness is performed.

LABORATORY AND IMAGING STUDIES

Blood type and antibody screen are important to obtain. Typically, a woman who is Rh negative will have received Rh immune globulin from the abortion provider. However, any woman who is Rh negative and has self-induced an abortion will need Rh immune globulin. If bleeding is heavy, a complete blood count (CBC) and coagulation studies must be ordered. If a woman shows signs of sepsis, also obtain lactic acid level, renal function tests, and blood cultures.

While a single quantitative serum beta-hCG does not aid in diagnosing an abortion complication, it may be useful to follow serial quantitative results for appropriate decline over time. Beta-hCG levels fall steadily after a first trimester aspiration abortion, halving at least every 48 hours. Because beta-hCG levels are as high as 150,000 in early pregnancy, levels may still be high enough to cause urine pregnancy tests to remain positive for as long as 60 days postabortion. With medication abortion, beta-hCG levels continue to increase after mifepristone is administered and then generally, but not always,

decline rapidly after misoprostol is administered. Even women with a successful medication abortion may continue to have elevated beta-hCG levels (Fjerstad & Edelman, 2011).

Ultrasound is useful for determining if a gestational sac or fetal parts remain in the uterus. Determining endometrial thickness with ultrasound is *not* clinically useful postabortion, as there is no thickness that correlates consistently with the need to intervene (Cowett, Cohen, Lichtenberg, & Stika, 2004; Reeves, Lohr, Harwood, & Creinin, 2008). Ultrasound may be used to assess for intra-abdominal hematoma when uterine perforation is suspected in a woman exhibiting signs of hypovolemic shock.

POSTABORTION BLEEDING

DIFFERENTIAL DIAGNOSIS

When the presenting complaint is abnormal postabortion bleeding, uterine atony is almost always the cause. Atony is most often related to retained POCs/incomplete abortion. If atony is ruled out, lacerations are the next most likely cause of abnormal bleeding.

CLINICAL MANAGEMENT OF UTERINE ATONY AND RETAINED POCS

The first step in managing uterine atony is to massage the uterus and administer uterotonics (Kerns & Steinauer, 2013; National Abortion Federation, 2016). Table 6.1 lists the appropriate uterotonics to administer. In addition, intravenous (IV) access must be maintained and vital signs must be monitored throughout.

Table 6.1 Standard Agents for Treating Postabortion Hemorrhage

MEDICATION	DOSAGE AND ROUTE	SIDE EFFECTS AND CONTRAINDICATIONS
Misoprostol	800–1,000 mcg per rectum or 800 mcg sublingual	Diarrhea and abdominal pain in >10%
Methergine (methylergonovine maleate)	0.2 mg PO or IM. PO dose may be given 4 times/day for up to 1 week. IM dose may be repeated every 2–4 hours	Produces sustained contractions of smooth muscles. Contraindicated in patients with hypertension, Do not give IV due to hypertensive crisis/stroke
Hemabate (carboprost tromethamine)	250 mcg IM. May be given every 15–90 minutes up to 8 doses	Diarrhea, nausea, and vomiting in 33%–66%. Contraindicated in patients with active cardiac, pulmonary, renal, or hepatic dysfunction. May cause transient pyrexia and elevated blood pressure
Oxytocin	10 units IM or 10–40 units IV	Antidiuretic effect in high doses (rare)

Abbreviations: IM, intramuscular; IV, intravenous; mcg, micrograms; PO, per os (orally).

Adapted from Kerns and Steinauer (2013); National Abortion Federation (2016).

If on speculum examination POCs are seen at the cervical os, they may be removed with a ring forceps. If bleeding is *not* heavy and the woman shows *no signs of infection*, misoprostol is another option to bring about expulsion of the POCs (Paul & Stein, 2011). If no POCs are seen on ultrasound, the decision to aspirate the uterus is based on the clinical findings, not on an ultrasound measurement of endometrial thickness. It is normal for the uterus to contain hyperechoic tissue such as blood clots, and this rarely indicates a need for uterine evacuation (ACOG Practice Bulletin No. 143, 2014; Reeves et al., 2008). If POCs are identified in the uterus on ultrasound, and bleeding is heavy, aspiration may be indicated. After the uterus is emptied, specimens are rinsed in a strainer and viewed—ideally backlit and floating in water. Specimens can be sent to pathology for further identification and analysis as needed. If uterotonics and aspiration fail to control the bleeding, intrauterine tamponade with foley balloon or packing may be attempted.

CLINICAL MANAGEMENT OF CERVICAL LACERATION

A cervical laceration is treated by tamponading the laceration with a ring forceps for several minutes, and/or applying silver nitrate or Monsel's solution. Suturing is necessary if the bleeding does not stop with these interventions or if the laceration is extensive (Kerns & Steinauer, 2013; Lichtenberg & Grimes, 2009).

RARE COMPLICATIONS

If bleeding continues after the previously described clinical management, other diagnoses must be considered. These include uterine perforation, coagulopathy, placenta accreta, and arteriovenous malformations.

POSTABORTION PAIN

DIFFERENTIAL DIAGNOSIS

Pain, by itself, is rarely a sign of an abortion complication. However, pain is concerning when it is accompanied by other signs or symptoms, such as fever or heavy bleeding. If pain persists, an evaluation to rule out retained POCs (see the previous section for clinical management), endometritis, hematometra, or uterine perforation is necessary (National Abortion Federation, 2016).

CLINICAL MANAGEMENT OF ENDOMETRITIS

Postabortion endometritis with or without retained POCs must be considered in any woman who presents with lower abdominal pain postabortion. Other signs of endometritis include fever, enlarged tender uterus, abnormal bleeding, elevated white blood cell count, mucopurulent vaginal discharge, and malaise. Typically, these signs occur in the first few days postabortion (Lichtenberg & Grimes, 2009).

Maintain IV access and must be monitored vital signs throughout. It is essential to treat endometritis with broad spectrum antibiotics, as infection is likely to be polymicrobial in nature (Lichtenberg & Grimes, 2009). Exhibit 6.3

EXHIBIT 6.3

Antibiotic Treatment of Postabortion Endometritis

Inpatient

Recommended Regimen A

Cefotetan 2 g IV q 12 hr *OR* cefoxitin 2 g IV q 6 hr *plus* doxycycline 100 mg PO or IV q 12

Recommended Regimen B

Clindamycin 900 mg IV q 8 hr *plus* gentamicin loading dose IV or IM (2 mg/kg of body weight) followed by a maintenance dose (1.5 mg/kg) q 8 hr. May substitute single daily dosing (3–5 mg/kg)

Alternative Regimen

Ampicillin/sulbactam 3 g IV q 6 hr *plus* doxycycline 100 mg PO or IV q 12 hr

Outpatient

Ceftriaxone 250 mg IM × 1 *plus* doxycycline 100 mg PO bid × 14 days *with or without* metronidazole 500 mg PO bid × 14 days *OR*
Cefoxitin 2 g IM × 1 and probenecid 1 g PO concurrently × 1 *plus* doxycycline 100 mg PO bid × 14 days *with or without* metronidazole 500 mg PO bid × 14 days
OR
Other parenteral third-generation cephalosporins *plus* doxycycline 100 mg PO bid × 14 days *with or without* metronidazole 500 mg PO bid × 14 days

Source: Adapted from CDC (2015).

IM, intramuscular; IV, intravenous; PO, per os (orally).

details the antibiotic treatment of endometritis. Women with mild infection may be treated with oral antibiotics on an outpatient basis and then reexamined in 3 days to assure substantial clinical improvement. IV antibiotic therapy is indicated in women with severe illness, suspected pelvic abscess, immunocompromise, inability to tolerate oral medication, or failed outpatient treatment (Centers for Disease Control and Prevention [CDC], 2015; Paul & Stein, 2011).

CLINICAL MANAGEMENT OF HEMATOMETRA

Pain may also be due to clots remaining in the uterus. A woman with hematometra will have an enlarged, tender uterus and minimal to no bleeding. Reaspiration and the administration of uterotonics are the indicated treatments, and symptoms usually resolve quickly (Paul & Stein, 2011).

CLINICAL MANAGEMENT OF UTERINE PERFORATION/RUPTURE

Uterine perforation is a very rare complication of abortion. Clinically significant uterine perforations are likely to be suspected or recognized during the abortion

procedure. In managing a uterine perforation, IV access must be maintained and vital signs must be monitored throughout. Serial CBCs and coagulation labs are obtained. If a woman is transferred to the hospital with a suspected perforation but no abdominal pain or evidence of internal bleeding, observation without intervention may be appropriate. Uterine rupture requiring surgical intervention is more likely to occur during procedures performed later in gestation. It becomes a surgical emergency when trauma to organs other than the uterus is suspected. If there is suspicion of internal bleeding, surgery is needed to identify and repair the injury (Paul & Stein, 2011). A uterine perforation that is not diagnosed in the perioperative period may present as severe anemia or peritonitis, and those complications must be treated, in addition to evaluating the perforation itself.

RARE COMPLICATIONS

Toxic Shock

Medication abortion rarely results in infection. However, *Clostridium sordellii* has caused a few cases of fatal toxic shock syndrome in women undergoing medication abortion. Women with this atypical infection tend to be afebrile with little uterine tenderness and present with flu-like symptoms, tachycardia, hypotension, a marked increase in white blood cell count, and a high hemoglobin level (ACOG Practice Bulletin No. 143, 2014).

Clinical Management of *C. sordellii* Infection

There is little information to guide treatment in cases of *C. sordellii* infection and death usually occurs rapidly. It is believed that initiating antibiotics that suppress toxin synthesis (i.e., clindamycin) could be helpful in addition to usual resuscitative measures. Emergency surgery to remove necrotic tissue is necessary (Aldapel, Bryant, & Stevens, 2006; Eschenbach, 2015).

Sepsis

Since the legalization of abortion in the United States, septic abortion has become an exceedingly rare postabortion complication. Signs and symptoms vary, but patients who have some combination of abdominal tenderness, high fever, hypotension, tachycardia, tachypnea, bleeding, and low urine output must be treated with aggressive therapy that includes urgent evacuation of the uterus, broad spectrum IV antibiotics, IV fluids, and intensive care unit (ICU) level care (Eschenbach, 2015).

EMOTIONAL RESPONSE

In general, women end pregnancies because they do not desire to continue a particular pregnancy at a particular time. Such situations can cause distress and elicit feelings of sadness and loss (National Abortion Federation, 2006). Unwanted pregnancy and abortion correlate with conditions like poverty, exposure to violence, and drug use, which can all negatively affect mental health. It has been shown that abortion does not pose a threat to women's mental health. In fact, relief is the most commonly felt emotion after abortion. In a comprehensive review of the literature for the American Psychological

Association Task Force on Mental Health and Abortion, no significant difference was found between the psychologic outcomes of women with unplanned pregnancies who terminated pregnancies and those who continued pregnancies. Previous mental health status and absence of social supports are the strongest negative predictors of postabortion mental health status (Major et al., 2008).

CLINICAL PEARLS

- Major complications from abortion are rare (<1%).
- It is critical to differentiate normal postabortion bleeding and crampy pain from abnormal symptoms such as fever, uterine tenderness, and heavy bleeding.
- The postabortion uterus normally contains hyperechoic tissue, but this rarely indicates a need for uterine evacuation. Treat the patient, not the ultrasound.

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Abdominal Pain and Masses in Pregnancy

7

Moune Jabre Raughley

Adnexal masses complicate between 1 in 81 and 1 in 8,000 pregnancies (Leiserowitz, 2006; Whitecar, Turner, & Higby, 1999). Of these, less than 1% to 13% are malignant (Leiserowitz, 2006; Mukhopadhyay, Shinde, & Naik, 2016; Whitecar et al., 1999). Most adnexal masses in pregnancy are found incidentally on routine obstetric ultrasound (US) as they typically do not cause symptoms, and physical examination is limited by the gravid uterus (Leiserowitz, 2006). Pregnant women presenting with abdominal pain to an emergency department or obstetric triage setting frequently have a diagnostic US to assess the fetus, placenta, and adnexae.

The majority (50%–70%) of adnexal masses in pregnancy resolve spontaneously (Hoover & Jenkins, 2011; Webb, Sakhel, Chauhan, & Abuhamad, 2015). Those that persist into the second trimester pose the greatest concern, as they can be malignant, rupture, torse, or obstruct labor (Hoover & Jenkins, 2011). The actual risk of these complications, however, has been reported as less than 2% (Webb et al., 2015; Whitecar et al., 1999). In the symptomatic woman, one must determine if the adnexal mass necessitates urgent surgical intervention versus observation and pain management.

PRESENTING SYMPTOMATOLOGY

In the first trimester, symptomatic adnexal masses typically present with unilateral or bilateral pelvic cramping or pressure. Larger masses persisting into the second trimester tend to cause unilateral pelvic pain. Midline abdominal pain can occur if the gravid uterus displaces the mass. Severe pain may be associated with nausea and vomiting from peritoneal irritation. In rare cases, a ruptured mass can cause significant internal hemorrhage such that the woman reports dizziness in addition to pain. Uterine irritability or contractions may be seen in the late second and third trimester. In pregnant women with pain secondary to an adnexal mass, vaginal bleeding, rupture of membranes, or impact on fetal status are exceedingly rare. However, symptoms may reflect other underlying obstetric conditions with the incidental finding of an adnexal mass.

HISTORY AND DATA COLLECTION

Obtaining a history in a pregnant woman with abdominal pain is similar to doing so for the nonpregnant patient. Important factors to ascertain are time of onset and duration of pain, inciting or mitigating factors, quality, severity, location, and

radiation. Associated symptoms can include fever, nausea/vomiting, urinary symptoms, bowel changes, vaginal bleeding, leaking amniotic fluid, contractions, or flank pain. If nausea and/or vomiting are present, long-standing symptoms may represent nausea and vomiting of pregnancy, whereas an acute onset could be associated with the current clinical presentation. Accurate determination of gestational age is critical. Does the woman have a known intrauterine gestation or must ectopic pregnancy be excluded? Obtain the remaining history such as obstetrical, medical, surgical, and social history as per routine. Recent ultrasounds need to be reviewed to help determine how long a mass has been present.

PHYSICAL EXAMINATION

Physiologic changes in pregnancy can affect vital signs. For example, mild tachycardia may be normal in the third trimester but would be atypical in early gestation. Likewise, blood pressure reaches its nadir in the second trimester. Tachycardia and hypotension can also result from significant internal hemorrhage.

In addition to routine cardiopulmonary examination, abdominal examination, and assessment for costovertebral angle tenderness, a sterile speculum and vaginal examination are performed to evaluate for adnexal or uterine tenderness, cervical dilation, and potential rupture of membranes. It is important to ensure an empty bladder prior to abdominal exam to optimize palpation of the adnexa. Also, include an evaluation for presence of lymphadenopathy, pleural effusion, and ascites, as well as a breast examination, should be performed if malignancy is suspected (Mukhopadhyay et al., 2016). Further examination is performed as directed by history.

At 6 weeks gestation, the uterus is similar in size to the nonpregnant state and the adnexa may be palpable in a nonobese patient. The uterine fundus is at the level of the pubis symphysis by 12 weeks and at the umbilicus at 20 weeks. Therefore, clinical examination of the adnexa is extremely limited after 12 weeks gestation.

LABORATORY AND IMAGING STUDIES

If a mass is suspected, US is the preferred imaging modality as it allows for optimal characterization of the mass and determination of its malignant potential (Hoover & Jenkins, 2011; Whitecar et al., 1999). Several studies have shown that antenatal US correctly diagnosed all the malignant tumors in these series (Hoover & Jenkins, 2011; Schmeler et al., 2005; Whitecar et al., 1999). US can be used to examine the kidneys and to assess free fluid in the pelvic cul-de-sac, abdominal ascites in Morison's pouch, and hemoperitoneum. US has the additional benefit of being cheaper and faster to obtain in most circumstances compared to other modalities.

Magnetic resonance imaging (MRI) can be employed if additional imaging is needed and is especially useful to delineate the extent and nature of masses that are too large to visualize completely on US or for surgical planning. An MRI should also be considered if appendicitis or other gastrointestinal causes such as inflammatory bowel disease and diverticulitis are suspected (Naqvi & Kaimal, 2015). As with US, MRI avoids maternal and fetal exposure to radiation.

Nonobstetric causes of abdominal pain are best evaluated by computed tomography (CT), as it provides higher resolution imaging of the gastrointestinal tract. Although CT is generally considered relatively safe in pregnancy, it should only be performed when absolutely necessary, as it does expose the mother and

fetus to 2 to 4 rads per abdominopelvic study (Hoover & Jenkins, 2011). With regard to the use of iodinated contrast media for CT and gadolinium for MRI, both the American College of Radiology and American College of Obstetricians and Gynecologists (ACOG) note the limited data on safety in pregnancy and advise limiting use to when benefits greatly outweigh risks (Jaffe, Miller, & Merkle, 2007).

Laboratory testing includes a complete blood count to assess for leukocytosis and/or anemia, as these may be present in the setting of torsion or ruptured ovarian cyst. Urinalysis may help exclude urinary tract causes of pain.

Serum tumor markers are of limited utility in the initial assessment of pregnant women as cancer antigen 125 (CA-125) levels are normally elevated in pregnancy with a peak in the first trimester (range, 7–251 units/mL) followed by a steady decrease. Other serum tumor markers such as alpha-fetoprotein (AFP), beta-human chorionic gonadotropin (beta-hCG), and lactate dehydrogenase (LDH) are likewise significantly affected by pregnancy (Hoover & Jenkins, 2011). Tumor markers are largely used to follow disease progression and control in women in whom a malignancy has already been diagnosed (ACOG, 2007; Hoover & Jenkins, 2011).

DIFFERENTIAL DIAGNOSIS

In addition to the adnexal mass as the source of abdominal pain, the differential diagnosis of abdominal pain in pregnant women must include other obstetric and nonobstetric causes of pain. Common sources of pain, unrelated to adnexal masses, include physiologic abdominal pain of early pregnancy, spontaneous abortion, round ligament pain, appendicitis, gastroenteritis, nephrolithiasis, urinary tract infections, and pyelonephritis. Ectopic pregnancy must be included in the differential diagnosis in women with unlocated pregnancies.

Functional cysts such as corpus luteum are among the most common adnexal masses in pregnancy (Hoover & Jenkins, 2011). Other benign masses include mature cystic teratoma, serous or mucinous cystadenoma, endometrioma, paraovarian cysts, and leiomyoma. Malignant tumors are rare. Of these, the most common types are germ cell, stromal, or epithelial tumors of low malignant potential (ACOG, 2007). See Table 7.1 for incidence of common adnexal masses.

Table 7.1 Incidence of Common Adnexal Masses in Pregnancy

TYPE OF MASS	PERCENTAGE (%)
Mature cystic teratoma	25
Corpus luteum and functional cysts	17
Serous cystadenoma	14
Mucinous cystadenoma	11
Endometrioma	8
Carcinoma	2.8
Low malignant potential tumor	3
Leiomyoma	2
Paraovarian cysts	<5
Pelvic kidney	<0.1

Sources: Cinman, Okeke, and Smith (2007); Hoover and Jenkins (2011).

The fundamental question in the acute management of pregnant women with adnexal masses is whether to observe or intervene surgically (and when to do so emergently). Factors to consider include the following: degree of suspicion for malignancy, hemodynamic stability, concern for torsion, and pain severity. Most hemodynamically stable women presenting to an emergency department without evidence of torsion may be observed acutely and then managed on an outpatient basis. This allows time to obtain additional imaging or subspecialist consultation, as needed. Abdominopelvic pain may be treated with acetaminophen or oral narcotics in the interim.

Given the inherent risks of surgery, there is a growing body of evidence to support observation and delay of surgery until the postpartum period. The vast majority of adnexal masses noted in pregnancy spontaneously resolve, thus obviating the need for surgical intervention (Hoover & Jenkins, 2011; Schmeler et al., 2005; Whitecar et al., 1999).

Surgery may increase the risk of spontaneous abortion, preterm labor, and rupture of membranes. However, observation can increase risk of torsion, rupture of the mass, peritonitis, hemorrhage, delay in diagnosis of cancer, and obstruction of delivery. Compared with pregnant women not undergoing surgery, the overall risk of premature delivery increased by 22% in those who had surgery, regardless of the surgical approach (Hoover & Jenkins, 2011).

There is conflicting evidence as to whether emergent versus scheduled surgery carries an increased risk of fetal adverse effects. Whitecar et al. (1999) reviewed 130 cases of pregnant women with adnexal masses that required laparotomy. Of these, 16 were emergent. They found that laparotomy at less than 23 weeks gestational age was associated with significantly fewer adverse pregnancy outcomes than at greater than 23 weeks, but there were no significant differences in maternal morbidity or fetal outcomes between emergent and scheduled laparotomy. A later study of 89 women with adnexal masses in pregnancy similarly showed no statically significant difference in adverse pregnancy outcomes following elective versus emergent surgery (Lee, Hur, Shin, Kim & Kim, 2004). A large systematic review of 12,542 procedures in 54 papers assessing pregnancy outcomes after emergent versus elective surgery for non-obstetric indications (e.g., appendicitis, adnexal mass, cholecystitis) concluded that current anesthetic and surgical techniques do not significantly increase the risk of spontaneous abortion, major birth defects, or maternal mortality (Cohen-Kerem, Railton, Oren, Lishner, & Koren, 2005). Reliable assessments of preterm birth and fetal loss rates are difficult to ascertain in this review and others as adverse fetal outcomes in emergent surgery are more likely to be related to the underlying condition that necessitated surgery (e.g., appendicitis) rather than the surgery itself (Cohen-Kerem, et al., 2005; Hoover & Jenkins, 2011). An ACOG Committee Opinion on nonobstetric surgery during pregnancy recommends performing urgent surgery at any gestational age but to delay nonurgent surgery until the second trimester or, preferably, until after delivery (ACOG, 2011).

A study by Schmeler et al. (2005) reviewed 127,177 deliveries and identified 59 women (0.05%) with an adnexal mass 5 cm or greater. Median gestational age at diagnosis was 12 weeks and 80% were diagnosed on US; the rest were identified at the time of the cesarean section. Seventeen women (29%) underwent surgery. Of these, the majority were planned laparotomies for suspected malignancy with the emergent surgeries being performed for torsion. One woman in the surgical group had preterm premature rupture of membranes at 23 weeks with subsequent delivery at 28 weeks. No other adverse fetal outcomes were reported. Forty-two women in the observation group were observed expectantly in the antenatal period and then had surgery either intrapartum

or postpartum. The median gestational age at delivery for all women was 39 weeks. There was no statistically significant difference in obstetric outcomes between the surgical and observation groups. All the malignant masses had concerning sonographic findings that prompted antenatal surgery. The authors concluded that the risk of malignancy is less than 1% in pregnant women with incidentally identified masses with low-risk features on US, which is similar to rates in nonpregnant women. As such, expectant management may be a reasonable option in appropriately selected women.

In 2010, the Society for Radiologists in Ultrasound (SRU) released a consensus statement on the recommended management and follow-up for adnexal masses that are incidentally seen on US in asymptomatic, nonpregnant women (Levine et al., 2010). Although the guidelines are intended for masses in the nonpregnant population, other studies have utilized similar management in pregnant women (Hoover & Jenkins, 2011; Schmeler et al., 2005; Zanetta et al., 2001). These guidelines allow stratification of adnexal masses into those that require further follow-up and those that do not on the basis of the presence of features suggestive of malignancy or benignity. The guidelines for premenopausal women include the following: normal ovaries are typically less than 3 cm in size, round or oval with thin smooth walls, anechoic spaces, and no flow seen on color Doppler US. Ovaries may contain multiple physiologic follicles or simple cysts that are considered normal if they measure less than 3 cm. The corpus luteum appears as a thick-walled cyst with or without crenulated inner margins, measures less than 3 cm, and often has internal echoes with a peripheral ring of vascularity on color Doppler US. Physiologic cysts (Figure 7.1) and corpus luteum cysts (Figure 7.2) do not require further follow-up.

Simple cysts as noted in Figure 7.3 that are anechoic with smooth thin walls measuring 5 to 7 cm without any features of complexity may be followed with annual repeat imaging in premenopausal women. Those measuring greater than 7 cm can be further evaluated with additional imaging or surgical evaluation if clinically indicated.

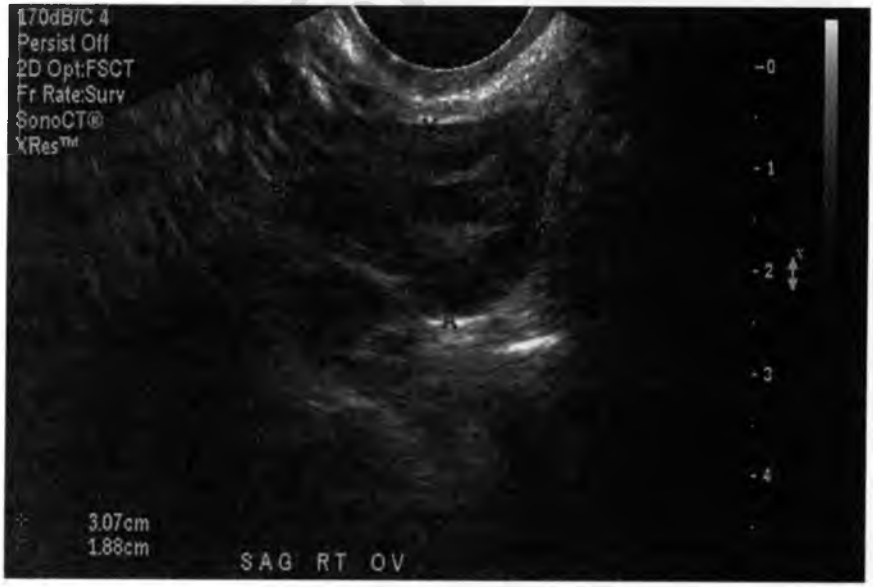

Figure 7.1 Normal ovary with physiologic follicles

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

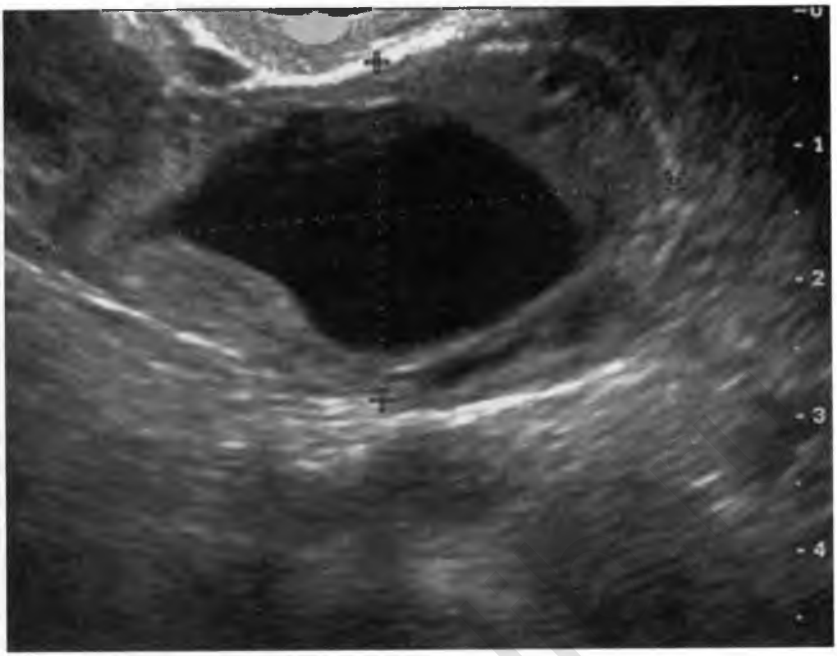

Figure 7.2 Corpus luteum cyst

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

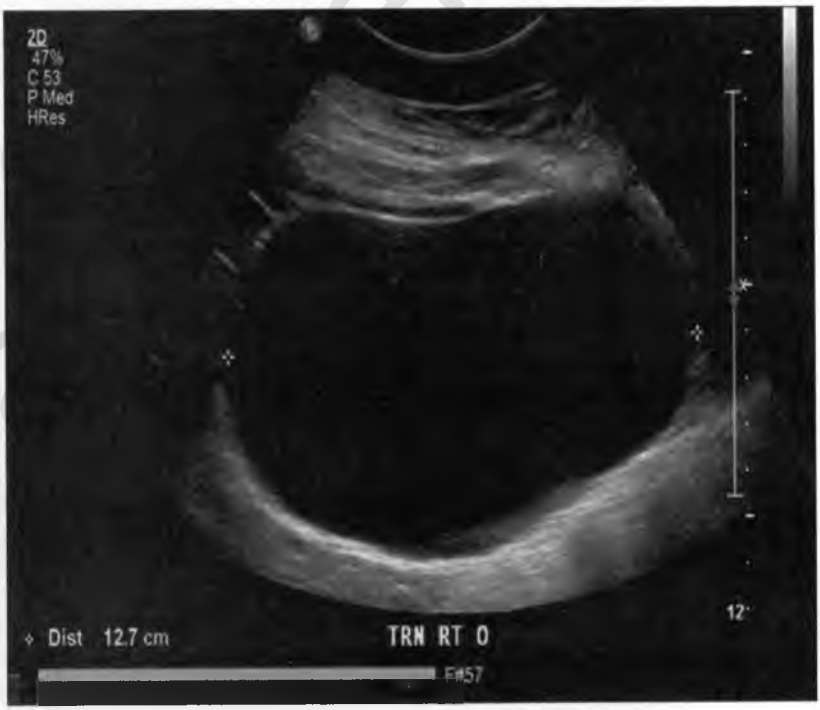

Figure 7.3 Simple cyst

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

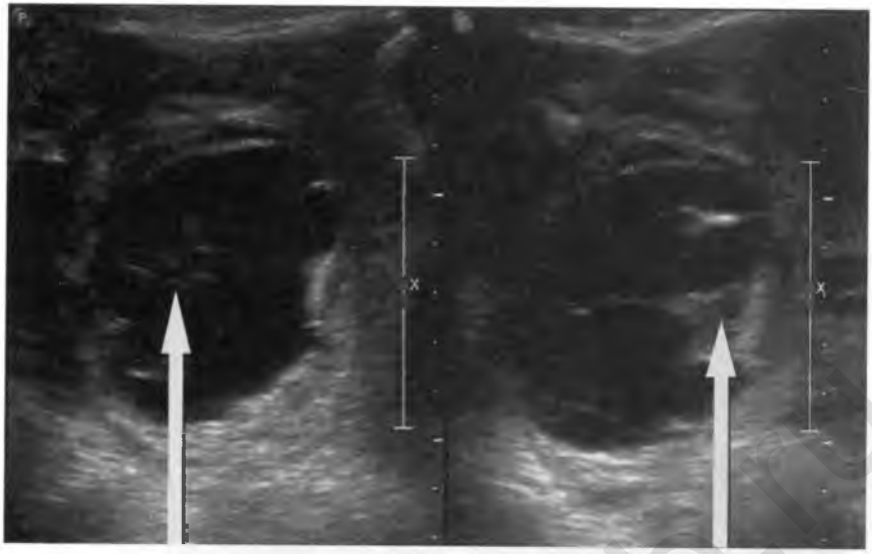

Figure 7.4 Hemorrhagic cyst

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

Hemorrhagic cysts (Figure 7.4) have a reticular pattern of internal echoes or multiple irregular hyperechoic structures within the cyst. They may have solid-appearing areas with concave margins without internal flow on color Doppler US. No follow-up is necessary for hemorrhagic cysts measuring less than 5 cm, but those greater than 5 cm should be reimaged at 6 to 12 weeks to document resolution.

Endometriomas (Figure 7.5) have homogeneous low-level internal echoes that give the classic "ground glass" appearance. Although they do not have a solid component, endometriomas can have small echogenic foci in the walls. Mature cystic teratomas (Figure 7.6) have a focal or diffuse hyperechoic component and may have hyperechoic lines or dots as well as areas of acoustic shadowing. Both endometriomas and mature cystic teratomas should be followed annually to document stability if not surgically removed. Peritoneal inclusion cysts and hydrosalpinx can be reimaged as clinically indicated.

Sonographic features concerning for neoplasm include nodularity, calcifications, and septations. Thin septations and solitary nodules without flow are likely to be benign neoplasms, whereas thick septations or nodules with blood flow are worrisome for malignancy. A review of sonographic scoring systems to predict malignancy in nonpregnant patients found that abnormal wall structure of adnexal masses most consistently predicted malignancy (Klangsin, Suntharasaj, Suwanrath, Kor-anantakul, & Prasartwanakit, 2013). Any of the previous findings warrant subspecialist consultation and/or additional imaging with MRI for possible surgical evaluation (Levine et al., 2010).

When emergent surgical intervention is warranted, the surgical approach must be determined. If suspicion for malignancy is high, pre- or intraoperative gynecologic oncology consult and frozen pathology must be considered. Frozen-section accuracy varies between 72% and 89% (ACOG, 2007).

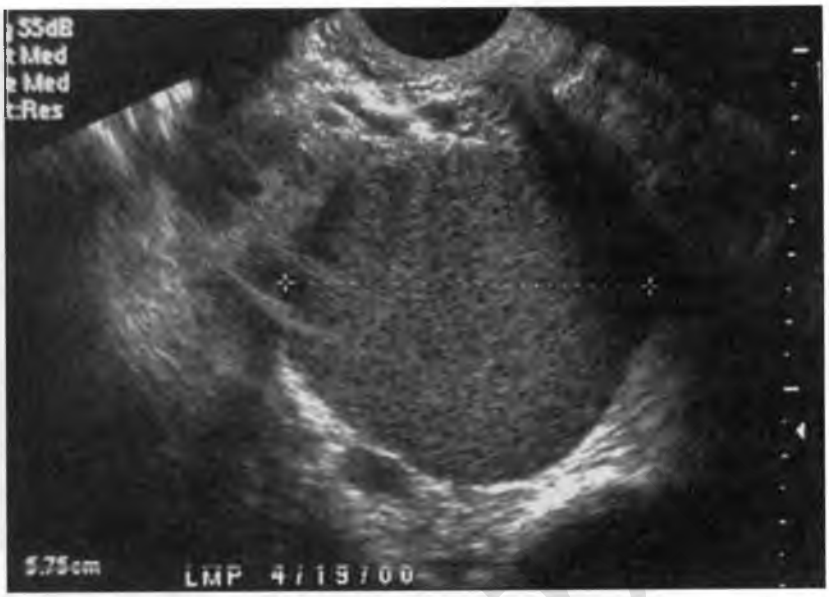

Figure 7.5 Endometrioma

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

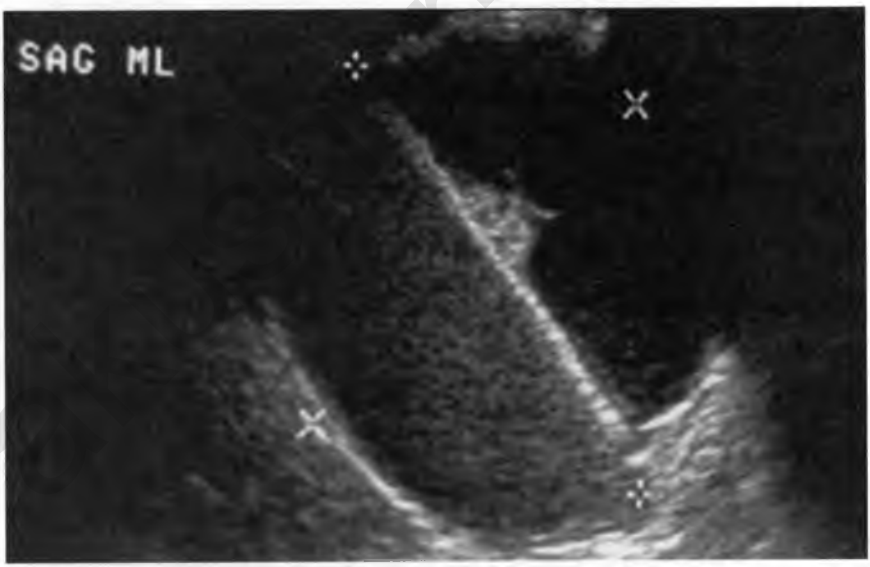

Figure 7.6 Mature cystic teratoma (dermoid)

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

It is unclear whether laparoscopy or laparotomy is preferable in the gravid woman. However, since laparoscopy has become the standard approach in the nonpregnant woman with an adnexal mass, its use in pregnancy has become common, safe, and effective (Ngu, Cheung, & Pun, 2014).

The hypothetical concerns with laparoscopy during pregnancy stem from a paucity of data on effects of pneumoperitoneum, potential for fetal acidosis from maternal conversion of insufflated carbon dioxide gas to circulating carbonic acid, injection of carbon dioxide into the uterus, and potential for uterine injury from the Veress needle or trochar (Hoover & Jenkins, 2011). Several studies evaluating laparoscopy have demonstrated maternal and fetal safety (Balthazar, Steiner, Boggess, & Gehrig, 2011; Cohen-Kerem, et al., 2005; Koo et al., 2012; Ngu et al., 2014). Laparotomy must be performed in certain clinical scenarios, such as extensive adhesive disease, in the third trimester or to permit staging, and so forth (Naqvi & Kaimal, 2015). Laparoscopy has several significant advantages over laparotomy however, such as shorter recovery period with faster postoperative ambulation, less postoperative pain requiring less narcotic use, less need for uterine retraction, and thus less uterine irritability (Hoover & Jenkins, 2011; Ngu et al., 2014).

In 2008, the Society of American Gastrointestinal and Endoscopic Surgeons issued the following guidelines for use of laparoscopy in pregnant women (Yumi, 2008): laparoscopy is safe at any gestational age, though 16 to 20 weeks is optimal. The woman is placed in the left lateral decubitus position to minimize vena caval compression. An open (Hasson) technique can be safely performed for initial abdominal access, though use of the Veress needle may be considered if performed under US guidance, and the location is adjusted to the fundal height (at least 6 cm above or in the left upper quadrant). Intra-abdominal pressure of 10 to 15 mmHg with Trendelenburg position may be safely used. Capnography should be used for intraoperative CO_2 monitoring. Routine blood gas monitoring is not indicated. Pneumatic compression devices can be used during and after surgery along with early ambulation for prophylaxis against deep venous thrombosis.

In recent years, robotic surgery has also been successfully used in pregnancy. A 2013 retrospective cohort study by Eichelberger, Cantrell, Strauss, and Boggess compared the safety of robotic versus laparoscopic surgery for adnexal masses in pregnancy and found no significant differences in operative time, rate of conversion to laparotomy, intraoperative or postoperative complications, or maternal-fetal outcomes. The robotic group did have significantly shorter hospital stays and less blood loss (Eichelberger et al., 2013).

The American College of Obstetricians and Gynecologists recommends fetal status be assessed before and after the procedure with fetal heart tones for a previable fetus and electronic fetal monitoring with tocometry for a viable fetus. Monitoring may be continued intraoperatively if technically feasible (ACOG, 2011). Though ACOG does not specifically address the use of prophylactic tocolysis, it may be considered perioperatively for signs of preterm labor on an individualized basis.

In summary, based on the existing evidence, ACOG recommends evaluating the pregnant woman with an adnexal mass similarly to the premenopausal nonpregnant woman. Ultrasound should be the first imaging modality followed by MRI if further imaging is necessary. Cancer antigen 125 levels are usually mildly elevated in pregnancy (<250 units/mL) and not typically associated with malignancy. Persistent, large adnexal masses are frequently surgically removed in the second trimester to prevent emergent intervention at a later time for torsion or rupture, though there is a lack of supporting data for this. Given the low risk for both malignancy and acute complications, expectant management can be considered in pregnant women with adnexal masses.

Periviable Obstetric Management

8

Lindsay Maggio

PERIVIABILITY

The limit of viability has been a moving target in the past several decades. With improvements in neonatal care and interventions that have reduced morbidity and mortality, there has been a shift in viability to earlier gestational ages. Assessment and management of a periviable gestation is one of the most complex problems encountered in an obstetric triage unit. While 0.5% of births occur before the third trimester, prematurity and its complications account for more than 40% of neonatal deaths (Ecker et al., 2016; Raju, Mercer, Burchfield, & Joseph, 2014). In 2014, a joint workshop of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the Society for Maternal-Fetal Medicine (SMFM), the American Academy of Pediatrics, and the American College of Obstetricians and Gynecologists (ACOG) convened and defined periviability: 20 0/7 weeks of gestation through 25 6/7 weeks of gestation (Raju et al., 2014).

Births during these gestational ages are wrought with complex decisions for the obstetric and neonatal teams. These decisions are ethically challenging and, because the clinical situation often evolves quickly, decisions must be made expediently. Adding to this complexity is the heterogeneity in the literature regarding the types of interventions used, as well as the degree and consistency of resuscitative efforts. Institutions also vary greatly in the accessibility to tertiary neonatal care. These issues further complicate and add to the already difficult challenge of counselling parents.

Neonatal Morbidity and Mortality

Prior to the 1980s, neonatal death was almost 100% assured if delivery occurred prior to 24 weeks of gestation, regardless of birth weight (Koops, Morgan, & Battaglia, 1982). Over the past 20 years, improvements in neonatal survival have been most marked from 23 to 24 weeks of gestation (Stoll et al., 2015). Survival rates are also improved when delivery and resuscitation occur at a tertiary center (Lubchenco et al., 1989). Several studies have demonstrated increasing neonatal survival to hospital discharge rates with increasing gestational age, as noted in Table 8.1 (Costeloe et al., 2012; Ishii, Kono, Yonemoto, Kusuda, & Fujimura, 2013; Kyser, Morriss, Bell, Klein, & Dagle, 2012; Mehler et al., 2012; Rysavy et al., 2015; Stoll et al., 2010; Wood, Marlow, Costeloe, Gibson, & Wilkinson, 2000).

Even in the setting of survival in extremely preterm neonates, there are high rates of moderate to severe long-term disability. These rates decline with increasing gestational ages and range from 30% to 60% at 22 weeks, 25% to 55% at 23 weeks, 28% to 45% at 24 weeks, and 17% to 38% at 25 weeks (Ecker et al., 2016; Ishii et al., 2013; Marlow, Wolke, Bracewell, & Samara, 2005; G. P. Moore, Lemyre, Barrowman, & Daboval, 2013; T. Moore et al., 2012; Rysavy et al., 2015; Wood et al., 2000).

Table 8.1 Survival to Hospital Discharge by Gestational Age at Delivery

AUTHOR	22 0/7–22 6/7	23 0/7–23 6/7	24 0/7–24 6/7	25 0/7–25 6/7
Stoll et al. (2010)	6%	26%	55%	72%
Rysavy et al. (2015)	5.1%	23.6%	54.9%	72%
Costeloe et al. (2012)	2%	19%	40%	66%
Mehler et al. (2012)	41%	76%	82%	80%
Kyser et al. (2012)	33%	58%	87%	85%
Wood et al. (2000)	1%	11%	26%	44%

Birthweight and gestational age are the most common factors used in predicting survival and severe morbidity. There are many more factors that have been associated with perinatal outcomes, such as fetal gender, plurality, location of delivery (Lasswell, Barfield, Rochat, & Blackmon, 2010; Lubchenco et al., 1989), use of magnesium sulfate, and use of antenatal corticosteroids (ACS). In an effort to help clinicians counsel patients at risk for periviable birth, the NICHD Neonatal Research Network created a tool that combines five variables (gestational age, birthweight, exposure to ACS, sex, and plurality). This tool can be found at https://neonatal.rti.org. Although this tool has some limitations, it is the most widely available resource at the current time (Ecker et al., 2016). Clinicians must check with the neonatology department to determine if there are site-specific estimates of survival, as these may be more accurate. Finally, a multidisciplinary approach to counseling with obstetricians, perinatologists, and neonatologists must be employed for these difficult and sensitive scenarios to ensure the parents receive consistent information. The most common reasons for pre- and periviable births are listed in Table 8.2 and will be reviewed individually.

PREVIABLE AND PERIVIABLE PRETERM LABOR

PRESENTING SYMPTOMATOLOGY

Spontaneous preterm labor is defined as regular uterine contractions that cause a change in cervical dilation, effacement, or both, or initial presentation of regular uterine contractions and dilation of at least 2 cm (ACOG, 2016a). Traditionally, preterm labor was defined as occurring between 20 0/7 weeks of gestation and 36 6/7 weeks of gestation. Since the mechanisms causing preterm labor and delivery between 16 0/7 and 20 0/7 are believed to be similar to the mechanisms that exist beyond 20 0/7 weeks, the recommendations for treatment are likewise similar (Iams, 2014). Women will present with pain, ranging from intermittent menses-like cramping or pelvic pressure to painful uterine contractions. Vaginal spotting and an increase in vaginal discharge may be associated symptoms.

HISTORY AND DATA COLLECTION

One of the most common risk factors for preterm birth is infection. As such, a thorough review of systems and documentation of the presence or absence of fever, chills, abdominal pain, purulent vaginal discharge, dysuria, flank pain, nausea, vomiting, and diarrhea is needed on presentation. The treatment of

Table 8.2 Previable and Periviable Birth—Causes and Associated Findings

	PRETERM LABOR	PRETERM PREMATURE RUPTURE OF MEMBRANES	CERVICAL INSUFFICIENCY	STILLBIRTH
Clinical presentation	Abdominal, back, or pelvic pain or discomfort Vaginal bleeding or spotting	Leakage of vaginal fluid Increased vaginal discharge	Pelvic or vaginal pressure Vaginal discharge Cramping/ backache Spotting Mild contractions	Absent fetal movement Vaginal bleeding Contractions
Risk factors	Prior preterm labor Infection Abruption PPROM Multiple gestations Uterine anomalies	Prior preterm premature ROM History of cervical conization Second trimester vaginal bleeding Connective tissue disorder Low BMI Cigarette smoking	History recurrent/ prior preterm delivery or midtrimester loss Cervical injury including cervical surgical procedures Exposure to DES	Advanced maternal age Obesity Multiple gestation Tobacco or drug use Abruptio placenta Hypertension Diabetes Infection
Physical examination findings	Cervical dilation or effacement Cervical change over 30–60 minutes	Vaginal pool Amniotic fluid pool pH > 7 Ferning on dry slide	Cervical dilation > 4 cm Membranes through cervical os	Nonspecific
Ultrasound findings	Not applicable	+/– Oligohydramnios	Cervical length < 25 mm in women with previous preterm birth and singleton gestation Cervical length < 15 mm in women without previous preterm birth	Absent fetal cardiac activity

Abbreviations: BMI, body mass index; DES, Diethylstilbestrol; PPROM, preterm premature rupture of membranes; ROM, rupture of membranes.

some infections, such as pyelonephritis, can halt preterm labor. Additional risk factors for preterm labor include abdominal trauma, placental abruption, history of preterm birth, multiple gestation, premature rupture of membranes, uterine fibroids, tobacco use, low body mass index, low socioeconomic status, and Black race (Goldenberg, Culhane, Iams, & Romero, 2008).

PHYSICAL EXAMINATION AND DIAGNOSTIC STUDIES

The diagnosis of preterm labor is made when there are regular contractions with active cervical change, or regular contractions and cervical dilation greater

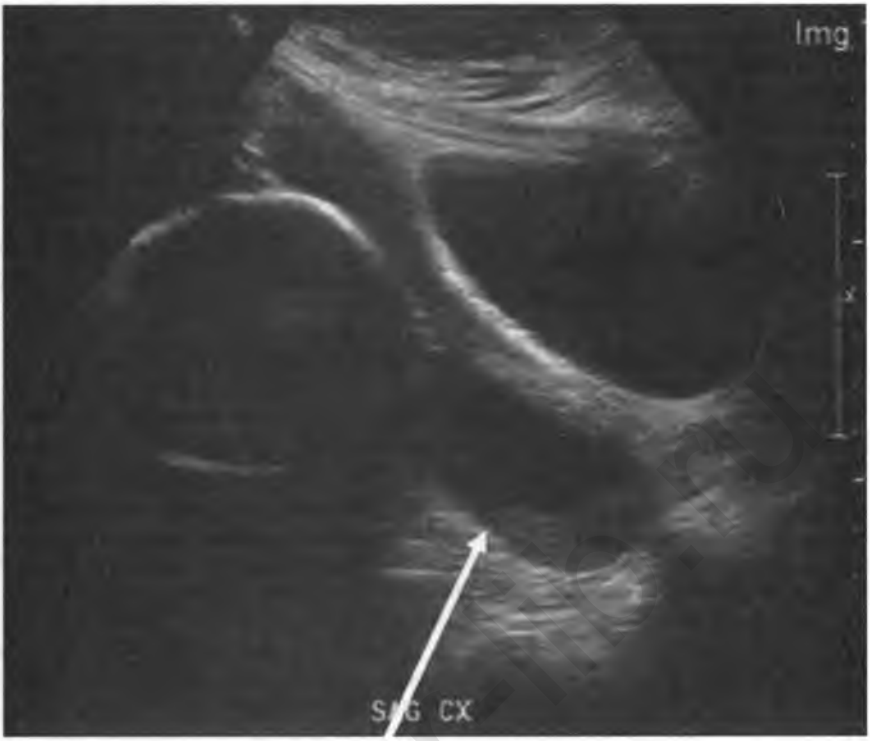

Figure 8.1 Cervical shortening with funneling

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

than 2 cm (ACOG, 2016a). Evaluation of vital signs and a physical examination are performed to rule out infection or other causes of preterm labor. If the gestational age is uncertain, biometry is performed so that a best gestational estimate can be attained, which will help guide treatment, management decisions, and counselling. Transvaginal cervical length monitoring is another tool that can be used in determining risk for preterm birth. However, this tool has been evaluated mainly for gestations after 24 weeks (Fuchs, Henrich, Osthues, & Dudenhausen, 2004; Ness, Visintine, Ricci, & Berghella, 2007). An example of a shortened cervix with funneling of membranes through the internal os is noted in Figure 8.1.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for labor in the periviable gestation includes obstetric/gynecologic causes such as preterm contractions (without cervical change or dilatation), round ligament pain, degenerating fibroids, ovarian cyst rupture, or torsion. Gastrointestinal, musculoskeletal, and genitourinary causes must also be considered. Infectious causes, such as cervicitis, pelvic inflammatory disease, cystitis, pelvic abscesses, appendicitis, and intra-amniotic infections, must also be ruled out.

If an intrauterine infection is confirmed, delivery must occur to prevent maternal sepsis. In the absence of an intrauterine infection, a pregnant woman can be offered expectant management and be allowed to progress through labor without intervention. Women who desire active management can be admitted to labor and augmented with prostaglandins, such as misoprostol. In both scenarios, women must be offered adequate pain control.

PERIVIABLE CONSIDERATIONS

Antenatal Corticosteroids

Antenatal corticosteroids (ACS) use has been shown to reduce perinatal mortality and decrease neonatal morbidity (ACOG, 2016a; Carlo et al., 2011; Chawla et al., 2010, 2013; Mori, Kusuda, Fujimura, & Neonatal Research Network Japan, 2011; Raju et al., 2014). Initially ACS use was targeted at pregnancies with gestational ages of 24 to 34 weeks; however, there are also data showing benefit from ACS when given prior to 24 weeks of gestation (Abbasi, Oxford, Gerdes, Sehdev, & Ludmir, 2010). An observational study by the *Eunice Kennedy Shriver* NICHD Neonatal Research Network revealed a reduction in death and neurodevelopmental impairment in infants exposed to ACS and born at 23 weeks of gestation (AOR, 0.58; 95% CI [0.42–0.80]), 24 weeks of gestation (AOR, 0.62; 95% CI [0.49–0.78]), and 25 weeks of gestation (AOR, 0.61; 95% CI [0.50–0.74]), but not at 22 weeks of gestation (Carlo et al., 2011). In addition, there was a decreased incidence of death, intraventricular hemorrhage, periventricular leukomalacia, and necrotizing enterocolitis in those born between 23 and 25 weeks of gestation (Carlo et al., 2011). For this reason, the ACOG and SMFM consensus guidelines recommend ACS at 24 weeks of gestation, suggest considering them at 23 weeks of gestation, and recommend not using them prior to 23 weeks of gestation. A summary table of the complete consensus guidelines is noted in Table 8.3.

Magnesium Sulfate for Fetal Neuroprotection

The use of antenatal magnesium sulfate has been shown to improve neurologic outcomes in premature infants (Conde-Agudelo & Romero, 2009; Costantine & Weiner, 2009; Doyle, Crowther, Middleton, Marret, & Rouse, 2009; Rouse et al., 2008). Although these studies have not included women with pregnancies prior to 24 weeks gestation, there is no increased risk of mortality (RR 1.04; [0.92–1.17]) when magnesium sulfate is given (Doyle et al., 2009). The ACOG and SMFM have recommended that it be used at 24 weeks of gestation and considered at 23 weeks of gestation.

Tocolytic Therapy

While most tocolytic therapy has been shown to reduce the rate of preterm birth within 48 hours (Flenady et al., 2014; Neilson, West, & Dowswell, 2014), these studies have not been performed in women at periviable gestations. While a brief delay in delivery could promote the use of ACS, the use of tocolytics has not consistently shown improvements in neonatal outcomes (ACOG, 2016a). Both the ACOG and SMFM recommend tocolytics after 24 weeks of gestation

Table 8.3 General Guidance Regarding Obstetric Interventions for Periviable Gestations

INTERVENTION	20 0/7 TO 21 6/7 WEEKS	22 0/7 TO 22 6/7 WEEKS	23 0/7 TO 23 6/7 WEEKS	24 0/7 TO 24 6/7 WEEKS	25 0/7 TO 25 6/7 WEEKS
Neonatal Assessment for Resuscitation	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
ACS	Not recommended (Level 1A evidence)	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
Limited tocolysis for ACS administration	Not recommended (Level 1A evidence)	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
Magnesium sulfate for neuroprotection	Not recommended (Level 1A evidence)	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
Antibiotics during expectant management of PPROM to prolong latency	Consider (Level 2C evidence)	Consider (Level 2C evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
Group B Streptococci antibiotic prophylaxis	Not recommended (Level 1A evidence)	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Recommended (Level 1B evidence)	Recommended (Level 1B evidence)
Cesarean delivery for fetal indications (abnormal testing or malpresentation in labor)	Not recommended (Level 1A evidence)	Not recommended (Level 1A evidence)	Consider (Level 2B evidence)	Consider (Level 1B evidence)	Recommended (Level 1B evidence)

ACS, antenatal corticosteroids; PPROM, preterm premature rupture of membranes.

Source: Ecker et al. (2016).

and consider them at 23 weeks of gestation. The main purpose of tocolytics in this setting is to allow for the administration of ACS.

Cesarean Delivery

Cesarean delivery is not indicated in the periviable period as routine, as it has not been shown to decrease morbidity and mortality (Alfirevic, Milan, & Livio, 2013), or improve 2-year neurodevelopmental scores (Običan et al., 2015). In the setting of malpresentation, cesarean delivery may offer improved short-term survival and decreased morbidity, but at 6 months there is no difference in survival (Tucker Edmonds, McKenzie, Macheras, Srinivas, & Lorch, 2015). Cesarean

deliveries at the periviable gestation frequently require classical uterine incisions. Because these incisions are associated with increased maternal morbidity, the mode of delivery is individualized for each patient depending on the clinical circumstances. Careful counselling regarding the risks of surgery compared to the limited benefit to the neonates must be undertaken, and cesarean delivery ought to be reserved only for maternal indications (e.g., placenta previa) prior to 22 weeks of gestation (Ecker et al., 2016).

PREVIABLE AND PERIVIABLE PREMATURE RUPTURE OF MEMBRANES

PRESENTING SYMPTOMATOLOGY

A pregnant woman with preterm premature rupture of membranes (PPROM) may present with a variety of symptoms. She may experience a distinct gush of fluid from the vagina or give a history of several days of increased vaginal discharge and spotting. Intra-amniotic infection often precedes PPROM (Gabbe, Niebyl, & Simpson, 2016). Women with infections may also present with fever, nausea or vomiting, exquisite abdominal or pelvic pain, and/or foul-smelling vaginal discharge. The following risk factors are associated with PPROM: prior history of PPROM, history of second trimester vaginal bleeding, history of cervical conization or shortened cervix, amniocentesis, low body mass index, low socioeconomic status, cigarette smoking, connective tissue disorder, and multifetal gestations (ACOG, 2016b).

PHYSICAL EXAMINATION AND DIAGNOSTIC STUDIES

Ruling out an infectious etiology for the rupture of membranes is imperative. Fever, hypotension, tachycardia, and tachypnea all may be signs of an infectious process. The abdominal examination may reveal significant tenderness to palpation. Exquisite fundal tenderness, rebound tenderness, and guarding are all concerns for an infectious etiology.

On speculum examination, rupture of membranes can be determined by the presence of an amniotic fluid pool in the posterior fornix. Amniotic fluid will have a pH of approximately 7 and, when left to dry on a slide, a ferning pattern will be seen through the microscope. During the speculum examination, the cervix is visualized to ascertain whether the cervix is dilated. Occasionally, a prolapsed cord or fetal part may be found protruding through the cervical os. Finally, the presence of purulent vaginal discharge or fever will raise the provider's suspicion for septic abortion. If a speculum exam is negative or equivocal for ruptured membranes, a wet mount can be performed to evaluate for bacterial vaginosis, candidiasis, or trichomoniasis. If the status of amniotic membranes is unclear, the speculum examination can also be repeated in 1 hour to reevaluate the fluid for evidence of ferning.

Laboratory studies include a complete blood count (CBC) to evaluate for any leukocytosis suggesting infection and to establish a baseline hemoglobin level. Rh status is also collected and a urinalysis is obtained. In addition, a type and screen is obtained, as there is an association with PPROM and placental abruption, which can be associated with significant hemorrhage. A transabdominal ultrasound can be performed to measure the amount of amniotic fluid within the uterus, to confirm fetal viability, and to measure an

estimated fetal weight, especially in the periviable setting or when due date estimates are uncertain.

DIFFERENTIAL DIAGNOSIS

In the second trimester, the differential diagnosis of vaginal discharge or leaking includes PPROM, cervicitis or vaginitis, or recent intercourse. Urinary tract infections or incontinence may also lead to the sensation of leaking fluid.

CLINICAL MANAGEMENT AND FOLLOW-UP

Preterm premature rupture of membranes (PPROM) is a devastating diagnosis for pregnant women to receive. Perinatal morbidity and mortality are commonly seen. Neonatal outcomes in the setting of PPROM may include pulmonary hypoplasia and fetal deformation, particularly when rupture occurs early in the second trimester or lasts more than 2 weeks. One study followed 152 expectant managed women with PPROM less than 24 weeks gestation (Manuck et al., 2009). Approximately 41% ended with a fetal demise, previable delivery, or neonatal death. Of the 59% who survived to hospital discharge, half of these experienced serious neonatal morbidity. Expectant management can be pursued as an outpatient prior to 23 to 24 weeks of gestation as long as the woman is counseled regarding signs of infection, labor, and placental abruption (ACOG, 2016b).

In women who are proven to have ruptured membranes, yet are hemodynamically stable and without evidence of infection, there is no urgency to move toward an immediate management decision. Time is allowed for the mother and partner to have all questions addressed, speak in private, and process the importance of what has occurred. Management options include expectant management, induction of labor, or dilatation and evacuation (D&E). Expectant management is offered only to those women with PPROM prior to viability who demonstrate no evidence of infection or significant hemorrhage from abruption. Expectant management, however, does carry the risk of delivery outside a clinical facility, infection, and, rarely, coagulopathy and hemorrhage. Therefore, women may be managed in the outpatient setting only if they are able to return for emergency care quickly. Active management requires consultation by experienced obstetric providers at appropriately equipped facilities.

In the setting of septic abortion, fluid resuscitation, broad spectrum antibiotic therapy, and surgical uterine evacuation must be administered expeditiously. Intravenous (IV) antibiotic regimens include clindamycin 900 mg IV q 8 hours with gentamicin 5 mg/kg IV q 24 hours with or without ampicillin 2 g IV q 6 hours (Stubblefield & Grimes, 1994). Antibiotic therapy is continued for 48 hours after the last temperature elevation.

PERIVIABLE CONSIDERATIONS

Antibiotics for Pregnancy Latency

Latency antibiotics have been shown to increase pregnancy prolongation and reduce rates of short-term neonatal morbidities (Kenyon, Boulvain, & Neilson, 2013). Although there are no data specific to the periviable period, broad spectrum antibiotic coverage to prolong pregnancy can be offered to all women with PPROM who are being expectantly managed at 24 weeks of gestation and beyond, and can be considered after 20 weeks of gestation (ACOG, 2016b).

PRESENTING SYMPTOMATOLOGY

The diagnosis of cervical insufficiency has no clear diagnostic criteria. Women with a history of painless cervical dilation with expulsion of the pregnancy prior to 24 weeks of gestation, without labor or contractions in the absence of other clear pathology, are believed to have cervical insufficiency (ACOG, 2014). A short cervical length (<2.5 cm) is a marker for an increased risk of preterm birth, but is not sufficient for the diagnosis of cervical insufficiency (ACOG, 2014).

HISTORY AND DATA COLLECTION

There are several known factors that increased the risk of cervical insufficiency. Congenital causes include collagen disorders, such as Ehlers–Danlos syndrome (Leduc & Wasserstrum, 1992) and type I collagen expression disorders (Iwahashi, Muragaki, Ooshima, & Umesaki, 2003). Exposure to diethylstilbestrol (DES) in utero has been linked to pregnancy loss from cervical insufficiency (Kaufman et al., 2000). Acquired causes of cervical insufficiency include prior obstetric trauma (cervical laceration), mechanical trauma (curettage, termination of pregnancy), and management of cervical dysplasia (loop electrosurgical excision procedure [LEEP], cold knife conization; Kyrgiou et al., 2006).

PHYSICAL EXAMINATION AND DIAGNOSTIC STUDIES

Sterile speculum examination is performed to test for chlamydia, gonorrhea, and for any rupture of membranes. Visualization of the cervix may reveal membranes prolapsing through the external cervical os. If premature rupture of membranes is excluded, sterile digital examination of the cervix is performed for dilatation and effacement.

Assessment for contractions can help to differentiate between preterm labor, abruptio placenta, and cervical insufficiency. Documentation of the presence of a fetal heart rate needs to be performed; however, continuous fetal monitoring is not indicated in previable pregnancies.

In the obstetric triage setting, CBC and urinalysis are obtained. When there is evidence for infection or a high suspicion for infection, then amniocentesis can be considered.

If membranes are not visualized on physical examination, then transvaginal ultrasound can be considered to evaluate for cervical length and funneling. During transvaginal ultrasound, fundal pressure may be applied for better visualization of the internal os. Funneling itself has been shown to define cervical insufficiency or increase the likelihood of preterm delivery (Berghella et al., 2007). Ultrasound can also be used to assess the state of fetal membranes, extrachorionic hemorrhage, cervical polyps, uterine/cervical anomalies, or intra-amniotic debris.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for women presenting with these complaints and findings include previable preterm labor, previable premature rupture of membranes, abruptio placenta, and chorioamnionitis. Gynecologic conditions such as cervicitis and sexually transmitted diseases need to be considered.

CLINICAL MANAGEMENT AND FOLLOW-UP

Women with a prior preterm birth and a current singleton pregnancy with a cervical length on transvaginal imaging of less than 25 mm may be offered cerclage (Berghella, Rafael, Szychowski, Rust, & Owen, 2011; Owen et al., 2009).

When cervical shortening is found incidentally and there is no history of prior preterm delivery (especially mid-trimester loss), evidence supports use of vaginal progesterone (either 200 mg micronized progesterone or 90 mg progesterone gel) with improved neonatal outcomes and prolonged pregnancy (Hassan et al., 2011). For these women with incidental cervical shortening, cerclage has not been found to reduce preterm delivery (Berghella, Odibo, To, Rust, & Althuisius, 2005) or reduction in maternal or perinatal morbidity/mortality (To et al., 2004).

PERIVIABLE CONSIDERATIONS

Exam-Indicated Cerclage

Women can be offered an exam-indicated cerclage (emergent or rescue cerclage) when cervical dilatation and fetal membranes are visible, in the absences of uterine contractions, PPROM, or other contraindications, if less than 24 weeks of gestation (ACOG, 2014). Randomized trial data show that cerclage in this setting improves pregnancy prolongation and improves neonatal survival (Althuisius, Dekker, Hummel, & van Geijn, 2003; Daskalakis, Papantoniou, Mesogitis, & Antsaklis, 2006; Debby, Sadan, Glezerman, & Golan, 2007). There is also some suggestion that placing an exam-indicated cerclage after 24 weeks of gestation may be beneficial; however, robust randomized studies evaluating this are currently lacking (Dahlke, Sperling, Chauhan, & Berghella, 2016; Stupin, David, Siedentopf, & Dudenhausen, 2008).

STILLBIRTH

PRESENTING SYMPTOMATOLOGY

When fetal demise is diagnosed prior to viability, it is often found incidentally on ultrasound. Occasionally, women will present to the obstetric triage setting with complaints of decreased or absent fetal movement, vaginal bleeding, or uterine contractions. The possible risk factors for fetal demise are extensive, as shown in Exhibit 8.1.

PHYSICAL EXAMINATION AND DIAGNOSTIC STUDIES

The prenatal record and all ultrasounds are reviewed, as well as any significant medical and surgical history. Questions regarding any known chromosomal abnormalities, history of infections during the pregnancy, abnormal fetal testing, known intrauterine growth restriction, or illicit drug use must be addressed.

Routine vital signs and an overall evaluation are performed once the woman has been diagnosed with a fetal demise. If vital signs are stable without evidence of preeclampsia, abruptio placenta, or disseminated intravascular

EXHIBIT 8.1

Risk Factors and Causes of Stillbirth

- Non-Hispanic Black race
- Nulliparity
- Advanced maternal age (AMA)
- Obesity
- Smoking
- Drug and alcohol use
- Comorbidities:
  - Hypertension, preeclampsia
  - Diabetes mellitus
  - Thrombophilia
  - History of thromboembolism
  - Systemic lupus erythematosus
  - Renal disease
  - Thyroid disease
  - Cholestasis of pregnancy
- Multiple gestation
- Congenital anomalies
- Growth restriction
- Infection (parvovirus B19, syphilis, listeria)

Source: Adapted from ACOG (2009).

coagulopathy (DIC), then it is appropriate to limit the initial physical examination and perform the pelvic exam once the woman has had time to process the diagnosis. On speculum examination, any vaginal bleeding is evaluated and a bimanual exam is performed to determine cervical dilatation and effacement. With no complaint of bleeding, a bimanual exam is performed to determine cervical dilatation and effacement.

When fetal demise is suspected, it is recommended that a bedside ultrasound confirmation of absent cardiac activity be conducted, with two providers present. If a woman requests a further ultrasound, this can be performed for confirmation of findings, as necessary. Laboratory studies recommended at the time of diagnosis of fetal demise include: CBC, lupus anticoagulant, anticardiolipin antibodies, human parvovirus B19 IgG/IgM antibodies, and thyroid stimulating hormone (ACOG, 2009). In selected cases, additional studies could include indirect Coombs, glucose screening, and evaluation for preeclampsia.

DIFFERENTIAL DIAGNOSIS

When a woman presents with the complaint of decreased and/or absent fetal movement, ultrasound findings may indicate oligohydramnios or anterior placenta. In addition, medical etiologies such as chronic hypertension, preeclampsia, diabetes mellitus, gestational diabetes, and acquired thrombophilias must be considered.

CLINICAL MANAGEMENT AND FOLLOW-UP

Pregnancy loss in the second trimester is devastating and quite often unexpected. Typically, the timing of delivery does not need to occur immediately, providing the maternal condition is stable. It is critical to initially rule out the following conditions that may pose a serious threat to maternal health: abruptio placenta, intrauterine infection, preeclampsia, and DIC. The type of delivery is frequently dependent on the gestational age at which the fetal demise occurred, maternal preference, and history of prior uterine scar. For women with a second trimester fetal loss, D&E can be offered; however, this method would limit the utility of fetal autopsy. Labor induction before 28 weeks gestation is often performed with vaginal misoprostol and appears to be the most efficient regardless of the Bishop score (Neilson, Hickey, & Vazquez, 2006; Tang, Lau, Chan, & Ho, 2004). The most common dose for misoprostol is 200 to 400 mcg vaginally every 4 to 12 hours. Even in women with a prior uterine scar, misoprostol was still an acceptable choice for women with a previous uterine scar prior to 28 weeks (Dickinson, 2005). As pyrexia, nausea, vomiting, and diarrhea are common side effects of misoprostol in these doses, consider prophylactic or early treatment for these side effects.

Fetal autopsy is offered to all women with the understanding that it will provide information in 30% of cases (ACOG, 2009). If a full autopsy is declined, chromosome analysis can be obtained. The placenta can also be sent for pathologic evaluation after stillbirth to determine if infections or an abruption contributed to the demise. Other options to evaluate the delivered fetus include gross external evaluation and potentially diagnostic imaging by a trained perinatal pathologist.

ETHICAL CONSIDERATIONS

The traditional framework for ethical decision making is that of informed consent (Arora & Miller, 2014). The traditional tenets of this include beneficence, autonomy, and justice, and in the case of perinatal ethics, must also include the interests of the fetus (Skupski et al., 2010). Neonatal outcome data provide some indication of survival and/or morbidity based on the gestational age; however, each fetus is unique and its individual course cannot be predicted, which adds to the complexity of these conversations.

Obstetric complications that occur in the periviable period are difficult not only for the patients, but also for the providers. The decisions the pregnant women and the family must make are filled with medical complexities. Additional considerations include the patients' religious and moral beliefs. If there are no signs of infection or hemodynamic instability, women must be given adequate time to process loss and review their options. If time allows, a shared-decision model between the family and a multidisciplinary team of professionals provides the optimal way to counsel women in these situations. Ideally, this team needs to assess the unique aspects of each clinical situation and must function collaboratively to present clear and consistent information that will aid the family in making the best decision. Social services can assist in informing women of local services and support groups to assist in the grieving process, postdelivery.

CLINICAL PEARLS

- Management of periviable pregnancies, recently defined as gestations between 21 0/7 weeks and 25 6/7 weeks, is fraught with medical and ethical complexities.
- Most obstetric interventions are not recommended prior to 24 0/7 weeks of gestation. There are clinical circumstances, however, when interventions at these gestations can be considered and optimally these situations are decided by a multidisciplinary approach involving parents, obstetricians, neonatologists, perinatologists, and other support professionals.
- Careful counselling is required when discussing the route of delivery of periviable gestations. Most cesarean deliveries at these gestational ages require classical incisions and have increased maternal morbidity and impact on future reproductive outcomes, without benefit to the neonate.

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Early Complications of Multiple Gestations

9

Karen Archabald

The incidence of twin gestations has increased over time, with data from the 2014 Centers for Disease Control National Vital Statistics revealing a twin birth rate of 33.9 per 1,000. The triplet and higher order birth rate has been slowly decreasing from its peak in 1998 of 1.93 per 1,000 live births to 1.13 per 1,000 live births in 2014. These percentages correlate to 135,336 twin, 4,233 triplet, 246 quadruplet, and 47 quintuplet or higher births in the United States in 2014 (Hamilton, Martin, Osterman, Curtin, & Mathews, 2015). The increase in twin gestations is attributed to increased use of assisted reproductive technology (ART), as well as an increasing number of women becoming pregnant at an advanced maternal age. The decrease in higher order multiples is attributed to modification of ART practices with an increase in single embryo transfer. Given the prevalence of multiple gestations, associated complications are very likely to present to an obstetric triage unit.

The focus of this chapter will be on the complications specific to multiple gestations. Complications from partial pregnancy loss due to spontaneous or planned fetal reduction, shortened cervix, preterm premature rupture of membranes (PPROM), and preterm labor will be addressed.

SPONTANEOUS OR ELECTIVE FETAL REDUCTION

Both spontaneous and elective fetal reductions are common in women with multiple gestations. Spontaneous reduction is more likely to occur before 10 weeks, whereas planned elective fetal reduction is commonly performed between 10 and 14 weeks gestation (Stone et al., 2008).

PRESENTING SYMPTOMATOLOGY

The majority of women will be asymptomatic when spontaneous fetal reduction is noted. A retrospective cohort study found 5.3% of 38 women who experienced spontaneous fetal reduction had vaginal bleeding, compared with 8.3% of controls (Steinkampf, Whitten, & Hammond, 2005).

HISTORY AND DATA COLLECTION

Gestational age is established by last menstrual period, transfer date, or early ultrasound. The number of fetuses as well as the chorionicity and amnionicity are documented if possible. If the pregnant woman has recently undergone a planned multifetal reduction, the procedure note will include complications. If vaginal bleeding occurs, the duration and amount, as well as associated uterine cramping, need to be documented.

PHYSICAL EXAMINATION

If a woman presents with vaginal bleeding, a complete pelvic examination is warranted. A speculum examination will allow quantification of the amount of vaginal bleeding, as well as the presence of any active bleeding. Visual inspection of the cervix will allow assessment of cervical dilation as well as any bleeding from the cervical stroma. A bimanual examination will allow assessment of cervical dilation and uterine tenderness.

LABORATORY AND IMAGING STUDIES

Documentation of blood type, antibody screen, and Rh antigen status is critical. If the amount of vaginal bleeding is significant, a complete blood count (CBC) is warranted. A transvaginal ultrasound is necessary to assess fetal viability and to establish chorionicity and amnionicity if not previously established. In the first trimester, two separate placentas confirm the diagnosis of dichorionicity. If only one placenta is visualized, the presence of the "twin peak" or "lambda" sign is highly predictive of dichorionicity. Sonographically, the groove between the dividing membranes as they insert into the placenta appears thickened because this potential space is filled with amniotic and chorionic mesoderm unlike in monochorionic pregnancies where the space remains empty. Please see Figure 9.1 for a sonographic image of the lambda sign.

If the pregnant woman has undergone a fetal reduction, it is imperative to carefully note which fetuses have cardiac activity. Imaging may reveal two gestational sacs with only one yolk sac or fetus, as noted in Figure 9.2.

CLINICAL MANAGEMENT AND FOLLOW-UP

Spontaneous reduction of twin or higher order multiple gestations are common. A large retrospective study in a fertility clinic followed pregnancies from 5.5 to 6 weeks every 2 weeks with transvaginal ultrasound. At 12 weeks, 62% of twin pregnancies conceived naturally and 31% of twin pregnancies conceived with ART had spontaneously reduced to singleton pregnancies (Dickey, 2005). In the same cohort, spontaneous reduction of one or more gestational sacs and/or embryos occurred before the 12th week of gestation in 53% of triplet (95% CI, 44%–61%) and 65% of quadruplet (95% CI, 46%–85%) pregnancies (Dickey et al., 2002). Overall, prognosis of the pregnancy is good; however, observational studies show a decrease in length of pregnancy and lower birth weight in infants born to women whose pregnancies spontaneously reduced compared with unreduced pregnancies (Dickey, 2005; Pinborg, Lidegaard, la

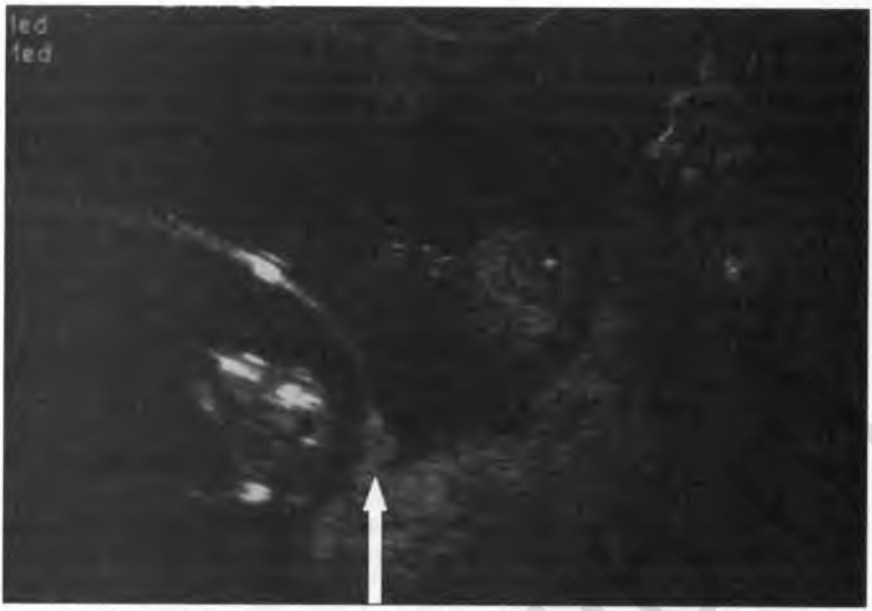

Figure 9.1 Twin peak or lambda sign in dichorionic gestation

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

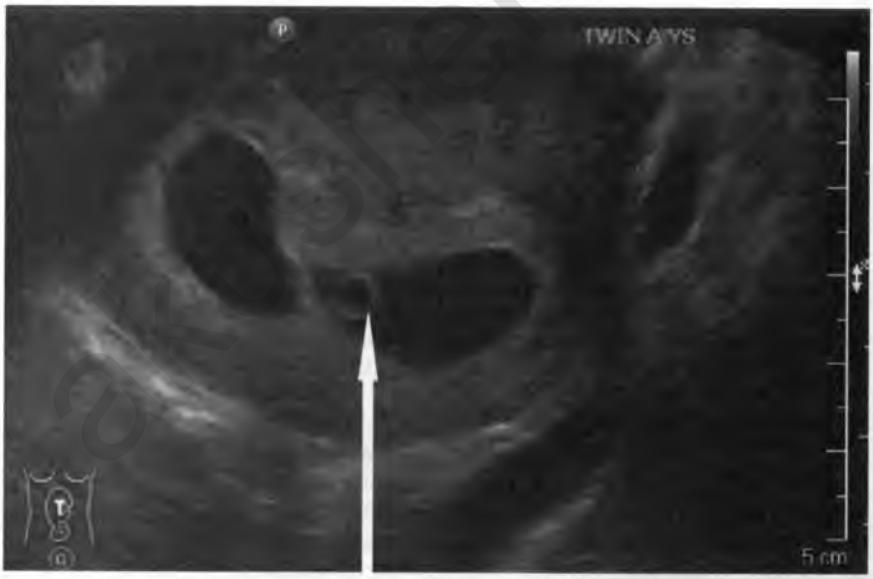

Figure 9.2 Vanishing twin with only one yolk sac visible

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

Cour Freiesleben, & Andersen, 2007). The woman and her family will require emotional support because loss of a fetus, even with a remaining viable pregnancy, can be devastating.

Women who have undergone a planned fetal reduction from twins to singleton have a higher risk of pregnancy loss at less than 24 weeks (11.9%) than those with ongoing twin pregnancies (3.1%; van de Mheen et al., 2015), whereas the risk of loss at less than 24 weeks in triplets reduced to twin gestations (3.3%) does not appear to be different from that for unreduced triplets (4.9%; Raval, Naglak, Igbal, Ramsey, & Craparo, 2015). In women who have undergone multifetal reduction, prognosis for the pregnancy is good with a decrease in preterm delivery (Raval et al., 2015). Regardless, women are encouraged to follow up with their provider or to seek care in an obstetric triage unit for worsening vaginal bleeding or uterine cramping. Women may experience increased anxiety after multifetal reduction, making emotional support and reassurance critical throughout the pregnancy (Dodd & Crowther, 2015).

SHORTENED CERVIX

Women with multiple gestations routinely undergo serial ultrasonographic examinations. Whether the cervical length is a planned part of the evaluation or a shortened cervix is noted incidentally, women may arrive in obstetric triage for evaluation and management of a shortened cervix. Shortened cervix is defined as a cervix measuring less than 25 mm, which is smaller than the 10% expected reduction in multiples (Iams et al., 1996).

PRESENTING SYMPTOMATOLOGY

A shortened cervix noted incidentally on ultrasound is often asymptomatic. However, it may also be associated with symptoms of preterm labor.

HISTORY AND DATA COLLECTION

The gestational age must be established by the last menstrual period, transfer date, or early ultrasound. A careful obstetric history is obtained, focusing on history of any deliveries before 37 weeks or second trimester losses. History of a cold knife cone biopsy or loop electrosurgical excision procedures is obtained as these have been associated with a shortened cervix in the mid-trimester (Fischer, Sveinbjornsson, & Hansen, 2010) and preterm delivery (Ørtoft, Henriksen, Hansen, & Petersen, 2010).

PHYSICAL EXAMINATION

Determining the presence of uterine contractions on tocometry is helpful for distinguishing preterm labor from asymptomatic shortened cervix. If the fetuses are viable, a nonstress test (NST) will provide information regarding fetal well-being. An abdominal examination with particular attention to the fundus is completed to evaluate for chorioamnionitis. A sterile speculum examination with visual assessment of the cervix will provide information on the rupture of membranes, and if no rupture, then dilatation and effacement. A confirmatory digital examination will provide further information if there is no evidence of ruptured membranes.

LABORATORY AND IMAGING STUDIES

If there is concern for chorioamnionitis, a CBC is indicated. Ultrasonographic evaluation of the cervix has already been completed in this clinical scenario; however, the examination can be confirmed in the triage unit if a practitioner is available who is competent with evaluation of ultrasonographic cervical measurement. Cervical length is measured with an empty maternal bladder via the transvaginal approach. The probe is placed in the anterior fornix of the vagina until the cervix is visualized, and a sagittal long-axis view of the endocervical canal is obtained. The probe is then withdrawn until the image is blurred, then advanced with enough pressure to restore the image. The cervical length is measured from the internal to the external os along the endocervical canal.

CLINICAL MANAGEMENT AND FOLLOW-UP

A shortened cervix between 20 and 24 weeks was shown in a meta-analysis to have a pooled positive likelihood ratio of 9.6 to predict preterm delivery before 28 weeks in twins (Conde-Agudelo, Romero, Hassan, & Yeo, 2010). Although data on triplets are limited, a study of 51 triplet gestations found a cervical length of less than 2.5 cm between 21 and 24 weeks gestation had 86% sensitivity for prediction of spontaneous delivery at less than 28 weeks gestation (Guzman et al., 2000).

Despite the predictive value of a shortened cervix for preterm delivery, options for intervention in multiple gestations are limited. A meta-analysis of five randomized controlled trials of cerclage versus expectant management in twin gestation found neither history nor ultrasound indicated cerclage had an effect on perinatal mortality, neonatal morbidity, or preterm birth less than 34 weeks (Rafael, Berghella, & Alfirevic, 2014). In triplets, a randomized controlled trial of 24 women with triplet gestation and shortened cervix, defined as less than 25 mm, showed no impact on birth weight or gestational age at delivery (Moragianni, Aronis, & Craparo, 2011).

A recent study on physical exam indicated cerclage found a decrease in risk of spontaneous preterm birth at less than 34 weeks from 94.7% to 52.6% (aOR, 0.06; 95% CI, 0.03–0.34) and adverse neonatal outcomes (33.9% vs. 90.5%; aOR, 0.05; 95% CI, 0.01–0.66) with placement of cerclage (Roman et al., 2016). Despite this promising study, evidence for efficacy of cerclage in multiple gestations remains insufficient and is not currently recommended by the American College of Obstetricians and Gynecologists (ACOG) or the Society of Maternal Fetal Medicine (ACOG, 2014).

Cervical pessary is an emerging strategy for management in this high-risk population. A randomized controlled trial of a cervical pessary in women with a sonographic short cervix measuring less than 25 mm found a reduction in spontaneous preterm birth at less than 34 weeks from 39.4% to 16.2% (relative risk [RR], 0.41; 95% CI, 0.22–0.76), although there was no statistical difference in composite neonatal morbidity (5.9% vs. 9.1%; RR, 0.64; 95% CI, 0.27–1.50; Goya et al., 2016). These findings confirmed results from the earlier ProTWIN trial, which showed placement of a pessary in women with cervical length less than the 25th percentile or 38 mm reduced poor perinatal outcome (12% vs. 29%; RR, 0.40; 95% CI, 0.19–0.83; Liem, Schuit, et al., 2013). However, the largest randomized controlled trial to date found placement of a pessary in women with a short cervix measuring less than 25 mm did not affect the incidence of spontaneous preterm birth before 34 weeks

(31% vs. 26%; RR, 1.2; 95% CI, 0.8–1.8; Nicolaides et al., 2016). Further research is currently underway (Maternal Fetal Medicine Units Network) to determine whether placement of pessary is optimal clinical management.

Finally, the evidence for vaginal progesterone for the prevention of preterm birth with asymptomatic shortened cervix in twin pregnancies is increasing. A meta-analysis of five studies found a significant reduction in the rate of spontaneous preterm birth at less than 33 weeks (RR, 0.69; 95% CI, 0.55–0.88) as well as composite neonatal morbidity and mortality (RR, 0.57; 95% CI, 0.59–0.94; Romero et al., 2012). A second meta-analysis of 13 studies also found treatment of women with cervical length less than 25 mm at less than 24 weeks with vaginal progesterone decreased the risk of adverse perinatal outcomes (RR, 0.56; 95% CI, 0.42–0.75; Schuit et al., 2015). Supplementation with vaginal progesterone can therefore be considered in multiple-gestation pregnancies complicated by asymptomatic shortened cervix before 24 weeks.

Therefore, when pregnant women with multiple gestation and asymptomatic shortened cervix present to the obstetric triage unit, once preterm labor and PPROM have been ruled out, no acute intervention is necessary. Consultation with a maternal–fetal medicine specialist can be arranged to discuss outpatient management. Depending on the gestational age, discussion with neonatology regarding neonatal outcomes may be helpful.

PRETERM PREMATURE RUPTURE OF MEMBRANES

Preterm premature rupture of membranes (PPROM) is more common in twin pregnancies than in singleton pregnancies, complicating up to 8% of twin pregnancies compared with approximately 4% of singleton pregnancies (Mercer, Crocker, Pierce, & Sibai, 1993). Previable PPROM in twin gestation accounts for a disproportionately higher percentage (14%–21%) of twin PPROM (Dinsmoor, Bachman, Haney, Goldstein, & MacKendrick, 2004; Falk et al., 2004). The impact of management decisions in multifetal gestation is complicated by the outcome of not only the fetus with ruptured membranes, but also the remaining fetuses.

PRESENTING SYMPTOMATOLOGY

Women with multiple gestations present with similar complaints when compared with women with PPROM in singleton gestations. Women may report a gush of fluid, but may also report intermittent or continuous leakage of clear or yellow fluid.

HISTORY AND DATA COLLECTION

A careful history regarding the timing of possible rupture of membranes, the color of the amniotic fluid, and any signs of chorioamnionitis including maternal or fetal tachycardia, fever, general malaise, or abdominal tenderness will help guide management.

PHYSICAL EXAMINATION

Documentation of maternal temperature and pulse, as well as fetal heart rate, is important when evaluating for chorioamnionitis. In viable fetuses, heart rate monitoring will provide information on fetal well-being and tocometry will

provide information regarding signs of preterm labor. Assessment of uterine tenderness can be completed by abdominal examination. A sterile speculum examination will confirm ruptured membranes by the findings of pooling of the amniotic fluid in the posterior fornix or direct egress from the cervical os, pH of vaginal fluid of 7.0 to 7.3 by nitrazine paper, and ferning.

LABORATORY AND IMAGING STUDIES

If ruptured membranes are confirmed, recommendations for laboratory assessment include CBC, type, and screen. Ultrasonographic evaluation can be helpful in determining which fetus has ruptured its membranes, as the presenting twin is not always the twin that is ruptured. A study of 291 women with PPROM evaluating the impact of oligohydramnios on pregnancy outcomes found that 67% of singletons had oligohydramnios by amniotic fluid index (AFI) less than 5.0 and 46.9% by maximum vertical pocket (MVP) of less than 2.0 at the time of diagnosis (Mercer et al., 2006). Although no studies on twins exist, it can be assumed that ultrasonographic evidence of rupture can help differentiate the twin with the ruptured sac. In addition to evaluating the amniotic fluid, the ultrasonographic evaluation can document fetal growth, as well as presentation of all fetuses, in order to help counsel on mode of delivery.

CLINICAL MANAGEMENT AND FOLLOW-UP

In PPROM between 23 and 34 weeks, options for management in twin pregnancy are similar to those for singletons. The latency period appears to be shorter in twins compared with singletons, particularly for women presenting after 28 weeks of gestation (5.0 ± 0.8 vs. 7.0 ± 0.4 days, $p = .01$) with an OR of 2.7 (95% CI, 1.7–4.2) of delivering within 48 hours (Kibel et al., 2017). In the obstetric triage unit, (a) antenatal steroids, (b) latency antibiotics, and (c) magnesium sulfate (Rouse et al., 2008) for neuroprophylaxis can all be initiated if gestational age is less than 32 weeks and delivery appears imminent. Use of tocolytic medications to allow time for administration of antenatal steroids is controversial and is not recommended. Inpatient management until delivery is recommended. Given the short latency period, observation on the labor unit for 24 hours to monitor for signs of labor is recommended. If the maternal–fetus status is stable, consideration may be given to subsequent transfer to the antepartum unit.

Management of previable PPROM is complicated in multifetal gestation. Neonatal survival of twins with previable PPROM between 20 and 24 weeks does not appear to be different from singletons, with a recent study finding 49.0% (95% CI, 39.4–58.6) newborns survived to discharge, of whom 24 (47.1%, 95% CI, 33.4–60.8) experienced severe neonatal morbidity (Kibel et al., 2016). In cases of previable rupture, management is complicated by the impact of management decisions on the fetus or fetuses with intact membranes. Depending on the gestational age, admission with the administration of broad-spectrum antibiotics and observation for signs of developing chorioamnionitis or labor are recommended. The woman can then be managed as either an inpatient or outpatient until viability, at which point administration of corticosteroids can be discussed (Waters & Mercer, 2009). Delivery of the ruptured twin with delayed-interval delivery of the remaining fetus or fetuses has been shown to improve 1-year survival from 24% to 56% (Zhang, Hamilton, Martin, & Trumble, 2004); however, improved survival rates are accompanied by increased

maternal morbidity (Roman et al., 2011). Consultation with a maternal–fetal medicine specialist and a neonatologist is recommended before proceeding with nontraditional management.

PRETERM LABOR

Preterm contractions and subsequent preterm delivery are common in twin and higher order multiple pregnancies. Data from the National Vital Statistics System for 2014 reveal that 59% of the 135,226 twin pregnancies were delivered before 37 weeks and 10.6% were born before 32 weeks. Of triplet pregnancies, 98.4% of the 4,233 triplet gestations were born before 37 weeks and 39.2% before 32 weeks (Hamilton et al., 2015). Appropriate evaluation of the woman with multiple gestations complaining of preterm contractions in obstetric triage is essential to ensure appropriate disposition.

PRESENTING SYMPTOMATOLOGY

Symptoms of preterm labor can be varied. The range of symptoms includes uterine contractions, menstrual-type cramping, low back pain, pelvic or vaginal pressure, increased discharge, or blood-tinged discharge with associated passing of a "mucus plug."

HISTORY AND DATA COLLECTION

Women with multiple gestations are at increased risk for preterm labor due to increased uterine distension. However, other known risk factors for preterm birth may also contribute to the preterm birth rate. Documentation of gestational age is essential. A thorough obstetric history must be obtained, focusing specifically on risk factors for preterm labor and any history of cervical surgery or preterm birth, because these increase the patient's risk for preterm delivery. Any history suggestive of abdominal trauma or abruption, and signs or symptoms of infection, either uterine or urinary, must be elicited. Duration and frequency of contractions, if present, must be documented, as well as signs and symptoms of PPROM.

PHYSICAL EXAMINATION

External fetal monitoring will provide valuable information on uterine contractions and fetal well-being. An abdominal examination will help to assess for uterine tone and tenderness, or the presence of another intra-abdominal process. A sterile speculum examination is performed to assess for PPROM, as well as to obtain swabs for labs (see next paragraph). If rupture is ruled out, a digital examination to assess cervical dilatation and effacement can be performed. Continued external fetal monitoring and repeat cervical exam will help differentiate preterm labor from preterm contractions.

LABORATORY AND IMAGING STUDIES

Infection as a possible cause for preterm labor can be evaluated with a urinalysis, urine culture, and cervical swabs for gonorrhea and chlamydia. A swab should also be obtained for Group B Streptococcus. If the woman has not had

intercourse, vaginal bleeding, or a vaginal exam in the previous 24 hours, a fetal fibronectin (FFN) collected from the posterior fornix will also help guide management. Ultrasound is used to evaluate presentation of each of the fetuses and for estimated fetal weight if delivery appears imminent.

CLINICAL MANAGEMENT AND FOLLOW-UP

Women with documented cervical change by digital examination require admission to the labor unit, as well as (a) antenatal steroids, (b) tocolytics, and (c) magnesium sulfate for neuroprophylaxis if gestational age is less than 32 weeks and delivery appears imminent.

In women with twins without evidence of cervical change with preterm contractions, FFN has been shown to be an effective method to predict preterm birth. A meta-analysis of three studies on 168 women with symptoms of preterm labor with twin pregnancies found that women with a negative FFN had only 1.6% probability of delivering within the next 7 days, compared with 24.5% for those with a positive FFN (Conde-Agudelo et al., 2010). Among women with preterm contractions and twins, a meta-analysis of five studies found limited evidence of the ability of cervical length to predict preterm delivery within 7 days (Liem, van de Mheen, et al., 2013). Fetal fibronectin is therefore recommended for triage of women with multiple gestations and symptoms of preterm contractions, but no cervical change. If the woman has no documented cervical change and a negative FFN, she can be safely discharged home with close follow-up. The disposition of a woman with a positive FFN is less clear because the positive predictive value is only 24.5%. However, given the increased risk of preterm delivery, depending on gestational age, inpatient observation can be considered.

CLINICAL PEARLS

- Chorionicity must be established by ultrasound and assists in assessing risk for complications.
- Fetal fibronectin is a validated tool in multiple gestations and can be used to help guide disposition in an obstetric triage unit.
- Shortened cervix in the setting of multiple gestations is controversial, and input from maternal–fetal medicine is recommended.

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Nausea, Vomiting, and Hyperemesis of Pregnancy

Amy L. Snyder

Nausea and vomiting of pregnancy (NVP) is quite common, affecting between 70% and 85% of pregnant women (Jewell & Young, 2003). Although typically a benign condition, NVP may lead to interruption of family life and the inability to attend work. The distress surrounding NVP commonly causes women to seek care in an emergency room or an obstetric triage unit, especially since symptoms may begin before a prenatal visit has taken place. In only 2% to 5% of pregnant women will the symptoms be severe enough to lead to the diagnosis of hyperemesis gravidarum (HG; Eliakim, Abulafia, & Sherer, 2000). Although there is no commonly agreed definition for HG, most diagnostic criteria include the following: severe nausea and persistent vomiting, resulting in dehydration (as indicated by ketonuria and elevated urine specific gravity), electrolyte abnormalities (e.g., hypokalemia), and 5% or greater weight loss. Hyperemesis can cause severe morbidity for both fetus and mother. Pregnancies complicated by HG are at higher risk for adverse outcomes, including premature birth and/or birth weight below the 10% for gestational age (Roseboom, Ravelli, van der Post, & Painter, 2011).

Attard and colleagues (2002) found that, in a sample of 223 women, those who suffered HG were slightly younger, more often primiparous, of lower socioeconomic status, and prone to substance abuse. They had more often conceived through assisted reproduction techniques, and more often had preexisting hypertension, metabolic conditions (e.g., diabetes mellitus), or psychologic conditions than women who did not suffer from HG.

PRESENTING SYMPTOMATOLOGY

Pregnant women may present with nausea, vomiting, retching, fatigue, mild abdominal pain, heartburn, dyspepsia, hyperptyalism, and lightheadedness if dehydration has occurred. These symptoms can persist throughout the day. Syncopal episodes or weight loss represents other common complaints that prompt patients to seek medical care. Abdominal pain not associated with retching or a fever must prompt the provider to search for a diagnosis other than NVP.

The symptoms of HG include significant maternal weight loss of 5 or greater pounds, dehydration, and electrolyte abnormalities, all of which require

immediate medical attention and all of which may adversely affect the health of both the mother and infant. Extreme cases of HG have led to other medical complications including peripheral neuropathies secondary to vitamin B_6 and B_{12} deficiencies, Wernicke's encephalopathy (WE), splenic avulsion, esophageal rupture, pneumothorax, and acute tubular necrosis (American College of Obstetricians and Gynecologists [ACOG], 2009).

HISTORY AND DATA COLLECTION

A thorough history is taken relative to the onset of symptoms. Symptoms often begin as early as 4 weeks after the last menstrual period (LMP) and peak at 9 weeks from LMP. Sixty percent of symptoms resolve by the end of the first trimester and 91% resolve by 20 weeks gestation (Niebyl, 2010). Knowing the duration of symptoms is crucial, as WE has been reported after 4 or more weeks of chronic, intense vomiting. Wernicke's is a neurologic condition that results from a depletion of vitamin B_6. Women must be questioned about additional symptoms such as abdominal pain, fever, hematemesis, dysuria, hematuria, flank pain, diarrhea, and headache. Nausea and vomiting may cause mild upper abdominal pain from retching. Other, more severe types of pain will alert the clinician to seek an alternative diagnosis. Recent travel and exposure to food-borne illness must be documented, as well as remedies attempted and the results of such interventions.

PHYSICAL EXAMINATION

The physical examination in the obstetric triage or emergency room setting for women with NVP is typically benign. Mild epigastric tenderness may be present due to retching; however, the abdominal examination is otherwise normal without guarding, rebound, or organomegaly. Costovertebral angle tenderness may indicate renal pathology as the primary cause of the symptoms. The patient is typically afebrile, with a normal neurologic examination and no goiter palpable. Mucous membranes and skin turgor are useful in determining the severity of dehydration. Orthostatic vital signs are recorded, as well as weight. An increase in pulse of 20 beats per minute or a drop in systolic blood pressure by more than 20 or 10 mmHg diastolic, associated with a change from a sitting to standing position, indicates a hypovolemic state. Orthostatic hypotension identifies those women who will benefit from intravenous (IV) fluid administration.

LABORATORY TESTING AND IMAGING STUDIES

Laboratory testing includes urinalysis and electrolyte evaluation. A complete blood count, liver function tests, amylase, lipase, and thyroid function tests are helpful in ruling out other causes of nausea and vomiting. Typical findings include suppressed thyroid stimulating hormone (TSH) levels and elevated free thyroxine, which resolves by 20 weeks gestation. These changes are likely due to stimulation of the thyroid gland by human chorionic gonadotropin. Elevated free thyroxine and free triiodothyronine can be measured to test for true hyperthyroidism. Other common blood work changes include elevated transaminases (usually <300 U/L); these mild elevations are likely due

to a combination of dehydration, malnutrition, and lactic acidosis. Levels in the 1,000s are atypical and may indicate viral hepatitis as the primary diagnosis. Elevated bilirubin (<4 mg/dL) and elevated amylase (up to 5 times normal values) are common findings. Amylase levels may be increased due to increased secretion of saliva, not from pancreatic production. If levels are 5 to 10 times greater than normal, pancreatitis must be considered as a potential diagnosis. A significantly elevated lipase is another laboratory finding suggestive of pancreatitis. Hematocrit and hemoglobin levels may be elevated due to hypovolemia or decreased from vitamin deficiency anemia (vitamin B_6 and B_{12}). A leukocytosis may indicate that infection is the underlying cause. Cholecystitis, pancreatitis, or pyelonephritis all need to be carefully considered. Electrolyte imbalances are common including hypokalemia, hyponatremia, and hypochloremic alkalosis. Ultrasound may disclose conditions that contribute to symptoms, such as multiple pregnancy or molar pregnancy.

DIFFERENTIAL DIAGNOSIS

Nausea and vomiting of pregnancy (NVP) is a diagnosis of exclusion. Other causes of vomiting must be carefully considered. These include various infectious, neurologic, and gastrointestinal causes for nausea and vomiting. Table 10.1 notes the extensive list of differential diagnoses when considering NVP.

Table 10.1 Differential Diagnoses for Nausea and Vomiting of Pregnancy

CONDITIONS	DIAGNOSES TO CONSIDER
Conditions related to pregnancy	Acute fatty liver of pregnancy, preeclampsia, premature contractions, hyperemesis gravidarum
Metabolic conditions	Addison's disease, diabetic ketoacidosis, hyperthyroidism, porphyria, thyrotoxicosis
Gastrointestinal causes	Achalasia, appendicitis, biliary tract disease, diaphragmatic hernia, gastroenteritis, gastroparesis, cholecystitis, cholelithiasis, hepatitis, intestinal obstruction, pancreatitis, stomach cancer, stomach or duodenal ulcer, dumping syndrome (postgastric bypass)
Urogenital tract conditions	Degenerative uterine fibroids, nephrolithiasis, pyelonephritis, uremia, ovarian torsion
Neurologic disorders	Acute alcohol withdrawal, migraine headache, vestibular disorders, central nervous system tumors, pseudotumor cerebri, Wernicke's encephalopathy
Miscellaneous conditions	Drug toxicities, food poisoning, iron imbalance, psychogenic causes

Sources: Adapted from ACOG (2009) and Jueckstock, Kaestner, and Mylonas (2010).

The goal of therapy is to reduce symptoms, correct the consequences of vomiting such as dehydration and electrolyte imbalance, and prevent serious complications to the woman and fetus. If the patient has not already received education through the office setting, dietary interventions can be discussed with the patient such as multiple smaller meals as opposed to larger meals, avoidance of spicy foods, and taking prenatal vitamins at night. If conservative measures are unsuccessful or the pregnant woman's symptoms are worsening, then antiemetics may be indicated. In more severe cases, rehydration with IV fluids may be necessary and vitamins and electrolytes may need to be repleted.

Medication Management

If a patient appears to be dehydrated either by elevated urine specific gravity, findings on physical examination, or orthostatic vital signs, IV fluids will need to be initiated. Sodium chloride 0.9% is the preferred IV solution; 1.8% sodium chloride is not advised, even in the setting of hyponatremia, as rapid correction may lead to central pontine myelinolysis. Thiamine must be administered along with glucose if vomiting has persisted for longer than 3 weeks as thiamine depletion can result in WE. Wernicke's triad of symptoms includes ataxia, confusion, and ophthalmoplegia. This complication absolutely must be identified, as it carries a 10% to 20% mortality rate and can cause persistent neurologic findings. A dose of 100 mg of thiamine IV followed by daily oral supplementation is recommended. The shortest duration of vomiting that has been shown to result in WE is 4 weeks (Togay-Isikay, Yigit, & Mutluer, 2001).

The antiemetic Bendectin® was removed from the U.S. market in 1983 due to the cost of defending legal accusations of congenital malformations. The drug continued to be used in Canada, under the name Diclegis®. To date, none of these allegations has been confirmed. The combination of the antihistamine doxylamine and vitamin B_6, the two ingredients in Bendectin, reduces nausea up to 70% (Niebyl, 2010). The attempts to duplicate Bendectin by using combinations of over-the-counter (OTC) medications are not exact, as OTC doxylamine is not time-released. In 2004, the U.S. Food and Drug Administration (FDA) approved the U.S. release of Diclectin®, which is a delayed-release formulation of 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride (HCl), for treatment of NVP. Diclectin remains a first-line treatment option recommended by the American College of Obstetricians and Gynecologists, when NVP does not respond to dietary or lifestyle changes (ACOG, 2015). The most common side effects are drowsiness, dry mouth, blurred vision, constipation, and urinary retention. Diclectin is taken twice at bedtime, once in the morning, and once in the afternoon. Women are encouraged to continue usage, as beneficial results may not occur for several days. Separate trials have also shown efficacy of using vitamin B_6 alone to treat nausea with good results (Niebyl & Goodwin, 2002; Sahakian, Rouse, Sipes, Rose, & Niebyl, 1991). In some circumstances, the cost of Diclectin remains a barrier to its usage.

Several dopamine antagonists may also be used to treat NVP. Promethazine and prochlorperazine are two commonly used agents. Both agents have demonstrated efficacy, as well as little or no risk for major malformations to offspring (Magee, Mazzotta, & Koren, 2002). In a trial comparing promethazine with metoclopramide, both were found to have similar results in treating nausea and vomiting and increasing overall well-being; however, promethazine had more side effects, including drowsiness (83.6%), dry mouth (43.8%) , headaches

(30.2%), and dystonia (19.2%), versus metoclopramide (Tan, Khine, Vallikkannu, & Omar, 2010). Compazine is available as a buccal tablet, which is associated with less drowsiness. Other side effects include extrapyramidal symptoms and Parkinsonian-like symptoms usually seen with higher doses or extended usage. These symptoms can be treated with diphenhydramine or lorazepam.

Metoclopramide is a dopamine antagonist with prokinetic properties. It is highly effective as described in the previous study and accepted by most pregnant women. Continuous use for more than 12 weeks has been linked to tardive dyskinesia. No increase in malformations or poor obstetric outcomes has been seen in studies performed to date, including an Israeli study of 3,458 women exposed to metoclopramide in the first trimester (Matok et al., 2009). Metoclopramide stimulates smooth muscle in the intestine and must be avoided in those women with bowel obstruction, perforation, or gastrointestinal bleeding.

Ondansetron is a HT3 antagonist commonly used to treat nausea and vomiting. This agent acts on both the peripheral vagal nerve terminals as well as centrally in the chemoreceptor trigger zone (Siminerio, Bodnar, Venkakataramanan, & Caritas, 2016). In recent years, published retrospective studies raise a controversial link between early exposure to ondansetron and birth defects, specifically cleft palate and cardiac anomalies (Einarsen, Maltepe, Navloz, Kennedy, Tan, & Koren, 2004). One of the largest studies to date, performed by using the Danish Birth Registry, also took into account family and maternal history and showed no evidence of increased risk for birth defects in infants exposed to ondansetron (Pasternak, Svanstrom, & Hviid, 2013). A subsequent review article suggests a possible small association between use of ondansetron in the first trimester of pregnancy and the increased incidence of neonatal cardiac septal defects and concludes ondansetron should only be used when other methods have failed (Carstairs, 2016). To summarize, current evidence suggests ondansetron is an option for treatment of nausea and vomiting when symptoms are unresponsive to first-line therapies. As always, risks and benefits must be discussed with pregnant women. Of note, ondansetron can prolong the QT complex and needs to be avoided in patients who have underlying heart problems, hypokalemia, hypomagnesemia, or are taking other medications such as anticholinergics, antihistamines, narcotics, metronidazole, or macrolide antibiotics. A summary of antiemetic treatment options is contained in Table 10.2.

Alternative Treatments

A review of six controlled trials by Borrelli and Capasso (2005) supports ginger use as an efficacious treatment for emesis without any significant side effects. Ginger showed beneficial effects for women after admission for hyperemesis when compared to placebo. About 250 mg four times daily by tablet and syrup both showed beneficial effects. In syrup form, nausea decreased by 77% in the ginger group versus 20% in the placebo group. Sixty percent of the ginger group and 20% of the placebo group stopped vomiting after 6 days of usage. No negative outcomes for mother or fetus were reported. When compared to vitamin B_6, ginger had equal reductions in nausea and number of vomiting episodes. Side effects of ginger were minor, including reflux and heartburn.

Acupressure is related to acupuncture and aims to heal by applying pressure to designated points throughout the body. Pressure to P6 or Neiguan is located three fingers or 4.5 cm above the wrist and is thought to treat nausea. Use of wristbands and electrical stimulation of P6 for treatment show conflicting results (Matthew, Dowswell, Haas, Doyle, & O'Mathuna, 2015). There are no consistent data to support acupuncture. A trial comparing acupuncture, sham acupuncture,

Table 10.2 Antiemetic Treatment Options for Nausea and Vomiting in Pregnancy

MEDICATION/DOSAGE	SIDE EFFECTS
First-line therapy	
Pyridoxine (vitamin B_6) 10–25 mg po q 8 hr	Nausea, headaches, somnolence
Antihistamines	
Doxylamine 12.5 mg PO 3 or 4 × per day Diphenhydramine 25–50 mg PO q 4–6 hr 10–50 mg IV q 4–6 hr Meclizine 25 mg PO q 4–6 hr	Drowsiness, thickened bronchial secretions Anticholinergic effects (tachycardia, constipation, confusion, urinary retention, decreased sweating, xerostomia)
Combination therapy	
Diclegis® (10 mg Doxylamine/10 mg Pyridoxine) 2 tablets each night and 1 tablet every morning	Somnolence, palpitations, urinary retention
Dopamine antagonists	
Prochlorperazine 5–10 mg PO, IV, IM q 6 hr 25 mg PR bid Metoclopramide 10 mg PO, IV, IM q 6–8 hr Promethazine* 12.5–25 mg PO, IM, pr q 4 hr	Dystonic reactions, akathisia, Drowsiness, sedation, diarrhea
Serotonin antagonists	
Ondansetron 4–8 mg PO, IM, IV q 8 hr	Headache, fatigue, constipation, drowsiness, QT interval prolongation

hr, hours; IM, intramuscular; IV, intravenous; PO, per os (orally); q, every; PR, rectally.
*Promethazine contraindicated for IV usage.

Source: Adapted from McParlin et al. (2016).

and no acupuncture showed a decrease in nausea for both sham and acupuncture groups; however, no change occurred in vomiting (Smith, Crowther, & Bellby, 2002).

Associated Gastrointestinal Symptoms

Gastroesophageal reflux symptoms such as heartburn, acid reflux, regurgitation, belching, flatulence, bloating, and indigestion are common during pregnancy and can compound symptoms of nausea and vomiting. Women with these symptoms perceived nausea to be more severe. Acid-reducing agents such as antacids, H-2 histamine blockers, and proton pump inhibitors are considered safe and effective in pregnancy. Antacids containing aluminum, calcium, and magnesium have all been found to be safe in pregnancy, though high dose, prolonged usage of magnesium trisilicate (Gaviscon®) is associated with nephrolithiasis, hypotonia, and respiratory distress in the fetus (Ebrahimi, Maltepe, & Einarson, 2010). The link between *Helicobacter pylori* and HG (Goldberg, Szilagyi, & Graves, 2007) has been documented. In a recent study, *H. pylori* was diagnosed by serum *H. pylori* IgG antibody in 71 of 80 patients

with HG versus 24 controls (Mansour & Nashaat, 2011). Endoscopy was performed on women with severe symptoms and *H. pylori* was confirmed by histopathology. Cases of confirmed infection were treated with ranitidine 150 mg twice daily, metronidazole 500 mg twice daily, and ampicillin 1,000 mg twice daily for 2 weeks. Improvement was seen in six of eight women. Screening for *H. pylori* must be considered in severe cases of hyperemesis and in women not responding to routine treatment regimens.

Management of Hyperemesis Gravidarum

Methylprednisolone is used in refractory cases of hyperemesis, when women continue to have symptoms and lose weight despite adequate treatment with antiemetics. A randomized trial comparing methylprednisolone 16 mg three times daily for 3 days followed by a 2-week taper compared to oral promethazine showed equal rates of improvement among hospitalized patients but higher rates of readmission with the promethazine group. A later study did not replicate these findings. Several studies have shown a link between steroid usage and oral clefts (ACOG, 2009; Carmichael & Shaw, 1999). The American College of Obstetricians and Gynecologists recommends usage after 10 weeks gestational age and in pregnant women who are being considered for enteral or parenteral feeding. The usual dosage is 48 mg daily for 3 days either IV or PO with a 2-week taper period. If symptoms recur, the woman may restart on the effective dose for up to 6 weeks.

Persistent refractory HG may necessitate consideration for feeding support. Many life-threatening risks are associated with parental feeding such as infections, thrombosis, and endocarditis. In a study that looked at 85 pregnant women with central catheters, 25% developed serious complications (Jueckstock et al., 2010). Enteral tube feeding is the preferable route, if tolerated.

CLINICAL PEARLS

- If the commonly occurring symptoms of nausea and vomiting persist despite dietary and lifestyle changes, antiemetic medications may prove beneficial as long as side effects and potential risks are carefully reviewed.
- When pregnant women present with more severe symptoms or clinically show signs of dehydration including lightheadedness, headache, tachycardia, and orthostatic hypotension, appropriate treatment includes IV rehydration, antiemetics, and potentially repletion of vitamins and electrolytes.
- HG represents an extreme variant and typically requires aggressive inpatient treatment, as it has been associated with significant maternal and fetal morbidities.

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Medical Conditions in Early Pregnancy

11

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Medical conditions can occur in early pregnancy and, although rare, can cause significant maternal and fetal morbidity. Often, women with these diseases can initially present to an obstetric triage or emergency room setting and may even necessitate referral to a tertiary care center. Prompt recognition and treatment of medical conditions during pregnancy can help to optimize maternal and fetal outcomes. The focus of this chapter will be on a few of the most common medical conditions that can present in early pregnancy: pyelonephritis, nephrolithiasis, and pancreatitis. Pregnancy is a risk factor for pyelonephritis, which may occur due to lack of treatment or incomplete treatment of bacteriuria. Nephrolithiasis and pancreatitis often present with nonspecific symptoms such as abdominal pain, nausea, and vomiting that can mimic other conditions seen in early pregnancy and are part of the differential when evaluating pregnant women in an obstetric triage or emergency room setting.

PYELONEPHRITIS

PRESENTING SYMPTOMATOLOGY

Pyelonephritis complicates approximately 1% to 2% of all pregnancies and can lead to significant maternal and fetal morbidity (Hill, Sheffield, McIntire, & Wendel, 2005). This can include sepsis, acute respiratory distress syndrome (ARDS), preterm birth, anemia, low birth weight, and renal insufficiency (Wing, Fassett, & Getahun, 2014). Pregnant women are thought to be more susceptible to pyelonephritis due to compression of the ureters by the gravid uterus, progesterone-mediated smooth muscle relaxation, increased glomerular filtration rate, and increased risk of bacteriuria during pregnancy. Approximately 21% of pyelonephritis during pregnancy occurs in the first trimester (Hill et al., 2005).

Pregnant women with pyelonephritis often have a history of a urinary tract infection or asymptomatic bacteriuria. Women with asymptomatic bacteriuria have an approximately 20- to 30-fold increased risk of developing pyelonephritis compared to women without bacteriuria (Jolley & Wing, 2010). Other risk factors for pyelonephritis include a previous history of pyelonephritis, sickle cell disease/trait, and diabetes. Approximately 13% of women with pyelonephritis in pregnancy may have at least one maternal risk factor (Hill et al., 2005).

Pregnant women with pyelonephritis may present with any of the following symptoms: fever, flank pain, dysuria, urinary frequency, costovertebral angle tenderness (CVAT), chills, nausea, or vomiting. In severe cases, they may present with signs and symptoms of septic shock including hypotension, tachycardia, shortness of breath, or multisystem organ failure. In contrast, women with a simple urinary tract infection may be asymptomatic or complain of localized symptoms only such as frequency, urgency, or dysuria.

PHYSICAL EXAMINATION

The diagnosis of acute pyelonephritis can be made on the clinical findings of fever (>38°C), flank pain, and CVAT with the laboratory finding of bacteriuria (Jolley & Wing, 2010). However, women with a simple urinary tract infection usually do not have any significant physical examination findings.

LABORATORY AND IMAGING STUDIES

A urinalysis can confirm that bacteriuria is present (>8 to 12 white blood cells/high power field) in a clean catch specimen (<2 to 4 epithelial cells). A urine culture obtained from a midstream clean catch specimen can isolate the microorganism and confirm the diagnosis by looking for greater than 100,000 colony forming units (Jolley & Wing, 2010). The most common pathogens associated with pyelonephritis are listed in Exhibit 11.1.

Other laboratory evaluation includes a complete blood count and serum chemistry evaluation. Elevation of the white blood cell count may be seen. In addition, there may be electrolyte abnormalities and transient renal insufficiency (Hill et al., 2005). The utility of obtaining blood cultures in the setting of pyelonephritis has been debated in the literature. Wing, Park, DeBuque, and Millar (2000) demonstrated that a change in management due to bacteremia alone occurred in only 1% of cases. There are no randomized controlled trials to comparing outcomes of pyelonephritis in pregnancy with or without blood cultures (Gomi, Goto, Laopaiboon, Usui, & Mori, 2015). However, blood cultures may be considered if the woman shows signs or symptoms of sepsis or has medical comorbidities.

EXHIBIT 11.1

Occurrence of Pathogens Associated With Pyelonephritis in Pregnancy

- *Escherichia coli* (83%)
- *Streptococcus* species (21.4%)
- *Klebsiella pneumoniae* (7.6%)
- *Staphylococcus* species (6.5%)
- *Proteus mirabilis* (4.9%)
- *Enterococcus* species (5.7%)

Source: Adapted from Wing et al. (2014).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for pyelonephritis in pregnancy includes other disorders of genitourinary, gastrointestinal, and pulmonary systems. Other conditions that can present in a similar fashion include acute cystitis, nephrolithiasis, viral syndrome, renal failure, pneumonia, pancreatitis, appendicitis, and gastroenteritis.

CLINICAL MANAGEMENT AND FOLLOW-UP

Unlike a simple urinary tract infection or asymptomatic bacteriuria, which can be managed as an outpatient with oral antibiotics, the standard management of pyelonephritis in pregnancy is admission to the hospital for inpatient management. Archabald, Friedman, Raker, and Anderson (2009) found that maternal morbidity and obstetric outcomes did not differ between first-trimester pyelonephritis compared with second-/third-trimester pyelonephritis. Given this data, it is recommended that all pregnant women with pyelonephritis, regardless of trimester, be admitted for parenteral antibiotics, antipyretics, and intravenous hydration.

Cephalosporins are recommended as first-line therapy for pyelonephritis during pregnancy (Jolley & Wing, 2010) due to the increasing resistance of *Escherichia coli* to ampicillin. An appropriate initial regimen is ceftriaxone 2g intravenously every 24 hours. Aminoglycosides (i.e., gentamicin) can be considered in cases of cephalosporin allergy, but it has been associated with ototoxicity following prolonged fetal exposure (Le, Briggs, McKeown, & Bustillo, 2004). Fluoroquinolones are avoided in pregnancy.

Parenteral antibiotics can be continued until the pregnant woman has shown clinical improvement and has been afebrile for 24 to 48 hours. Because of the risk of capillary endothelial damage from bacteria-mediated endotoxins and subsequent risk of respiratory insufficiency and acute respiratory distress syndrome (ARDS), aggressive hydration during this time should be used with caution and urine output monitored closely. Treatment with oral antibiotics tailored to the sensitivity of the microorganism can be continued for 14 days following intravenous treatment. It is recommended that a post treatment urine culture as a test of cure be sent (Glaser & Schaeffer, 2015).

If there is no clinical improvement seen in 48 to 72 hours, further evaluation for bacterial resistance, urolithiasis, renal abscess, and urinary tract abnormalities can be considered. In addition, broadening antibiotic coverage and imaging the urinary tract system with ultrasound or magnetic resonance imaging (MRI) may be warranted.

Recurrent pyelonephritis can occur in 6% to 8% of women with pyelonephritis in pregnancy (Lenke, VanDorsten, & Schifrin, 1983). Suppressive therapy is recommended for the duration of the pregnancy and up to 6 weeks postpartum with either nitrofurantoin 100 mg orally or cephalexin 250 to 500 mg orally at bedtime. Suppressive therapy may be considered in subsequent pregnancies.

NEPHROLITHIASIS

PRESENTING SYMPTOMATOLOGY

Symptomatic nephrolithiasis affects approximately 1 in 244 to 1 in 2,000 pregnancies (Rosenberg et al., 2011; Srirangam, Hickerton, & Van Cleynenbreugel, 2008). As noted previously, changes in the urinary tract during pregnancy include

an increased glomerular filtration rate, compression of the ureters due to the gravid uterus, and progesterone-mediated smooth muscle relaxation. Despite the normal physiologic changes in pregnancy, the prevalence of nephrolithiasis is thought to be similar to the nonpregnant population (Rosenberg et al., 2011). This may be due to increased production of citrate and magnesium during pregnancy, since both are thought to be urinary stone inhibitors (Meria, Hadjadj, Jungers, & Daudon, 2010). Symptomatic nephrolithiasis presents in the second or third trimesters in approximately 80% to 90% of cases (Butler, Cox, Eberts, & Cunningham, 2000).

Pregnant women with symptomatic nephrolithiasis may present with back or flank pain, lower abdominal pain, dysuria, or hematuria. Nausea and/or vomiting may also be present. Flank or abdominal pain is the most common symptom, occurring in approximately 85% to 100% of patients (Srirangam et al., 2008). Pain is often described as intermittent and colicky in nature. Frank hematuria is reported to occur in 15% to 30% of cases (Srirangam et al., 2008). Microscopic hematuria may not be present in up to 25% of women with diagnosed calculi (Travassos et al., 2009). Women may report a history of nephrolithiasis in the past.

On physical examination, pregnant women might appear uncomfortable and in visible pain. Palpation of the flanks is used to evaluate for CVAT. Tachycardia may be present as part of the pain response.

A urinalysis and urine culture can assess for hematuria and pyuria, suggestive of an underlying infection. A complete blood count may indicate evidence of systemic infection. A baseline creatinine is helpful to confirm normal renal function. Straining the urine of pregnant women with suspected nephrolithiasis may demonstrate the spontaneous passage of stones.

Imaging of the renal system may be helpful in confirming the diagnosis of renal calculi. Renal ultrasonography is often used as the first-line imaging modality. However, the sensitivity of ultrasound in confirming urolithiasis ranges from 34% to 86% (Srirangam et al., 2008). In addition, ultrasound may be unable to distinguish an obstruction due to calculi or physiologic hydronephrosis. Ultrasound may be used to see ureteral jets that would indicate the passage of urine at the uretero-vesical junction. The absences of ureteral jets is sensitive and specific for obstruction in the nonpregnant population but up to 15% of asymptomatic pregnant women may also have this finding (Masselli et al., 2013). In the setting of symptoms that are not improving or worsening, other imaging modalities that can be considered include an abdominal flat plate x-ray, MRI, or single-shot intravenous pyelography. Magnetic resonance imaging can differentiate physiologic hydronephrosis from obstruction but is expensive and may not be readily available (Masselli, Weston, & Spencer, 2015). It is, however, safe to use in pregnancy as it does not employ ionizing radiation.

The differential diagnosis of nephrolithiasis includes other genitourinary and gastrointestinal disorders as well as conditions related to pregnancy itself. The differential diagnoses for nephrolithiasis are listed in Exhibit 11.2.

If there is a clinical suspicion for nephrolithiasis in pregnancy, the first steps are aggressive hydration and pain control. Pregnant women may need to be admitted to the hospital for pain management. Opiates, either intravenously or orally, can be used for analgesia in pregnancy. Nonsteroidal anti-inflammatory drugs (NSAIDs) are to be avoided, especially in the third trimester, due to risks of oligohydramnios and premature closure of the ductus arteriosus. If a superimposed infection is suspected, antibiotic therapy can be initiated while awaiting final urine culture results. Antiemetics can also be administered if the woman's symptoms include nausea or vomiting. Approximately 64% to 84%

EXHIBIT 11.2

Differential Diagnosis of Nephrolithiasis in Pregnancy

- Pyelonephritis
- Urinary tract infection
- Labor
- Diverticulitis
- Appendicitis
- Pancreatitis
- Round ligament pain
- Gastroenteritis
- Abruption
- Ectopic pregnancy

Source: Adapted from Srirangam et al. (2008).

of renal calculi pass spontaneously (Srirangam et al., 2008). Urine is strained to assess for passage of calculi.

In approximately 15% to 30% of cases, further intervention may be needed (Srirangam et al., 2008). A urology consultation and/or further imaging with ultrasound or MRI may be considered for symptoms that are not improving with conservative management, evidence of compromised renal function, or concern for superimposed pyelonephritis. Medical expulsive therapy for symptomatic urolithiasis with tamsulosin is being used in the nonpregnant population. Bailey, Vaughan, Rose, and Krambeck (2016) studied 27 pregnant patients receiving tamsulosin during pregnancy. No adverse outcomes including preterm birth, low birth weight, spontaneous abortion, or congenital anomalies were found in the treatment group. Surgical interventions for persistent nephrolithiasis with obstruction during pregnancy include percutaneous nephrostomy, ureteral stent insertion, or ureteroscopy with stone retrieval (Srirangam et al., 2008). A recent series of ureteroscopy in pregnant women showed a 100% success rate (Travassos et al., 2009). A meta-analysis of ureteroscopy in pregnancy showed an 8.3% complication rate, similar to the nonpregnant population (Semins, Trock, & Matlaga, 2009).

In pregnant women with nephrolithiasis, pregnancy outcomes including spontaneous abortion and preeclampsia were not significantly different compared to women without nephrolithiasis (Butler et al., 2000). Similarly, the risk of congenital anomalies is not increased in women with nephrolithiasis in pregnancy (Bánhidy, Acs, Puhó, & Czeizel, 2007). One study, however, did find an increased risk of preterm birth in women admitted to the hospital for nephrolithiasis (Swartz, Lydon-Rochelle, Simon, Wright, & Porter, 2007).

PANCREATITIS

PRESENTING SYMPTOMATOLOGY

Acute pancreatitis is estimated to occur in approximately 1 in 1,000 to 1 in 12,000 pregnancies (Eddy, Gideonsen, Song, Grobman, & O'Halloran, 2008) and can initially present with nausea and vomiting, similar to hyperemesis of pregnancy.

EXHIBIT 11.3

Causes of Pancreatitis in Pregnancy

- Gallstones
- Alcohol
- Idiopathic pancreatitis
- Hyperlipidemia
- Hyperparathyroidism
- Trauma
- Medications
- Acute fatty liver of pregnancy

Source: Adapted from Eddy et al. (2008).

Therefore, it is critical to consider pancreatitis when evaluating nausea and vomiting of pregnancy. Approximately 57% of pancreatitis during pregnancy is estimated to occur in the first or second trimesters (Eddy et al., 2008).

Pancreatitis in pregnancy commonly presents with abdominal pain that is classically located in the epigastric region with radiation to the back. Other significant symptoms include nausea and vomiting, which can also occur secondary to pregnancy itself. In severe cases, pregnant women may present with signs of sepsis, including fever, tachycardia, hypotension, and hyperventilation.

The most common cause of pancreatitis in pregnancy is gallstones (66%; Eddy et al., 2008). Other causes of pancreatitis in pregnancy are listed in Exhibit 11.3.

Risk factors for pancreatitis include a history of gallstones, alcohol use, hyperlipidemia, or tobacco use. Physiologic changes during pregnancy such as smooth muscle relaxation of the gallbladder due to progesterone can induce bile stasis and gallstone formation. In addition, pregnancy is thought to be associated with a two- to four-fold increase in plasma triglyceride levels (Crisan, Steidl, & Rivera-Alsina, 2008). Medications that have been associated with pancreatitis include erythromycin, mesalamine, sulfasalazine, acetaminophen, didanosine, and steroids (Papadakis, Sarigianni, Mikhailidis, Mamopoulos, & Karagiannis, 2011).

PHYSICAL EXAMINATION

Vital signs of a patient with acute pancreatitis may be notable for fever, tachycardia, or tachypnea. Physical examination findings may include abdominal tenderness, especially in the epigastric area; signs of an acute abdomen; or signs of dehydration.

LABORATORY AND IMAGING STUDIES

The diagnosis of acute pancreatitis can be confirmed by increased serum amylase and/or lipase. Amylase and lipase levels in pregnancy are similar to levels in the nonpregnant state (Karsenti et al., 2001). An elevated amylase level can be a nonspecific finding as it can be elevated in other disease states.

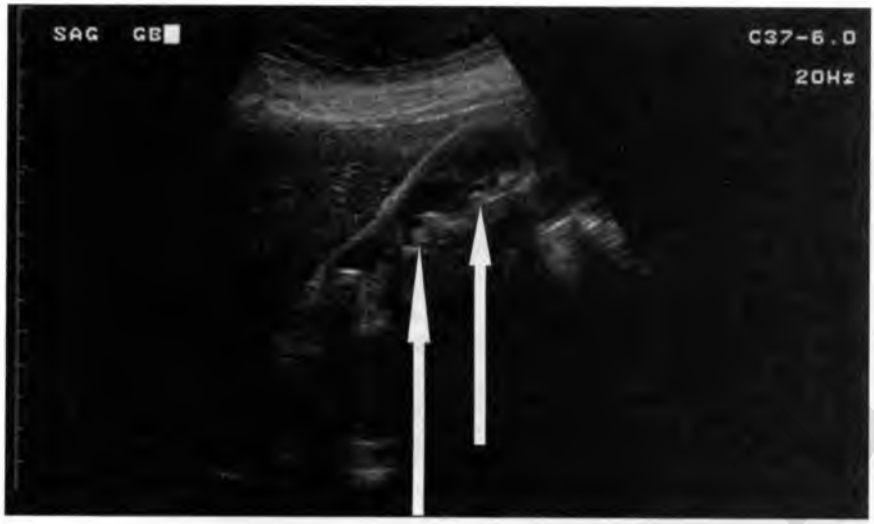

Figure 11.1 Gallstones on ultrasound

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

Typically in acute pancreatitis, the amylase level is three times the normal range. Serum lipase has also been found to be more specific than amylase in the evaluation of acute pancreatitis (Treacy et al., 2001). Other laboratory findings may include elevated liver function tests, leukocytosis, and increased serum cholesterol levels.

An ultrasound of the right upper quadrant may be performed as it is safe in pregnancy and can reliably detect gallstones and biliary duct dilation. Figure 11.1 illustrates gallstones in the gallbladder on ultrasound imaging.

However, ultrasound has low-diagnostic value for acute pancreatitis (Koo, Chinogureyi, & Shaw, 2010). Magnetic resonance cholangiopancreatography (MRCP) can allow for visualization of the pancreatic parenchyma and common bile duct with a sensitivity of over 90% (Roumieu et al., 2008). In addition, it avoids exposure to radiation for the patient and fetus.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of pancreatitis in pregnancy encompasses diseases from many organ systems. It includes cholecystitis, cholelithiasis, choledocholithiasis, preeclampsia, acute fatty liver of pregnancy, hyperemesis gravidarum, gastroenteritis, gastric ulcer, appendicitis, nephrolithiasis, and pyelonephritis.

CLINICAL MANAGEMENT AND FOLLOW-UP

Pregnant women with presumed acute pancreatitis are most often admitted to the hospital for further workup and clinical management. Clinical and laboratory risk factors or various severity grading systems can be used to access the severity of disease (Geng et al., 2011). If the woman is clinically stable and has a mild form of the disease, it is reasonable to proceed with conservative management

including intravenous fluid therapy, bowel rest, and pain control. The mean length of stay in the hospital is 6 days (Hernandez et al., 2007). Once symptoms resolve, the woman can be discharged home with close follow-up. A low-fat diet is encouraged in all patients with pancreatitis. The rate of recurrence of gallstone pancreatitis during pregnancy is approximately 30% to 50% (Eddy et al., 2008; Hernandez et al., 2007). A cholecystectomy can be performed safely in pregnancy, ideally during the second trimester, and may be considered once symptoms resolve (Date, Kaushal, & Ramesh, 2008).

If symptoms do not improve, enteral or parenteral nutrition may be needed after approximately 7 days. Women who are clinically unstable or have evidence of septic shock will need admission to the intensive care unit. Consultation with gastroenterology or general surgery to assist with further management may be considered.

Antibiotic prophylaxis in the setting of acute pancreatitis is controversial and debated in the literature. In cases of suspected sepsis or cholangitis, broad spectrum antibiotics are recommended. However, in mild pancreatitis, antibiotics can be deferred unless the clinical situation changes (Pitchumoni & Yegneswaran, 2009).

Later in gestation, women with acute pancreatitis are at-risk for preterm delivery. The rate of preterm delivery in pregnant women with a history of acute pancreatitis is estimated to be approximately 32% (Eddy et al., 2008). The risk of preterm delivery is thought to be increased in patients with nongallstone pancreatitis or in severe cases of pancreatitis (Geng et al., 2011). Pancreatitis during pregnancy has also been associated with adverse neonatal outcomes including jaundice, respiratory distress syndrome, and intrauterine fetal death (Hacker, Whalen, Lee, & Caughey, 2015). In addition, pancreatitis has been associated with preeclampsia during pregnancy (Hacker et al., 2015).

CLINICAL PEARLS

- Prompt recognition and treatment of medical conditions during pregnancy can help to optimize maternal and fetal outcomes, particularly in the relatively common condition of pyelonephritis in pregnancy.
- Nephrolithiasis in pregnancy is treated similarly in pregnant and nonpregnant patients.
- Pancreatitis has potentially serious consequences for both mother and fetus and is most frequently caused by gallstones in pregnancy.

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12 Fetal Evaluation and Clinical Applications

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Electronic fetal heart rate monitoring (EFM) technologies and ultrasound are the primary surveillance tools used for fetal evaluation in an obstetric triage setting. Approximately 85% of live births in the United States are assessed with EFM, making it one of the most widely used obstetric tools (Freeman, Garite, Nageotte, & Miller, 2012; Tucker, Miller, & Miller, 2009). Technologic advances have produced a machine that provides clinicians with a valuable tool to display fetal heart rate (FHR) patterns accurately. The benefits of EFM include decreased intrapartum death rates, improved Apgar scores, and the determination of well-being in the high-risk fetus. The goals of fetal evaluation are to accurately identify the well-oxygenated fetus so that unnecessary intervention is avoided as well as recognize the fetus at risk, thus preventing adverse perinatal outcomes (American College of Obstetricians and Gynecologists [ACOG], 2014; Devoe, 2008; L. A. Miller, Miller, & Cypher, 2017; Signore, Freeman, & Spong, 2009). Common maternal and fetal indications for EFM testing in an obstetric triage setting are presented in Exhibit 12.1.

EXHIBIT 12.1

Common Indications for Electronic Fetal Monitoring Evaluation in Obstetric Triage

- Postterm pregnancy
- Amniotic fluid abnormalities
- Preterm premature rupture of membranes (PPROM)
- Decreased fetal movement (DFM)
- Hypertensive disorders
- Abnormal serum markers
- Diabetes
- Multiple gestation
- Fetal growth restriction
- History of stillbirth
- Minor trauma

Sources: Adapted from ACOG (2014); L. A. Miller et al. (2017); and Signore et al. (2009).

Despite widespread use of these technologies, there is limited evidence to guide the type of test, testing intervals, gestational ages at which to initiate testing, or optimal frequency of testing (Signore et al., 2009). Key measures of the effectiveness of a test include the false negative rate (incidence of fetal death within 1 week of normal antepartum test) and the false positive rate (abnormal test that prompts delivery of a healthy fetus; L. A. Miller et al., 2017). These rates are presented for each of the current testing methods as described in Table 12.1.

FETAL TESTING METHODS AND EVALUATION

Nonstress Test

Nonstress tests (NSTs) are often the first cardiotocographic test performed in assessing fetal well-being and are initiated for a variety of maternal and fetal conditions. The characteristics of the baseline FHR unrelated to contractions are observed with healthy fetuses displaying normal fluctuations and oscillations in the baseline. In addition, the presence of accelerations correlates with fetal well-being (Freeman et al., 2012) and normal fetal autonomic functioning (ACOG, 2014). Absence of accelerations on a baseline FHR tracing can be associated with a fetal sleep cycle, medication administration, congenital abnormalities, or adverse fetal outcomes (Signore et al., 2009) and acidosis (ACOG, 2014; Freeman et al., 2012).

Both the external tocodynamometer and the ultrasound transducer are secured to the woman's abdomen to record uterine contractions and FHR, respectively. A separate "event marker" button is given to the mother to record perceived fetal movements. The fetal monitor tracing is recorded for 20 minutes during which clinicians can observe FHR baseline, variability, and the presence or absence of accelerations, decelerations, and contractions, along with maternal perception of fetal movements. A review of FHR nomenclature and definitions is given in Table 12.2.

Interpretation and Management

Accelerations of the FHR in response to fetal movements are the basis for interpretation and management of the NST. There is no universal agreement for defining a "reactive" NST, the number of accelerations, or the length of testing (Freeman et al., 2012). Generally, for a fetus beyond 32 weeks gestation, a normal or reactive NST consists of two accelerations of the FHR greater than 15 beats above baseline lasting at least 15 seconds occurring in 20 minutes. When the fetus is less than 32 weeks, the immature central nervous system may not respond as vigorously. In these fetuses, a reactive NST consists of two accelerations of greater than 10 beats above baseline lasting at least 10 seconds (L. A. Miller et al., 2017). The NST may continue for 40 minutes or more to account for a fetal sleep cycle.

Vibroacoustic stimulation, using an artificial larynx, may be used to stimulate fetal movement and shorten the test duration (Tan, Smyth, & Wei, 2013). FHR accelerations, in response to fetal scalp stimulation or fetal acoustic stimulation, are predictive of a normal fetal scalp pH (L. A. Miller et al., 2017). A reactive NST may occur without maternal perception of fetal movement (ACOG, 2014; Freeman et al., 2012; L. A. Miller et al., 2017).

TABLE 12.1 Comparison of Fetal Evaluation Techniques

NAME	COMPONENTS	RESULTS/SCORING	FALSE NEGATIVE (%)	FALSE POSITIVE (%)	COMMENTS
NST	Continuous FHR monitoring. FHR accelerations: ≥32 wk: reaching 15 bpm above baseline and lasting ≥15 sec <32 wk: 10 beat amplitude lasting ≥10 sec	**Reactive**: ≥2 accelerations within 20 min (may be extended to 40 min) **Nonreactive**: <2 accelerations in 40 min	0.2–0.65	55–90	Preterm fetus 24–28 wk, up to 50% of NSTs are nonreactive Preterm fetus 28–32 wk, 15% of NSTs may be nonreactive
Modified BPP	NST and AFI	**Normal**: Reactive NST and AFI >5 cm **Abnormal**: Nonreactive NST and/or AFI ≤5 cm	0.08	60	NST short-term indicator of fetal acid–base status Normal AFI >5 cm—indicator of long-term placental function
BPP	Presence or absence of five components within 30 min: Reactive NST ≥1 episode of fetal breathing movements lasting ≥30 sec ≥3 discrete body or limb movements ≥1 episode of extremity extension with return to flexion or opening or closing of a hand Maximum vertical AF pocket >2 cm or AFI >5 cm Continuous FHR monitoring	Each component present is assigned a score of 2 points; maximum score is 10/10 **Normal**: ≥8/10 or 8/8 excluding NST **Equivocal**: 6/10 **Abnormal**: ≤4/10	0.07–0.08	40–50	Assesses both acute (NST, breathing, fetal movement) and chronic (AFV/AFI) hypoxia. Correlates with fetal pH

(*Continued*)

TABLE 12.1 Comparison of Fetal Evaluation Techniques (*Continued*)

NAME	COMPONENTS	RESULTS/SCORING	FALSE NEGATIVE (%)	FALSE POSITIVE (%)	COMMENTS
Contraction stress test (Oxytocin challenge test)	At least three contractions of ≥40 sec duration within 10 min that occur spontaneously, with nipple stimulation or with IV oxytocin	**Negative**: No late or significant variable decelerations **Positive**: Late decelerations following ≥50% of contractions **Equivocal—suspicious**: Intermittent late decelerations or significant variable decelerations **Equivocal—hyperstimulatory**: Decelerations with contractions occurring more frequently than q 2 min or lasting greater than 90 sec **Unsatisfactory**—less than 3 contractions in 10 min or uninterpretable FHR tracing	0.04	35–65	Relative contraindications: PTL Preterm ROM Classical C/S Known placenta previa Repeat equivocal CSTs within 24°
Doppler indices					
Uterine artery	Evaluation of maternal flow to placenta	Increased resistance to uterine artery blood flow			Associated with development of future preeclampsia, IUGR, and/or perinatal death
Umbilical artery	Evaluation of high-velocity diastolic flow, that is, SD ratio	Decreased, absent, or reversed diastolic flow in early IUGR fetuses associated with fetal hypoxia			Indicated for early onset IUGR fetuses with uteroplacental insufficiently ACOG currently supports use with IUGR fetuses
Middle cerebral artery	Doppler measurement of flow	Detects blood redistribution from periphery to brain			Brain sparing Limited data available

ACOG, American College of Obstetricians and Gynecologists; AF, amniotic fluid; AFI, amniotic fluid index; AFV, amniotic fluid volume; BPP, biophysical profile; C/S, cesarean section; CST, contraction stress test; FHR, fetal heart rate; IUGR, intrauterine growth restriction; IV, Intravenous; NST, nonstress test; PTL, preterm labor; ROM, rupture of membranes; SD, systolic-to-diastolic.

Sources: Adapted from ACOG (2014); Cunningham et al. (2014); Devoe (2008); and Signore et al. (2009).

TABLE 12.2 Electronic Fetal Monitoring Standardized Definitions

PATTERN	DEFINITION
Baseline	Mean FHR rounded to the nearest 5 bpm in 10-min segment excluding accelerations, decelerations, or periods of marked variability Minimum of 2 min of tracing Normal baseline FHR: 110–160 bpm Tachycardia: >160 bpm Bradycardia: <110 bpm
Baseline variability	Fluctuations in baseline FHR in a 10-min window, peak-to-trough amplitude, and frequency quantified in bpm *Absent*—range undetectable *Minimal*—range detectable 5 bpm or less *Moderate (normal)*—range between 6 and 23 bpm *Marked*—range >25 bpm
Accelerations	*Abrupt* (onset to peak <30 sec) increase in FHR above baseline Peak of acceleration is 15 bpm above baseline and is sustained for ≥15 sec but less than 2 min Before 32 weeks gestation: 10 bpm amplitude for at least 10 sec but less than 2-min duration Prolonged acceleration: >2 min but <10 min if ≥10 min is a baseline change
Early deceleration	*Gradual* (onset to nadir >30 sec) decrease and return of FHR associated with a contraction Nadir of deceleration occurs with peak of contraction and returns to baseline with end of contraction
Late deceleration	*Gradual* (onset to nadir >30 sec) decrease in FHR below baseline occurring with a contraction "Delayed" timing: Nadir of deceleration occurs *after* the peak of the contraction and ends after contraction is finished "Repetitive": Occurs with >50% of uterine contractions
Variable deceleration	*Abrupt* (onset to nadir <30 sec) decrease in FHR ≥15 bpm drop below the baseline lasting ≥15 sec, but less than 2 min
Prolonged deceleration	FHR decrease ≥15 bpm lasting ≥2 min but <10 min; if ≥10 min, it is a baseline change
Sinusoidal pattern	Smooth, sine-like undulating pattern of FHR baseline with a cycle frequency of 3–5/min lasting for ≥20 min
Uterine contractions frequency	The number of contractions in a 10-min window averaged over 30 min ≤5 is "normal" >5 is "tachysystole" Management guided by presence or absence of deceleration

bpm, beats per min; FHR, fetal heart rate.

Sources: Adapted from ACOG (2009, 2010) and D. A. Miller (2010).

An NST is considered nonreactive when two accelerations do not meet the gestational age requirements in 40 minutes (ACOG, 2014). Nonreactive NSTs, along with reactive NSTs with decelerations, warrant additional testing including amniotic fluid (AF) assessment, contraction stress test (CST), or

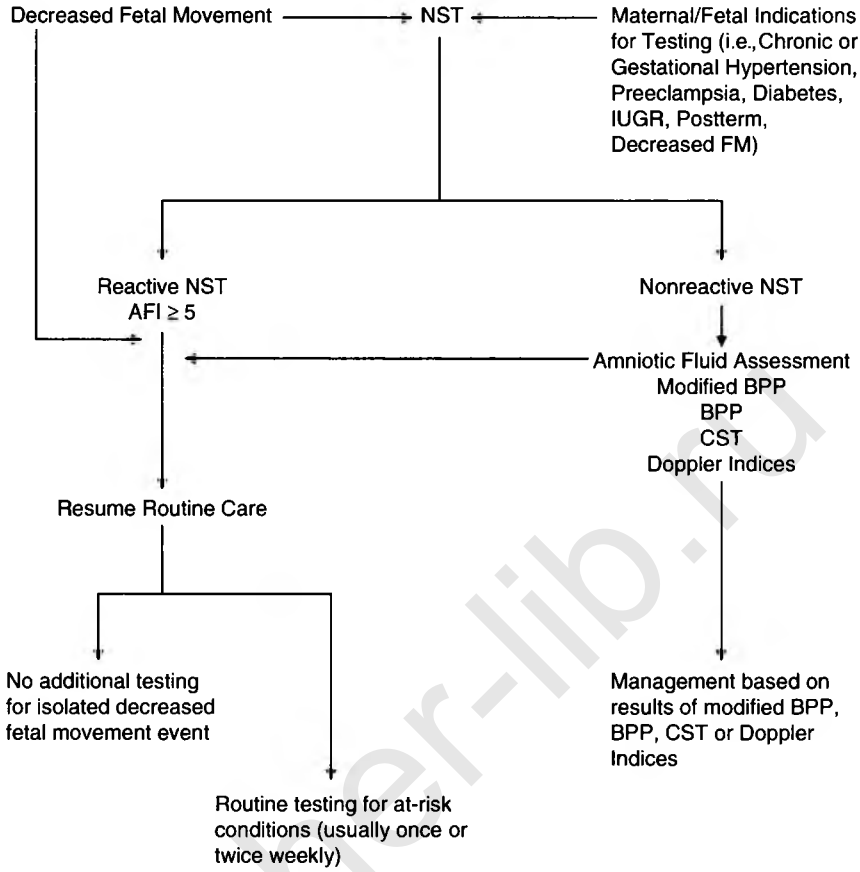

Figure 12.1 Algorithm for electronic fetal monitoring testing

Source: Adapted from L. A. Miller et al. (2017).

AFI, amniotic fluid index; BPP, biophysical profile; CST, contraction stress test; FM, fetal movement; IUGR, intrauterine growth restriction; NST, nonstress test.

biophysical profile (BPP; L. A. Miller et al., 2017). See Figure 12.1 for a sample management algorithm for EFM testing in the obstetric triage setting.

Amniotic Fluid Assessment

The assessment of AF is an important determinant of fetal well-being. It provides a protective environment for fetal development by shielding the fetus from trauma and infection, allowing for fetal movement, and preventing compression of the umbilical cord. Its volume is the sum of fluid flowing into and out of the amniotic cavity from fetal urine, fetal swallowing, and intramembranous absorption. As long as there is no rupture of membranes, oligohydramnios is believed to indicate a fetal response to chronic stress. It is associated with increased fetal and neonatal morbidity and mortality including fetal anomalies, growth restriction, postterm pregnancies, and maternal hypertensive disorders (Nabhan & Abdelmoula, 2008). Ultrasound measurement of AF is used during fetal surveillance by estimating an amniotic fluid volume (AFV) in a single vertical

pocket or the amniotic fluid index (AFI). Several AFV measurements have been suggested in the literature, but a 2-cm vertical pocket is the most commonly used lower limit of normal (ACOG, 2014; Nabhan & Abdelmoula, 2008). When calculating the AFI, the clinician divides the uterus into four quadrants. The AFI is the sum of the largest vertical fluid pocket in each of the four quadrants that does not contain umbilical cord (Nabhan & Abdelmoula, 2008).

Interpretation and Management

An AFI of 5 or less cm or the absence of a 2-cm vertical pocket identifies oligohydramnios and has been associated with fetal compromise, especially with high-risk pregnancies (Nabhan & Abdelmoula, 2008). No consensus exists for the best method of testing or for the ideal cutoff for intervention (ACOG, 2014). Many clinicians will plan delivery for oligohydramnios at term but will also consider maternal and fetal clinical condition as determined by other tests of fetal well-being (ACOG, 2014; Nabhan & Abdelmoula, 2008). Evaluate the pregnant woman for ruptured membranes based on clinical history. In the preterm pregnancy, expectant management may be the most suitable course of action but follow-up AF and fetal growth assessments are warranted (ACOG, 2014).

Modified Biophysical Profile

The modified biophysical profile (mBPP) uses two biophysical parameters, the NST to reflect current fetal oxygenation and the AFI that reflects chronic oxygenation (Devoe, 2008; L. A. Miller et al., 2017).

Interpretation and Management

A normal mBPP consists of a reactive NST and an AFI of greater than 5 cm (L. A. Miller et al., 2017), and the woman may resume her routine prenatal care regimen as directed by her risk status. An abnormal test result is obtained when either or both of these components are absent; additional testing is then necessary. Further assessment usually consists of the complete BPP or the CST. Management is directed by the results of these additional tests.

Biophysical Profile

The original research for the BPP in 1980, published by Manning and coworkers, endorsed the combined use of multiple biophysical components measured by ultrasound as a more accurate assessment of fetal well-being than the NST alone (Cunningham et al., 2014). The elements of the BPP consist of an NST, fetal movement, fetal tone, and fetal breathing as indicators of acute central nervous system functioning. An ultrasound assessment of AFV indicates long-term placental functioning (L. A. Miller et al., 2017).

Four ultrasound components of the BPP are assessed over a 30-minute time frame with the NST obtained using a fetal monitor. Each of the tests is assigned a score of 0 or 2 according to specific criteria. Two points are assigned for a reactive NST, three distinct fetal movements, 30 continuous seconds of fetal breathing, and an AFV greater than 2 cm in a single vertical pocket. In addition, the presence of at least one episode of flexion and extension of an extremity or opening and closing of a hand provides two points for tone. The absence of any of these five components provides a score of 0 for

that assessed parameter. The presence of all five components yields a score of 10/10. The NST may be omitted if all components of the BPP are normal (ACOG, 2014).

Interpretation and Management

A BPP result of 8 or 10 out of 10 is considered a normal test, and the woman will continue a routine testing schedule if the fetus is felt to be at risk. A score of 6 is equivocal and warrants repeat testing within 6 to 24 hours. The BPP is abnormal if the score is 4 or less and necessitates evaluation for delivery. Management may be gestational age dependent with later gestations considered for delivery and very early gestations managed with daily, ongoing fetal assessment. The presence of oligohydramnios necessitates additional evaluation (ACOG, 2014; Signore et al., 2009).

Contraction Stress Test

The CST, or oxytocin challenge test (OCT), was originally based on observations of the FHR during labor (Cunningham et al., 2014) when examiners observed periods of heart rate decelerations occurring with contractions as a result of impaired oxygenation. When uteroplacental pathology existed during some at-risk pregnancies, the fetus would exhibit recurrent late decelerations.

The external tocodynamometer and the ultrasound transducer are secured to the woman's abdomen to record uterine contractions and FHR, respectively. Contractions may be spontaneously occurring or they may be induced with oxytocin or with nipple stimulation. When Pitocin or nipple stimulation is used, EFM monitoring is continuous until three contractions in 10 minutes are achieved and the test is completed. Clinicians observe FHR response to uterine contractions.

Interpretation and Management

A negative test occurs with the absence of late decelerations. A positive test exhibits the presence of persistent late decelerations occurring with more than 50% of the contractions. Depending on gestational age, the woman may be evaluated for delivery. Equivocal tests are repeated within 24 hours (Signore et al., 2009).

Doppler Velocimetry

Research is expanding in the field of Doppler assessment, which is used as an adjunct to fetal evaluation (Freeman et al., 2012). Doppler measurement of blood flow in the maternal and fetal vessels provides information about the fetal response to diminished uteroplacental blood flow (L. A. Miller et al., 2017; Signore et al., 2009). Abnormal blood flow is characterized by absent or reversed end-diastolic flow, and this abnormal flow has been associated with fetal growth restriction, acidosis, and perinatal morbidity (L. A. Miller et al., 2017). Further assessment and timing of delivery are suggested with abnormal testing results. At present, umbilical artery Doppler velocimetry is recommended in pregnancies complicated by fetal growth restriction (ACOG, 2014), whereas middle cerebral artery (MCA) testing is used for detection and management of fetal anemia (Cunningham et al., 2014).

A challenge faced by clinicians in obstetric triage settings is to understand and fulfill the legal requirements for care of the pregnant woman. The Emergency Medical Treatment and Active Labor Act (EMTALA) was enacted so that patients with medical emergencies, including labor, are not denied treatment and are not inappropriately transferred (Angelini & Mahlmeister, 2005). EMTALA requires that obstetric triage clinicians perform a medical screening exam in a timely fashion to determine if a medical condition exists, provide necessary stabilizing treatments, and, if warranted, provide proper transfer to another hospital (Angelini & Mahlmeister, 2005).

The minimal initial assessment includes maternal vital signs, FHR tracing, and the presence or absence of contractions. The obstetric triage clinician additionally assesses for the presence or suspicion of vaginal bleeding, acute abdominal pain, fever greater than 100.4°F, preterm labor, preterm rupture of membranes, hypertension, or abnormal EFM pattern (Simpson, 2009). Concise and complete documentation of screening examinations, stabilizing treatments, and consultation with the referring hospital is necessary to reduce liability and claims of an EMTALA violation (Angelini &Mahlmeister, 2005).

Care of the pregnant woman presenting to obstetric triage settings must adhere to national, evidence-based standards that are typically derived from recommendations from the ACOG and the American Academy of Pediatrics (AAP; Angelini, 2006). The topics mentioned in the following text have been identified as demonstrating increased liability in the obstetric triage environment (Angelini, 2006). These include decreased fetal movement (DFM), minor trauma, and liability of assessing fetal status in labor or upon discharge.

Decreased Fetal Movement

Most women perceive fetal movements between 16 and 20 weeks, with a woman's perception of fetal movement frequency increasing as gestational age approaches term. Movements decrease in response to fetal hypoxemia (Signore et al., 2009) and have been thought to be associated with impending fetal death (Freeman et al., 2012). Many clinicians have encouraged fetal movement counting but results of clinical trials for routine fetal movement counting are mixed (Signore et al., 2009). One randomized trial in Denmark noted that fetal movement counting had a 73% reduction in stillbirths (relative risk [RR] = 0.27, 95% CI [0.08–0.93]; Signore et al., 2009). However, a large international study found no difference in avoidable fetal deaths when women were instructed to count movements routinely versus women who were not given specific instructions for counting (Signore et al., 2009).

The diagnosis of DFM is based on the woman's subjective perception of a decline in fetal activity. When a pregnant woman of 24 or greater weeks gestation presents to obstetric triage with DFM, an assessment of the woman's prenatal health and risk status along with fetal assessment and risk status is initiated as soon as possible. This woman is prioritized ahead of those with nonemergent problems and not kept waiting (Angelini & Mahlmeister, 2005). The clinical assessment of the woman with DFM includes evaluation of maternal or fetal risk factors with a NST, an ultrasound assessment of AF, and other biophysical parameters if warranted, as well as a review of fetal growth during the pregnancy (Preston et al., 2010). No consensus exists for the optimal management of DFM. However, the NST combined with ultrasound evaluation of AF are the most useful tests for fetal surveillance in DFM (Frøen et al., 2008).

Clinical Management

A nonreactive NST or decreased AF requires additional evaluation of fetal well-being such as with BPP, CST, or Doppler indices if growth restriction is revealed. An isolated episode of DFM requires no additional follow-up.

No trials have defined an agreed-upon method for fetal movement counting or at what threshold decreased movements signify increased risk. The current definition of DFM recommended by the AAP and the ACOG has the woman count 10 movements. If it takes longer than 2 hours for those movements to occur, the woman is instructed to call the provider or present to the obstetric triage unit as soon as possible for additional follow-up (AAP & ACOG, 2012). A recent Cochrane review of fetal movement counting for assessing well-being concluded that there is insufficient evidence to recommend routine counting to prevent stillbirth (Mangesi, Hofmeyr, Smith, & Smyth, 2015).

Minor Trauma in Pregnancy

Trauma affects up to 6% to 7% of all pregnancies with the majority accidental and noncatastrophic. Motor vehicle accidents, falls, and assaults are the most common causes. Most trauma is blunt trauma and often without direct fetal injury. However, injury may be noted in minor trauma and complications include not only direct maternal consequences but also pregnancy-related conditions such as placental abruption, preterm labor, fetal-maternal hemorrhage, and fetal demise (Chames & Pearlman, 2008).

Clinical Management

Timely and systematic care must be provided to the minor trauma patient who presents to obstetric triage. A complete physical examination and trauma clearance of the pregnant woman is necessary, evaluating for maternal injury along with contractions, vaginal bleeding, and fetal movement. Laboratory testing may be obtained for complete blood count, blood type, and antibody screen. The Kleihauer–Betke test may be ordered in the Rh-negative woman for appropriate dosing of Rh immune globulin. Once the woman's condition is considered to be stable, continuous fetal monitoring is recommended if the pregnancy is 24 or greater weeks. Four hours of continuous EFM is a widely accepted minimum duration of monitoring. Lateral displacement of the uterus is recommended to avoid compression of the vena cava by the gravid uterus. Women with 6 or fewer contractions per hour during this 4-hour period and no evidence of uterine tenderness, bleeding, significant maternal injury, or nonreassuring fetal tracing (i.e., tachycardia, bradycardia, decelerations) may be discharged with instructions and warning signs of abruption. Inpatient observation for 24 hours with continuous EFM has been recommended with 6 or greater contractions per hour or concern for abruption (Chames & Pearlman, 2008).

Liability in Assessing Fetal Status in Labor or Upon Discharge

Evaluation of the woman presenting to obstetric triage in labor includes assessment of maternal vital signs, uterine activity, fetal assessment, cervical examination, and membrane status (Simpson, 2009). Labor is established by progressive cervical change with regular contractions. EMTALA specifies that a woman experiencing contractions is in labor unless a qualified clinician certifies that, after a period of observation, the woman is in false labor

(Angelini & Mahlmeister, 2005; Simpson, 2009). Prior to discharging the woman in early or false labor, fetal well-being is established, usually by a reactive NST, when gestational age is appropriate (Simpson, 2009). Fetal assessment in the laboring woman uses nomenclature and interpretation as defined and revised by the National Institute of Child Health and Human Development (NICHD) consensus in 2008 (ACOG, 2014; D. A. Miller, 2010; L. A. Miller et al., 2017). Refer to Table 12.2 for EFM definitions (ACOG, 2009).

If the FHR tracing is considered to be nonreassuring, then additional evaluation methods such as an AFI, BPP, or CST are needed (Angelini & Mahlmeister, 2005). When fetal bradycardia, tachycardia, or repetitive decelerations occur in obstetric triage settings, intrauterine resuscitative measures including intravenous fluid administration, maternal oxygen therapy, and repositioning are employed to promote fetal well-being (Garite & Simpson, 2011). Recommended interpretation and management of FHR tracings are further delineated into three categories as noted in Exhibit 12.2.

EXHIBIT 12.2

Fetal Heart Rate

Three-Tiered FHR Classification System

Category I. Includes all of the following:

Baseline: 110–160 bpm
Moderate FHR variability
No late or variable decelerations
Early decelerations may be present or absent
Accelerations may be present or absent

Category II. All FHR tracings not specifically categorized as Category I or III:

Baseline rate: Bradycardia without absent variability; tachycardia
Baseline variability: Minimal or marked variability; absent variability without decelerations
Absence of accelerations with scalp stimulation
Recurrent variable decelerations with minimal or moderate variability
Prolonged deceleration
Recurrent late decelerations with moderate variability
Variable decelerations with "slow return to baseline," "overshoots," or "shoulders"

Category III. Includes either:

Absent baseline variability with the presence of any of the following:
  Recurrent late or variable decelerations
  Bradycardia
Or sinusoidal pattern

bpm, beats per minute; FHR, fetal heart rate.

Sources: Adapted from ACOG (2009, 2010); and D. A. Miller (2010).

The purpose of the categories is to assist clinicians in identifying EFM tracings that are normal versus those that require additional intrauterine resuscitation or delivery. In addition, the categories are integral to determining the necessity of timing the transport to a labor and delivery unit/facility and in alerting an operating room team. For example, Category 1 FHR tracings are considered normal and no specific action is required. Category 2 tracings are considered indeterminate. This category requires evaluation, surveillance, and possibly other tests to ensure fetal well-being. Category 3 tracings are considered abnormal and require prompt evaluation. An abnormal FHR tracing may require intrauterine resuscitation prior to transporting the pregnant woman (ACOG, 2009, 2010; D. A. Miller, 2010).

Many different fetal testing modalities are used prior to discharging the pregnant woman from obstetric triage. In all situations prior to discharge, clinicians must adequately assess the EFM tracing to obtain evidence of maternal and fetal well-being and have complete documentation that supports management of any non–Category 1 fetal tracing. Any pregnant woman discharged from an obstetric triage unit or emergency setting must have evidence of fetal well-being. Failure to adequately assess the FHR tracing or failure to respond to a non–Category 1 tracing can affect fetal and maternal outcomes.

CLINICAL PEARLS

- The goals of fetal evaluation are to accurately identify the well-oxygenated fetus so that unnecessary intervention is avoided as well as recognize the fetus at risk, thus preventing adverse perinatal outcomes.
- Despite widespread use of antepartum fetal assessment technologies, there is limited evidence to guide the type of test, testing intervals, gestational ages at which to initiate testing, or optimal frequency of testing.
- In the case of intrauterine growth restriction (IUGR), fetal testing with Doppler measurements indicate either absent or reversed end-diastolic flow has been associated with acidosis and perinatal morbidity.

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Limited or No Prenatal Care at Term

Linda Steinhardt

The essential elements of care for the pregnant woman at term who presents to the obstetric triage unit or emergency department with late or no prenatal care (PNC) is reviewed. The goals of such a visit include establishing maternal and fetal well-being; determining the gestational age of the pregnancy, number of fetuses, fetal presentation, and labor status; and addressing immediate needs. If a woman is not admitted to the hospital, enrollment into PNC needs to be expedited. The U.S. Department of Health and Human Services (DHHS) defines late or no PNC as births that occur to mothers in the third trimester with no documentation of PNC, or documented no PNC on the child's birth certificate (DHHS, 2015). This population includes a wide range of women, who for a variety of reasons experience barriers to obtaining PNC.

INCIDENCE

U.S. statistics from 2014 represent the most recent published data on this population. In that year, there were 3,988,076 live births (Centers for Disease Control and Prevention [CDC], 2014). Four to eleven percent of all reported births were to women with late or no PNC (DHHS, 2015). In 2014 American Indian and Alaska Native women were the most likely to receive late or no PNC (11%), followed by Black (10%) and Hispanic women (8%). On the other end of the spectrum during the same year, 6% of births among Asian or Pacific Islander women, and 4% of births among White women, received late or no PNC (DHHS, 2015). Young women in their teens are the least likely to receive timely PNC. In 2014 25% of births to females under age 15, and 10% of births to teens ages 15 to 19 were to those receiving late or no PNC (DHHS, 2015). In addition, women who have unplanned births are less likely to recognize pregnancy early or to receive adequate PNC (Guttmacher Institute, 2015). Almost 40% of the annual births in the United States result from an unintended pregnancy (Guttmacher Institute, 2015). These represent a large number of pregnant women who may present to the emergency department for a first and/or only PNC visit. Infants born to mothers who receive no PNC are three times more likely to be born with low birth weight, five times more likely to die (DHHS, 2015), and have twice the risk of preterm birth (Cunningham et al., 2014) than those whose mothers received PNC.

WHY WOMEN DO NOT SEEK PRENATAL CARE

Pregnant women may not seek PNC for a variety of social, economic, and medical reasons. Analysis of birth certificate data by the CDC found that risk factors for inadequate PNC included ethnicity, socio-economic status, age and method of payment for services (CDC, 2014; Every Mother Counts, 2014), undocumented status (Guttmacher Institute, 2016a), or other problems (Guttmacher Institute, 2016a). Common reasons cited were that a woman did not know she was pregnant, lacked money or insurance, and had no transportation (DHHS, 2013, 2015). The most recent statistics from 2015 show a marked decrease in the number of uninsured women of childbearing age (ages 15–44) in the United States from 19.6% in 2012 to 13.3%. This is largely due to the Affordable Care Act (Shartzer et al., 2015). Although this is an improvement, it still leaves approximately 530,400 women annually without insurance. Uninsured women are less likely to access PNC (Schartzer et al., 2015). Still, lack of money or insurance remains the second most likely reason for a woman to delay or not obtain PNC, the most common being late identification of pregnancy (Cunningham et al., 2014, p. 167). Access to care for minors can be a complicating factor (Guttmacher Institute, 2016b). Compared with women having planned births, those who have unplanned births are less likely to recognize pregnancy early, to receive early PNC or to breastfeed, and are more likely to have low-birth-weight babies (Guttmacher Institute, 2015). National trends toward restrictive access to abortion services can create a situation where a woman does not desire a pregnancy yet cannot terminate it (Guttmacher Institute, 2015). The 6.4 million women of reproductive age who are not U.S. citizens are much less likely to be insured, especially those who live in poverty and are often barred from Medicaid (Guttmacher Institute, 2016a). Still other barriers may include social pressures such as undocumented legal status, relocation, drug abuse, fear of interacting with "the system", difficulty with assessing care, or being a woman who has experienced intimate partner violence or reproductive coercion (Guttmacher Institute, 2016c). Social services often available in the emergency setting provide vital assistance in identifying/assessing barriers and expediting the process to obtain necessary documentation, insurance, mental health assessment, and referrals to appropriate agencies.

EMERGENCY MEDICAL TREATMENT AND ACTIVE LABOR ACT

The Emergency Medical Treatment and Active Labor Act (Centers for Medicare & Medicaid Services [CMS], n.d.) mandates a medical screening exam (MSE) for any pregnant woman, regardless of age, who presents to obstetric triage with uterine contractions, or who might be in active labor (CMS, n.d.). The examination includes, at a minimum, assessment of vital signs, fetal heart tracing (FHT) status, frequency and intensity of uterine contractions, fetal presentation, cervical dilatation, status of membranes, and rapid assessment of the presenting complaint (CMS, n.d.). The MSE examination must be performed by a "qualified medical examiner" (QME; CMS, n.d.). The QME must be someone who is credentialed to perform this function within this setting and who meets hospital credentialing requisites, as well as state rules and regulations for practice (CMS, n.d.). The QME may include physicians, certified nurse midwives, nurse practitioners, physician assistants, or RNs (CMS, n.d.). Nurses

must be credentialed to perform the MSE within their respective hospitals, and in addition, they must meet individual state rules and regulations for nursing practice (CMS, n.d.).

CARE OF MINORS

State law is superseded by EMTALA in the case of pregnant minors who are pregnant and contracting (CMS, n.d.). In the case of a minor who is pregnant but not contracting, regulations differ by state. The great majority of states and the District of Columbia currently allow a minor to obtain confidential PNC, including regular medical visits and routine services for pregnancy (Guttmacher Institute, 2016b). State by state information is available at www.guttmacher.org (Guttmacher Institute, 2016b).

EXAMINATION OF THE WOMAN WITH LATE OR NO PRENATAL CARE AT TERM

PRESENTING SYMPTOMATOLOGY

Even when a woman is obviously pregnant, the presenting complaint may not include pregnancy (Minnerop, Garra, Chohan, Troxell, & Singer, 2011). The history alone is not a reliable method of confirming pregnancy. Key questions for a relevant pregnancy history are summarized in Exhibit 13.1.

EXHIBIT 13.1

Key Questions to Ascertain Relevant Pregnancy History

1. When was your last menstrual period?
2. Do you know when your due date is?
3. Were you using contraception?
4. What number pregnancy is this for you?
5. What happened with your previous pregnancies?
   a. Were they term?
   b. Were they normal vaginal deliveries or cesarean sections?
6. Have you received any prenatal care anywhere? If so, where?
7. Do you have any medical problems?
8. Do you take any medications? Any drug usage?
9. Do you have any allergies?
10. Do you feel fetal movement?
11. Do you have vaginal bleeding?
12. Are you having contractions, if so, how frequently?
13. Have you noticed leaking of fluid?
14. Intimate partner violence or control screening questions
15. Travel history and corresponding symptomology including specific questions regarding areas where Zika, Ebola, or tuberculosis are endemic
16. Drug and alcohol screen questions

Sources: Adapted from CDC (2016) and Cunningham et al. (2014).

The most frequent presenting symptomology includes: gastrointestinal and gynecologic complaints, urinary issues, trauma, psychiatric problems, syncope, chest pain, or respiratory difficulty. In addition to determining the chief complaint, it is crucial to obtain as much information as possible about the pregnancy to date.

PHYSICAL EXAMINATION

Vital signs are performed at the point of care to evaluate maternal status and confirm a viable, intrauterine pregnancy. Establishing gestational age is crucial at this time. Ideally, this is performed and confirmed by ultrasound identifying the following: fetal presenting part, number of fetuses, placental location, amniotic fluid index, and biometry. Biometry is the measurement of fetal head circumference, abdominal circumference, and femur bone length that are used to calculate an estimated fetal weight (EFW). Fetal weight loosely corresponds to gestational age although the accuracy of ultrasound for estimation of EFW decreases as pregnancy advances, as the margin of error is 8% (Cunningham et al., 2014). Figure 13.1 shows a near-term fetus with cephalic presentation.

The abdominal examination consists of observing for any scars suggestive of previous cesarean section or other uterine surgeries, palpation of fundal height for an estimation of gestational age, and evaluation for uterine contractions. Leopold's maneuvers are performed, which are a series of gentle and deliberate palpations of the abdomen that can help to establish fetal position, lie, presentation, and EFW of the fetus (Cunningham et al., 2014).

An external fetal monitor is applied to assess the fetal heart rate and frequency/intensity of uterine contractions. Establishing fetal well-being is a vital part of the evaluation. A normal fetal heart rate baseline is between 110 to 160 beats per minute. Fetal Doppler or external fetal monitor is used to ascertain the fetal heart rate and assess for baseline, variability, and presence or absence of accelerations and decelerations.

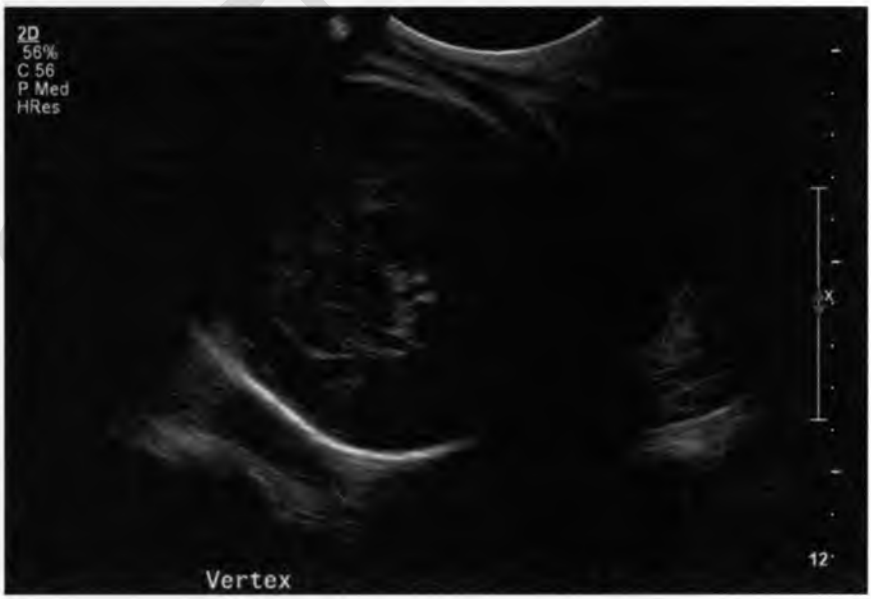

Figure 13.1 Ultrasound image of cephalic presentation, at term

Source: Courtesy of Women & Infants Hospital, Department of Radiology, Providence, RI.

An abdominal ultrasound is performed to eliminate the finding of placenta previa. A vaginal examination performed in the presence of placenta previa can cause a life-threatening hemorrhage to mother and fetus. A speculum examination is performed to observe for the following: lesions, bleeding, fluid pool, vaginal discharge, signs of infection, cervical dilation, presenting part, or prolapsing umbilical cord. A vaginal examination is performed to assess cervical dilation, effacement, station, and fetal presentation.

LABORATORY AND IMAGING STUDIES

Specimens collected during the sterile speculum examination might include amniotic fluid testing for nitrazine and ferning, as well as a wet mount. When an abnormal vaginal discharge is observed, a swab may be collected for Affirm™ testing, which uses DNA probes to detect and identify the three most common sources of vaginal infection: *Candida* species, *Gardnerella vaginalis*, and *Trichomonas vaginalis*. Cultures for gonorrhea and chlamydia as well as a Group B Strep (GBS) culture need to be obtained. A urine drug screen may be warranted, and the woman's consent is usually necessary before this can be collected and sent for analysis.

GBS is a bacterium associated with neonatal infection and sepsis. It is transmitted from mother to fetus during the birth process. In order to minimize this complication, women with unknown GBS status are treated based on risk factors; however, a confirming culture may prove useful in care of the neonate. Treatment is comprised of appropriate antibiotics administered during labor and until the infant is born. Exhibit 13.2 summarizes risk factors for GBS when a woman's status is unknown.

In addition to the routine prenatal laboratory panel, which is listed in Table 13.1, additional labs may be necessary based on individual cases.

For instance, if a woman has recently been out of the country or is a recent immigrant, she might have been exposed to a variety of infectious or communicable diseases. These can include a wide range of possibilities including viral or parasitic infections. Measles, mumps, diphtheria, and other infections, such as malaria, not commonly seen in the United States may also present and will need to be considered in the emergency setting. In addition, women may present with previously undiagnosed conditions such as tuberculosis and will

EXHIBIT 13.2

Group B Strep (GBS) Risk Factors

If GBS status is unknown, the recommendation is to give intrapartum prophylaxis by risk factors.

1. Preterm labor less than 37 weeks
2. Preterm premature rupture of membranes less than 37 weeks
3. Rupture of membranes greater than 18 hours
4. Maternal fever during labor greater than 38°C or 100.4°F
5. Previous infant with GBS sepsis
6. GBS bacteriuria during current pregnancy

Source: ACOG Committee Opinion, No. 485, April 2011 (Reaffirmed 2015).

Table 13.1 Prenatal Laboratory Panel for Women With No Prenatal Care at Term

	INFORMATION YIELDED
Blood	
Complete blood count	Anemia, inherited anemias, thrombocytopenia
Blood type and Rh	Need for Rhogam
Blood antibody screen	Hemoglobinopathies
Hepatitis B surface antigen	Screen for hepatitis B
Hepatitis C virus	Screen for hepatitis C
Rapid plasma reagin or Veneral Disease Research Lab	Syphilis status
Human immunodeficiency virus	Special care plan and medications
Rubella titer	Screen need for PP vaccination
Hemoglobin electrophoresis	Sickle cell syndromes or thalassemias
Vaginal	
Chlamydia, gonorrhea cultures	STI testing
Group Beta Strep culture	Screen for prophylaxis in labor if greater than or equal to 35–37 weeks gestation
Nitrazine	Vaginal pH and screen for ruptured membranes
Dry slide of vaginal discharge	Ferning for ruptured membranes
Wet prep slide	Screen for infections (*Candida*, bacterial vaginosis, *Trichomonas*)
Urine	
UA	Screen for infection, ketones, proteinuria, blood
Urine culture and sensitivity	Rule out infection if you suspect based on symptoms or UA
Urine drug screen (consent needed)	Screen for substance abuse

PP, postpartum; STI, sexually transmitted infections; UA, urinalysis.

Source: Adapted from Cunningham et al. (2014).

need appropriate precautions and isolation as indicated. Testing for tuberculosis, malaria, Ebola, or Zika may be considered in women from areas where these diseases are endemic.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses often include assessment of labor, evaluation of ruptured membranes, and monitoring of other pregnancy or medical conditions. Other conditions such as placental abruption, umbilical cord prolapse, and chorioamnionitis need to be addressed accordingly.

CLINICAL MANAGEMENT AND FOLLOW-UP

Clinical management and follow up care can take several pathways. Some pregnant women presenting to obstetric triage at term with scant or no previous

PNC may be in active labor or could be close to delivery when they present for care. In the case of those women not in active labor but with reassuring fetal status, referral for a prompt formal ultrasound and access to PNC are critical. Some women may simply have been unaware of services available to them. Social services may identify needed supports and establish access to services and/or insurance. Still other women require substantial social services to address homelessness, abusive situations, drug use, or mental health problems.

The key factors in the assessment of the woman with little or no PNC at term include identifying labor and addressing immediate needs. Appropriate follow up care includes admission to the hospital or referral for appropriate services.

CLINICAL PEARLS

- The essential elements of care for the pregnant woman at term with late or no PNC include establishing maternal and fetal well-being; determining the gestational age of the pregnancy, number of fetuses, fetal presentation, and labor status; travel history; and addressing immediate needs.
- Four to eleven percent of all reported births were to women with late or no PNC.
- The risk factors for unknown GBS status include preterm labor at less than 37 weeks, preterm premature rupture of membranes, rupture of membranes at term greater than 18 hours, maternal fever, prior infant with GBS sepsis, and GBS bacteriuria during current pregnancy.

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Preterm Labor

14

Linda A. Hunter

Defined as a delivery that occurs prior to 37 weeks gestation, preterm birth is the leading cause of perinatal mortality and long-term infant morbidity worldwide (Frey & Klebanoff, 2016). According to the National Center for Health Statistics, the preliminary preterm birth rate in the United States for 2015 was 9.62% (Hamilton, Martin, & Osterman, 2016). Although this represents a small percent rise from 2014 (9.57%), the preterm birth rate in the United States has been steadily decreasing since 2006 when the rate peaked at 12.8% (Hamilton et al., 2016). Despite these trends, the preterm birth rate in the United States remains one of the highest among industrialized nations (Frey & Klebanoff, 2016). Although advances in perinatal and neonatal medicine have improved the survival rates for these infants, the consequences of prematurity still pose lifelong disability and economic burden (Frey & Klebanoff, 2016). Preterm births are classified as either *spontaneous* (i.e., premature rupture of membranes or preterm labor with cervical dilatation) or *indicated* (i.e., induction of labor for maternal or fetal complications). Preterm births are also categorized by gestational age at delivery. For example, preterm births occurring between 34 and 36 weeks are referred to as *late preterm births* (Hamilton et al., 2016). This chapter will present the diagnosis and management of spontaneous preterm labor in singleton pregnancies occurring between 24 and 34 weeks gestation.

PRESENTING SYMPTOMATOLOGY

Etiology and Risk Factors

Regular and painful uterine contractions that result in cervical change have been the long-accepted definition of labor. Until recently, this "common pathway of parturition" was thought to occur similarly in both full-term and preterm labor (Romero, Dey, & Fisher, 2014). Unlike labor at full-term gestations, however, spontaneous preterm labor is an enigmatic process that occurs when the normal labor pathway is triggered through various pathologic mechanisms. Intrauterine infection or inflammation, immunologic reactions, hormonal disorders, cervical insufficiency, and uterine ischemia, hemorrhage, or overdistention have all been implicated as associated factors in preterm labor (Romero et al., 2014). More recently, specific genetic and genome pathways have been linked to birth

timing, providing opportunities for future research aimed at understanding the mechanisms of preterm parturition (Monangi, Brockway, House, Zhang, & Muglia, 2015).

A number of contributing factors have been identified that increase a woman's chances of giving birth before 37 weeks. This comprehensive list represents years of epidemiologic investigation that has yet to establish a clear chain of causality with the sole exception of intra-amniotic infection (Romero et al., 2014). In addition, strategies to identify and treat medical risk factors during pregnancy have not reduced the preterm birth rate (Iams, 2014). A history of prior preterm birth or a short cervical length (measured by transvaginal ultrasonography) of less than or equal to 20 mm remain the most significant risk factors for preterm delivery (Iams, 2014). A summary of preterm birth risk factors can be found in Exhibit 14.1.

EXHIBIT 14.1

Risk Factors Associated With Spontaneous Preterm Birth

Major Risk Factors

- Previous preterm birth[a]
- Non-White race[b]
- Infection/inflammation[c]
- Cervical insufficiency[d]
- Multiple gestation
- Bleeding in second trimester
- Mullerian uterine anomalies

Associated Risk Factors

- Low socioeconomic status
- Maternal age less than 18 or greater than 40
- Limited maternal education
- Unmarried
- Poor nutrition/underweight
- Short interconception period (<6 months)
- Smoker
- Drug abuse
- Life stressors
- Occupational fatigue
- Family history of preterm birth
- Periodontal disease
- Sexually transmitted infections
- Shifts in vaginal ecosystem

[a]Induced or spontaneous.
[b]Black, African American, Afro Caribbean.
[c]Chorioamnionitis or systemic infections (pneumonia, pyelonephritis, appendicitis).
[d]Shortened cervix less than or equal to 2.5 mm on transvaginal ultrasound in second trimester.

Source: Adapted from Goldenberg, Culhane, Iams, and Romero (2008).

HISTORY AND DATA COLLECTION

Subjective Assessment

Women with threatened preterm labor often present with a myriad of nonspecific symptoms such as constant low backache, pelvic pressure, mild irregular uterine cramping, and increased watery vaginal discharge. While the majority of women admitted to the hospital for treatment of threatened preterm birth will go on to deliver at full-term gestations, any persistent abdominal, pelvic, or vaginal symptoms warrant a full obstetric evaluation to rule out preterm labor.

The diagnosis of true preterm labor can be challenging to determine clinically. Regular, painful contractions with a progressive change in cervical effacement and/or dilatation or cervical dilatation of at least 2 cm are reliable clinical indicators (American College of Obstetricians & Gynecologists [ACOG], 2016b). The presence of any vaginal bleeding or premature rupture of membranes greatly adds to the likelihood of impending birth. More importantly, the transition from subclinical parturition to overt preterm labor has been most likely triggered by one or more pathologic processes (Romero et al., 2014). Consequently, the presence of past or current risk factors for preterm birth is important to ascertain, as well as any recent associated symptoms such as fever, malaise, nausea, vomiting, diarrhea, urine symptoms, drug use, and trauma. Previous cervical assessments (digital or ultrasound) or recent sexual intercourse are also noted.

Gestational Age Assessment

A crucial next step in data collection is a thorough review of the dating criteria used to determine gestational age. Women who conceive with assisted reproductive technologies will have the most accurate pregnancy dating, followed by first trimester ultrasound assessment (Benson & Doubilet, 2016). Menstrual dating is still considered to be reliable, especially when corroborated by an ultrasound performed prior to 20 weeks gestation (Benson & Doubilet, 2016). Accuracy of fetal biometry ultrasound decreases with advancing gestational age. Consequently, women who present for care in the third trimester with an unsure menstrual history could potentially have a margin of error with ultrasound dating of anywhere from 21 to 30 days (ACOG, 2014; Benson & Doubilet, 2016). No matter how the gestational age was determined, some margin of error exists and clinicians must use the best evidence-based criteria to discern the boundaries for preterm labor treatment.

PHYSICAL EXAMINATION

Pregnant women with a gestational age of greater than 24 weeks who present with any symptoms suggestive of preterm labor require continuous external fetal monitoring for contractions and assessment of fetal well-being. Observation of the woman's demeanor and response to contractions is ongoing while the remainder of the physical examination is completed. Constitutional assessment includes temperature, pulse, respirations, and blood pressure, paying careful attention for the presence of any fever, tachycardia, or tachypnea. Auscultation of the heart and lungs is performed, as well as thorough palpation of the abdomen and uterine fundus for any signs of tenderness, rebound, or guarding. Percussion of the flank area for costovertebral angle tenderness is another requisite component of this evaluation to assess for signs of renal etiologies.

Lastly, a complete pelvic exam is performed. It is imperative that a digital examination is *not* performed until the vagina and cervix are first visually inspected using a sterile speculum. This enables the clinician to initially exclude the possibility of preterm premature rupture of membranes (PPROM) and obtain any necessary specimens for further evaluation. Cervical dilation, bleeding, or discharge can also be assessed during this inspection. Regardless of the appearance of the cervix, once PPROM is ruled out and the possibility of placenta previa is also excluded, a digital examination can be safely performed to more thoroughly assess cervical dilatation, effacement, consistency, and position.

LABORATORY AND IMAGING STUDIES

Since there are a number of pathologic processes that could lead to preterm labor, the physical examination must be accompanied by laboratory studies that will facilitate accurate diagnosis of etiologies such as intrauterine and extrauterine infections. A complete blood count and clean catch urinalysis (with micro) are basic first steps of this evaluation. During the pelvic examination, cultures for gonorrhea, chlamydia, and a vaginal swab for wet mount assessment are collected. Specifically, a wet mount is obtained to identify the presence of either bacterial vaginosis or trichomoniasis. These infections have been implicated as risk factors for preterm labor, especially in women with a history of preterm birth, although absolute causality has not been established (Koullali, Oudijk, Nijman, Mol, & Pajkrt, 2016).

Fetal Fibronectin

Fetal fibronectin (fFN) is an extracellular glycoprotein normally found in the amniochorionic membrane prior to 20 weeks gestation and again as labor approaches in full-term gestations due to physiologic cervical remodeling and effacement (Berghella & Saccone, 2016). For women presenting with threatened preterm labor between 24 and 34 weeks gestation, the presence or absence of fFN was thought to hold some predictive value in determining the risk of delivery within 7 days. The fFN sample must be collected prior to any other vaginal or cervical examination and its validity is greatly hampered by the presence of lubricants, bleeding, amniotic fluid, and sexual intercourse within 24 hours (Wax, Cartin, & Pinette, 2010). Proper technique requires that the swab is placed in the posterior vaginal fornix (avoiding the cervical os) during the speculum examination but can also be inserted blindly into the vagina (Wax et al., 2010). In either case, the swab is left in position for a minimum of 10 seconds and placed in the appropriate culture medium according to the manufacturer's instructions. The specimen can then be set aside and either sent or discarded as the clinical situation dictates.

Previous evidence on the clinical utility of fFN testing in threatened preterm labor has demonstrated a negative predictive value of almost 98%, providing reassurance that delivery is unlikely within the next 7 days (Sanchez-Ramos, Delke, Zamora, & Kaunitz, 2009). The positive predictive value of fFN unfortunately is only 25.9%, often leading to overtreatment and increased costs (Sanchez-Ramos et al., 2009). In a more recent systematic review, Berghella and Saccone (2016) state fFN testing has not been found to improve outcomes or decrease the incidence of preterm birth and should not be used routinely in the management of women with threatened preterm labor. They further conclude fFN is best utilized in screening protocols that include transvaginal ultrasound measurement of cervical length (Berghella & Saccone, 2016).

Initially, real-time abdominal ultrasound is performed to confirm the presenting part, identify placental location, or gauge an approximate gestational age, if needed. Ultrasound can also be utilized to provide a transvaginal measurement of cervical length (TVCL). When compared to digital assessments performed in early labor, transvaginal cervical sonography imparts a more consistent and objective measurement of the cervix (Nijman, van Vliet, Koullali, Mol, & Oudijk, 2016). Moreover, decreasing TVCL has been associated with increased risks of spontaneous preterm birth (Nijman et al., 2016). As a screening tool in selected asymptomatic high-risk women (those with a history of prior preterm birth), a second trimester TVCL measurement of 25 mm is considered the threshold discriminator for predicting future recurrence risk of preterm delivery and may indicate cervical insufficiency (Iams, 2014).

For women presenting with preterm contractions at 24 weeks or beyond, a TVCL measurement can distinguish a low (less than 5%) versus high probability of preterm delivery (Nijman et al., 2016). For example, a TVCL of 30 mm or greater precludes the likelihood of preterm birth within the next 7 days (Nijman et al., 2016; Van Baaren et al., 2014). The addition of an fFN culture further stratifies the risk category when the TVCL is between 15 to 30 mm. Symptomatic women with a TVCL of less than 15 mm or 15 to 30 mm with a positive fFN are at high risk to deliver within the next week and require prompt treatment (Nijman et al., 2016). Conversely, when combined with a negative fFN, a normal TVCL measurement can greatly reduce false positive diagnoses and provide a more cost-effective alternative to hospital admission (Nijman et al., 2016; Van Baaren et al., 2014). As a result, many hospitals have now incorporated protocols that include a combination of both TVCL and fFN in efforts to more accurately discriminate those women truly at high risk for delivery (Nijman et al., 2016; Van Baaren et al., 2014).

Mid trimester ultrasound can also assess other characteristics of the lower uterine segment and cervix that may provide additional risk stratification for the likelihood of a preterm delivery. Cervical funneling, for example, is a term used to describe a measurable opening of the internal os and has been associated with cervical insufficiency (Mella & Berghella, 2009). Protrusion of the amniotic membrane into the inner cervical canal can have a "V" or "U" shaped appearance (Mancuso et al., 2010). In the presence of a shortened cervix, a "U" shaped funnel in particular is an ominous sign and the risk of preterm birth is greatly increased (Berghella et al., 2007; Mancuso et al., 2010). See Figure 14.1 for a transvaginal measurement of shortened TVCL with funneling.

DIFFERENTIAL DIAGNOSIS

Women experiencing the wide array of symptoms associated with threatened spontaneous preterm labor will generate a broad list of differential diagnoses. This inventory includes fairly straightforward etiologies such as Braxton Hicks contractions and round ligament pain. More serious causes such as pyelonephritis or chorioamnionitis must be conclusively ruled out. Regardless of the presumed cause(s), overt preterm labor calls for expeditious treatment, especially in cases where birth seems imminent. A comprehensive list of differential diagnoses is noted in Exhibit 14.2.

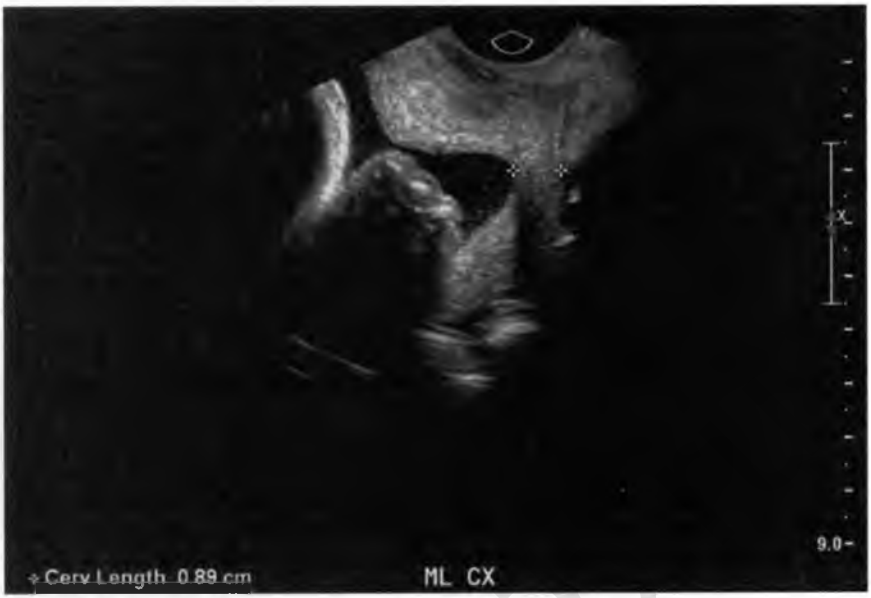

Figure 14.1 Sonographic image of shortened cervix with funneling

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

CLINICAL MANAGEMENT

Once the diagnosis of spontaneous preterm labor is made, clinical management is focused on strategies that have been shown to improve neonatal outcomes such as expeditious transfer to a neonatal intensive care facility. Other key interventions include antenatal corticosteroids, delay of delivery, administration of antibiotics, and fetal neuroprotection.

Antenatal Corticosteroids

Numerous studies conclusively uphold that a single course of antenatal corticosteroids administered to women in preterm labor between 24 and 34 weeks gestation significantly reduces the incidence of neonatal respiratory distress syndrome, intraventricular hemorrhage, and other morbidities associated with prematurity (Neilson, 2007; Nijman et al., 2016). Antenatal corticosteroids are most effective when given within a week of actual delivery; however, even one dose given within 24 hours of birth will convey some neonatal benefit (Neilson, 2007; Nijman et al., 2016). Currently, the ACOG advocates the use of either betamethasone or dexamethasone to hasten neonatal lung maturity for women between 24 and 34 weeks gestation at risk for delivery within 7 days (ACOG, 2016a). In addition, if delivery does not occur within 7 days, a single repeat course of "rescue steroids" can be given if (a) more than 2 weeks have passed, (b) the gestational age is less than 32 6/7 weeks, and (c) the risk of delivery is again within 7 days (ACOG, 2016a). See Table 14.1 for current corticosteroid options and dosing recommendations.

Another more recent consideration is now being given to the administration of corticosteroids to women who present with threatened preterm labor in the late preterm period (34–36 6/7 weeks gestation). The recently published

EXHIBIT 14.2

Differential Diagnoses for Spontaneous Preterm Labor

Physiologic

- Braxton Hicks contractions
- Uterine irritability
- Dehydration
- Lax vaginal tone
- Round ligament pain
- Sacroiliac joint instability
- Unknown cause

Pathologic

- Intrauterine infections
  - Chorioamnionitis
  - Decidual inflammation
- Extrauterine infections
  - Urinary tract infection
  - Kidney stone
  - Pyelonephritis
  - Appendicitis
- Genital tract infections
  - Gonorrhea/chlamydia
  - Bacterial vaginosis
  - Trichomoniasis
- Placental abruption
- Trauma

Note: This list is not all inclusive and does not imply causality.

Source: Adapted from Goldenberg et al. (2008).

Antenatal Late Preterm Steroid (ALPS) Trial demonstrated improved neonatal respiratory outcomes and shortened neonatal intensive care unit (NICU) stays in this subgroup (Gyamfi-Bannerman et al., 2016). As a result, ACOG has issued a Practice Advisory (2016b) that states antenatal corticosteroids can be considered for women in late preterm gestations presenting in labor if delivery is imminent within 7 days and they have not previously received steroids during this pregnancy. In addition, delivery will not be delayed or postponed in order to complete a full course of treatment (ACOG, 2016b). Antenatal corticosteroids are contraindicated in women who have been diagnosed with chorioamnionitis (ACOG, 2016b).

Intrapartum Antibiotics

Infants born prior to 34 weeks are particularly susceptible to early onset Group B Streptococcus (GBS) disease with a reported neonatal mortality rate of 20% to 30% (Centers for Disease Control and Prevention [CDC], 2010). Since routine GBS screening does not occur until 35 to 37 weeks gestation, most women presenting in preterm labor prior to this gestational age will have unknown colonization status. Consequently, if preterm delivery seems likely, a culture for

TABLE 14.1 Current Guidelines for Antenatal Corticosteroids[a]

BETAMETHASONE	DEXAMETHASONE
12 mg IM 2 doses given 24 hours apart	6 mg IM 4 doses given 12 hours apart

IM, intramuscular.

[a]Recommended for preterm labor 24 to 34 weeks gestation and birth likely within 1 week. Dosing guidelines are the same for rescue course.

Source: ACOG Practice Bulletin No. 171 (2016b).

GBS colonization should be obtained and prophylactic treatment with either intravenous penicillin or ampicillin initiated (CDC, 2010). Other antibiotics can be used when a penicillin allergy exists; however, if GBS colonization or sensitivities are unknown, vancomycin is the recommended alternative (CDC, 2010). Although published in 2010, these guidelines remain the current standard of care for GBS prophylaxis in impending preterm birth.

Delay of Delivery

One of the more controversial aspects of preterm labor management has continued to revolve around the utility, efficacy, safety, and side effects of tocolytic medications. Many different pharmacologic agents have been utilized over the past 50 years as researchers have fervently sought to prolong pregnancy in hopes of reducing the preterm birth rates. All of these medications have certainly demonstrated the ability to produce some degree of uterine quiescence, which in theory should have achieved this goal. Unfortunately, many of these drugs cause untoward side effects and increased risks of toxicity (Haas, Caudwell, Kirkpatrick, McIntosh, & Welton, 2012). More importantly, tocolysis has not been shown to prevent preterm births from occurring or reduce neonatal morbidity or mortality (ACOG, 2016b; Conde-Agudelo, Romero, & Kusanovic, 2011; Haas et al., 2012; Nijman et al., 2016). At best, tocolytic medications will delay preterm delivery from 2 to 7 days, allowing time for a full course of antenatal corticosteroids and transfer to a tertiary center if needed (Haas et al., 2012).

Until recently, the most commonly used tocolytic medications in the United States included calcium channel blockers (nifedipine), prostaglandin synthetase inhibitors (indomethacin), beta-mimetics (terbutaline), and magnesium sulfate (ACOG, 2016b; Haas et al., 2012; Nijman et al., 2016). Due to a higher incidence of maternal side effects, potential toxicity, and lowered comparative efficacy, magnesium sulfate and terbutaline have fallen out of favor and are no longer recommended for acute tocolysis by many authors (ACOG, 2016b; Haas et al., 2012; Nijman et al., 2016).

Despite ample evidence discouraging its continued use as a tocolytic, magnesium sulfate is still commonly used in the United States, especially in the context of preterm labor for fetal neuroprotection (ACOG, 2016b). In a recent Cochrane Review, magnesium sulfate was not found to have any benefit as a tocolytic over other treatment options (Crowther, Brown, McKinley, & Middleton, 2014). Most sources now recommend using either nifedipine or indomethacin as first-line therapies although indomethacin is recommended for gestations less than 32 weeks due to potential constriction of the fetal ductus arteriosus (Conde-Agudelo et al., 2011; Haas et al., 2012). Regardless, there is consensus agreement that tocolysis is discontinued after a full course of corticosteroids have been completely administered (ACOG, 2016b; Haas et al., 2012; Nijman et al., 2016). See Table 14.2 for tocolytic dosing guidelines.

TABLE 14.2 Guidelines for Tocolytic Medication Use

DRUG NAME	DOSING GUIDELINES	CONTRAINDICATIONS	MATERNAL SIDE EFFECTS	FETAL SIDE EFFECTS
Nifedipine	Loading dose: 30 mg orally[a] Maintenance: 10–20 mg orally every 4–6 hr for 48 hr	Cardiac disease, hypotension less than 90/50 **Caution with magnesium sulfate**[b]	Flushing, headache, dizziness, nausea, transient hypotension	None identified
Indomethacin[c]	Loading dose: 50–100 mg orally Maintenance: 25–50 mg orally every 6 hr for 48 hr	Significant renal or hepatic impairment	Nausea, heartburn	Constriction of ductus arteriosis, pulmonary hypertension, IVH oligohydramnios
Magnesium Sulfate[d]	Loading dose: 4–6 g IV Maintenance: 2–3 g/hr IV[e] for 48 hr (discontinue sooner if possible)	Myasthenia gravis **Caution with nifedipine**[b]	Flushing, lethargy, muscle weakness, cardiac or respiratory arrest	Lethargy, hypotonia, respiratory depression

hr, hour; IV, intravenous; IVH, intraventricular hemorrhage; mg, milligram.

[a]Alternative regime: 10 to 20 mg loading dose repeated every 3 to 6 hours until contractions slow, then 30 to 60 mg every 8 to 12 hours for 48 hours.
[b]Both drugs are calcium antagonists; careful monitoring is advised if used together (ACOG Committee Opinion No. 623; 2015).
[c]Recommended only for gestations less than 32 weeks.
[d]Not recommended for acute tocolysis unless nifedipine or Indomethacin are contraindicated.
[e]Must be administered via infusion pump with frequent monitoring of maternal respiratory rate and patellar reflexes.

Source: Adapted from ACOG Practice Bulletin No. 171 (2016b).

Fetal Neuroprophylaxis

One of the most promising perinatal discoveries in recent years has been the potential benefit of magnesium sulfate therapy in improving neurologic disability for infants born preterm. This neuroprotective role was first described in the 1990s by researchers who reported a decreased incidence of cerebral palsy in preterm infants exposed to antenatal magnesium sulfate (Nelson & Grether, 1995). Numerous studies including five randomized controlled trials have since been aggregated into a Cochrane Review indisputably confirming this hypothesis (Doyle, Crowther, Middleton, Maret, & Rouse, 2009). A recent review of this large body of evidence continues to support the neuroprotective benefits of magnesium sulfate for infants born before 32 weeks gestation (Rouse & Hirtz, 2016). As a mainstream practice in the management of spontaneous preterm labor, the administration of magnesium sulfate to women in these clinical situations has the potential to prevent 1,000 cases of cerebral palsy per year in the United States alone (Rouse & Hirtz, 2016).

The current ACOG Committee Opinion (2010) on fetal neuroprotection was reaffirmed in 2015 and continues to recommend that clinicians who elect to use magnesium sulfate for fetal neuroprotection develop specific guidelines in

accordance with one of the larger randomized controlled trials. Considered by some to be "the best single piece of scientific evidence available," the Beneficial Effects of Antenatal Magnesium Sulfate (BEAM) trial published in 2008 has subsequently become a favored option (Cahill, Stout, & Caughey, 2010). In this regime, intravenous magnesium sulfate is offered to pregnant women between 24 0/7 to 31 6/7 weeks gestation at high risk for impending delivery within 24 hours (Rouse et al., 2008). Using a shared decision-making approach, pregnant women and their families are also thoroughly informed of all risks and potential fetal benefits of this therapy (Cahill et al., 2010). As modeled in the BEAM trial (Rouse et al., 2008), magnesium sulfate is then administered intravenously first as a loading dose of 6 g/hr over 20 to 30 minutes. This bolus is followed immediately by a continuous intravenous infusion of 2 g/hr (via an infusion pump) for 12 hours. The full dosing protocol can be repeated after 6 to 12 hours if delivery again seems imminent and/or discontinued once delivery occurs.

FOLLOW-UP

Inpatient observation for advancing cervical dilatation is often continued for at least 24 hours following acute tocolysis or for as long as deemed clinically necessary. Continuing to prolong pregnancy beyond this point has not been shown to reduce preterm birth rates nor have interventions such as home contraction monitoring, sedation, or bedrest (ACOG, 2016b). Prior to discharge from the hospital, any potential infectious causes of preterm labor are treated and strategies to reduce preterm birth risks addressed. For those women who re-present at a later date with threatened preterm labor, the clinical appropriateness of rescue steroids, fetal neuroprophylaxis, and GBS prevention must all be reassessed.

CLINICAL PEARLS

- fFN testing is best utilized in preterm labor screening protocols that include transvaginal ultrasound measurement of cervical length.
- Evidence supports the neuroprotective benefits of magnesium sulfate administration to women presenting in preterm labor prior to 32 weeks gestation.
- The recently published ALPS trial demonstrated improved neonatal respiratory outcomes and shortened NICU stays in infants born in the late preterm period (34 to 36 6/7 weeks) who received betamethasone prior to delivery.

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Preterm Premature Rupture of Membranes

15

Alexander Friedman

Premature rupture of membranes (PROM) is defined as spontaneous rupture of the membranes prior to labor. When PROM occurs at less than 37 weeks gestational age, it is defined as preterm premature rupture of membranes (PPROM). Suspicion for PPROM is a commonly encountered clinical scenario in obstetric triage. PPROM occurs in 3% of pregnancies, causes one-third of preterm births, and is associated with brief latency from rupture of membranes to delivery (Mercer, 2003). Risk factors associated with PPROM include subclinical intrauterine infection, placental abruption, and uterine overdistention (Simhan & Canavan, 2005). However, most women who develop PPROM have no identifiable risk factors (Waters & Mercer, 2011). Timely diagnosis and treatment are necessary to optimize care. Even with conservative management, 50% to 60% of pregnant women will deliver within 1 week of rupture (Mercer, 2003). While several interventions have been shown to improve neonatal and maternal outcomes after PPROM, early preterm infants delivered after PPROM commonly face significant complications such as respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), and sepsis (Mercer, 2003).

PRESENTING SYMPTOMATOLOGY

The most common presenting symptom for PPROM is a gush of vaginal fluid. However, women may complain of increased discharge, urinary incontinence, perineal moisture, or leakage of small amounts of fluid (Simhan & Canavan, 2005). The differential diagnoses for leakage of fluid or increased perineal dampness include PPROM, urinary incontinence (which increases during pregnancy), increased vaginal discharge (physiologic secondary to pregnancy), and expression of cervical mucus.

HISTORY AND PHYSICAL EXAMINATION

A standard obstetric history in the setting of suspected PPROM includes a past medical, surgical, social, obstetric, gynecologic, and social history. Medications

and allergies are included in the history. Careful review of the prenatal chart is important. Clinical risk factors for spontaneous preterm birth such as prior preterm delivery, prior cervical surgery, or shortened cervix on transvaginal ultrasound are included in the history. Frequently, the gestational age is critical in decision making so medical records must be carefully reviewed to determine exact pregnancy dating. The history includes duration and amount of leakage of fluid, and whether fetal movement, contractions, and vaginal bleeding are present. Reports of the color of the fluid and odor need to be noted by the provider.

A physical exam in a pregnant woman with suspicion for PPROM is performed to confirm the diagnosis and assess maternal and fetal status. The physical examination includes all the components of a basic physical exam including vital signs, general appearance, and a cardiac and lung assessment. The abdominal exam, noting whether or not fundal tenderness is present, is critical because this finding may signify a diagnosis of chorioamnionitis.

Diagnosis of PPROM is made by sterile speculum exam. On speculum exam, the dilatation and effacement of the cervix are only visually inspected. Prolapsed umbilical cord needs to be ruled out. Fluid seen coming directly from the cervical os confirms the diagnosis. The finding of pooling of vaginal fluid in the posterior fornix increases the likelihood of PPROM having occurred. If present, cervical fluid is analyzed to confirm the diagnosis. However, small amounts of vaginal pooling can occur with urinary incontinence or severe vaginal infections such as herpes simplex virus (HSV). A second clue may be vaginal pH. The vaginal pH is usually acidic with a pH of 4.5 to 6.0, and amniotic fluid is slightly alkaline with a pH of 7.1 to 7.2. Amniotic fluid in the vagina will usually change the color of nitrazine paper from yellow to blue–green as the pH increases beyond 6.4 to 6.8. Blood, semen, bacterial vaginosis, and alkaline urine may all decrease the pH of the vagina and result in a false positive nitrazine test (Simhan & Canavan, 2005).

A final test of vaginal fluid is assessment for "ferning" or "arborization." Amniotic fluid obtained with a sterile swab from the posterior fornix of the vagina and placed on a clean slide and allowed to dry will produce fern-like crystals (secondary to salt content) when viewed with microscope magnification. The slide is allowed to dry for 10 minutes, and the false negative rate increases the less time left to dry. Cervical mucus may also cause ferning, although these crystals tend to be thicker and darker. Because of this risk for false positive results, care should be taken to avoid swabbing cervical mucus (Simhan & Canavan, 2005).

If a pregnant woman provides a clinical history highly suspicious for PPROM, but the diagnosis is not confirmed by initial speculum exam, the woman can be placed in a semi-upright position and reexamined after 1 hour to allow for vaginal pooling. As a last resort, if results are still equivocal, amniocentesis with injection of indigo carmine dye may be performed. A tampon is placed; if any dye leaked from the cervix, a blue staining would be noted on the tampon, confirming the diagnosis of PPROM.

The physical exam includes assessment of fetal well-being with continuous fetal heart rate monitoring. Contractions are assessed by palpation and/or tocometry. Since women with PPROM are at risk for chorioamnionitis, presence or absence of pertinent physical exam findings consistent with infection are noted. Exhibit 15.1 lists the clinical criteria for chorioamnionitis (Gibbs, Blanco, St. Clair, & Castaneda, 1982; Tita & Andrews, 2010).

EXHIBIT 15.1

Clinical Criteria for Chorioamnionitis

Maternal temperature 100°F or higher with no other explanation for fever and any two of the following:
Maternal heart rate over 120 beats per minute
Fetal heart rate over 160 beats per minute
Foul smelling amniotic fluid
Fundal tenderness
Maternal WBC count greater than 14K or bandemia (>9%)

WBC, white blood cell.

Sources: Adapted from Gibbs et al. (1982) and Tita and Andrews (2010).

LABORATORY AND IMAGING STUDIES

Multiple laboratory tests are currently marketed to assess findings in the diagnosis of PPROM. The AmniSure test for rupture of membranes is an immunoassay for placental alpha microglobulin (PAMG-1). There are low levels of PAMG-1 in vaginal secretions and blood, but very high levels in amniotic fluid. AmniSure has been shown to be 94% to 99% sensitive and 88% to 100% specific in detecting rupture of membranes across a range of studies (Birkenmaier et al., 2011; Cousins, Smok, Lovett, & Poeltler, 2005; Lee et al., 2007; Ng et al., 2013). Other tests include Actim PROM and ROM Plus, which assess for placental protein 12 and a combination of placenta protein 12 and alpha-fetoprotein, respectively. Test characteristics appear to be similar to AmniSure (Erdemoglu & Mungan, 2004; Thomasino, Levi, Draper, & Neubert, 2013). Because of the costs of these tests, they are primarily used either for women with unclear rupture of membrane status or if providers with appropriate clinical training are unavailable to assess for pooling, ferning, and nitrazine changes.

If a pregnant woman has unknown Group B Streptococcus (GBS) status, vaginal and rectal cultures will be collected during the pelvic exam. If sexually transmitted infections are suspected, appropriate cultures are also collected and sent. A digital cervical exam is contraindicated if the woman is less than 34 weeks gestation, unless active labor or imminent delivery is suspected. Research demonstrates that latency (time from rupture to delivery) is decreased when serial examinations are performed (Alexander et al., 2000).

If the woman is between 32 and 34 weeks gestational age and has significant vaginal pooling, amniotic fluid may be obtained for lung maturity testing. Fluid can be collected using a 5- or 10-mL syringe attached to an intravenous catheter (with the needle removed). As much fluid as possible is obtained from the vaginal pool to maximize the probability that the sample is adequate for laboratory analysis for any lung maturity studies.

Ultrasound examination is a critical part of the evaluation for PPROM. Oligohydramnios offers supporting evidence for PPROM having occurred but is not the gold standard for the diagnosis. Normal or increased fluid volume does not preclude the diagnosis. Fetal presentation and placentation are additionally noted. An estimated fetal weight determined by biometry is obtained. In terms of laboratory work, a complete blood count is performed, as well as a GBS culture if the woman's status is unknown.

CLINICAL MANAGEMENT

Viability to 34 Weeks Gestational Age

At many centers, viability is defined as early as 23 weeks 0 days gestational age. However, some fetuses at 24 to 26 weeks gestational age may not be considered viable because of associated conditions (severe intrauterine growth restriction, major congenital anomalies, genetic syndromes, or other conditions predisposing to poor prognoses). Care must be individualized, and determination of viability includes the entire clinical picture, as well as input from neonatologists and the family's goals for care. Not all centers have neonatal intensive care unit (NICU) facilities to manage extreme prematurity (neonates born at 28 or fewer weeks gestational age). Obstetrical providers should be aware of their center's NICU capabilities and potential benefit of maternal transfer for PPROM within a system of regionalized perinatal care if both the status of the mother and the fetus are stable.

The mainstays of management for viable PPROM until 34 weeks include hospital admission, administration of betamethasone, latency antibiotics, and close evaluation of maternal and fetal status. Women who present with PPROM are at risk for chorioamnionitis and abruption, both contraindications to expectant management. The pregnant woman is assessed on a daily basis for chorioamnionitis, abruption, preterm labor, and nonreassuring fetal status (either with a nonstress test or biophysical profile).

Steroid Administration

Evidence supports the administration of betamethasone or dexamethasone in the setting of PPROM from 24 to 34 weeks gestational age. Steroids reduce the risk of RDS, NEC, and IVH. There appears to be no increased risk of maternal infectious morbidity from steroid administration (Roberts & Dalziel, 2006). Leukocytosis occurs after steroid administration and may not be representative of infection. The American College of Obstetricians and Gynecologists (ACOG, 2016c) states that steroids may be considered for pregnant women as early as 23 0/7 weeks of gestation at risk of preterm delivery within 7 days. Regarding late preterm steroid administration between 34 0/7 weeks and 36 6/7 weeks for patients with PPROM, the ACOG states: "Recent data indicate that administration of betamethasone in the late preterm period between 34 0/7 weeks and 36 6/7 weeks reduces respiratory morbidity in newborns. Although subgroup analysis was not done, approximately 20% of study patients had preterm PROM. It is assumed that patients with preterm PROM will benefit from betamethasone in the late preterm period" (2016c). Regarding rescue steroids, the ACOG states: "Whether to administer a rescue course of corticosteroids with PROM at any gestational age is controversial, and there is insufficient evidence to make a recommendation for or against" (2016a). These recommendations may change as evidence regarding risks and benefits evolves and it is recommended to consult up-to-date documents from the ACOG.

Magnesium Administration

For patients presenting with PPROM prior to 32 weeks, maternal administration of magnesium sulfate may provide neuroprotective benefits for neonates. The beneficial effects of the antenatal magnesium sulfate (BEAM) trial demonstrated that pregnant women at risk for preterm delivery between 24 and 31 weeks because of PPROM or advanced preterm labor who were randomized to magnesium sulfate had a significantly lower risk of a child born with cerebral palsy (Rouse et al., 2008). While protocols and dosing regimens may vary by center,

administration of magnesium sulfate for 24 hours, in the absence of maternal contraindications, for patients presenting with PPROM prior to 32 weeks is a reasonable clinical strategy. If a patient with PPROM is not at risk of imminent delivery 24 hours after presentation, magnesium may be discontinued.

Latency Antibiotics

Administration of latency antibiotics improves neonatal outcomes. Level 1 evidence demonstrates that antibiotic administration reduces RDS, NEC, neonatal sepsis, bronchopulmonary dysplasia, and pneumonia, while increasing latency (Hutzal et al., 2008; Mercer et al., 1997). Latency antibiotics along with antepartum steroids likely reduce perinatal mortality. A typical antibiotic regimen includes 48 hours of intravenous ampicillin and erythromycin, followed by 5 days of oral ampicillin and erythromycin (Mercer et al., 1997). Ampicillin and amoxicillin cover Group B Streptococcus and provide gram-negative and some anaerobic coverage. Erythromycin offers coverage of genital mycoplasma along with some coverage of gram-positive cocci. Azithromycin, which has a better side effect profile than erythromycin, may be used as an alternate macrolide. Amoxicillin-clavulanic

EXHIBIT 15.2

Antibiotic Regimens for PPROM

Sample Antibiotic Regimens

Ampicillin 2 g IV every 6 hr for 48 hr followed by amoxicillin 500 mg PO three times daily for 5 d

Plus One of the Following:

Erythromycin 250 mg IV every 6 hr for 48 hr followed by erythromycin 333 mg PO every 8 hr for 5 d

OR

Azithromycin 1 g PO once

OR

Azithromycin 500 mg IV every 24 hr for 48 hr followed by azithromycin 250 mg PO daily for 5 d

Sample Antibiotic Regimens for True Penicillin Allergy

Clindamycin 900 mg IV every 8 hr for 48 hr

Plus

Azithromycin 1 g PO once

OR

Azithromycin 500 mg IV every 24 hr for 48 hr followed by azithromycin 250 mg PO daily for 5 d

IV, intravenous; PO, per os (orally).

Sources: Adapted from Mercer et al. (1997) and Brenna Hughes, MD (personal communication, 2011).

acid should be avoided because of a possible increased risk of NEC. Exhibit 15.2 offers proposed antibiotic regimens, which may vary by medical center.

Many women who present with PPROM at less than 34 weeks may have a prior history of prior preterm birth and may be receiving 17-hydroxyprogesterone (17P). While researchers have hypothesized that 17P may work by an anti-inflammatory mechanism, no evidence exists that receiving 17P in the setting of PPROM increases maternal or neonatal infectious morbidity. No benefit to continuing 17P in the setting of PPROM has been established. Currently, there is insufficient evidence to recommend for or against continuing 17P in the setting of PPROM in women less than or equal to 34 weeks gestational age.

34 to 37 Weeks Gestational Age

At most clinical centers, the fetal and maternal risks of prolonging pregnancy in the setting of PPROM greater than or equal to 34 weeks outweigh fetal benefits of expectant management, and delivery is recommended. However, in remote locations without intensive neonatal care, expectant management may be warranted up until 36 weeks. Alternately, if fetal lung maturity is demonstrated at 32 to 33 weeks, the risks of prolonging the pregnancy may outweigh the benefits gained from an extra week to 2 weeks of latency, and delivery may be indicated prior to 34 weeks.

The Antenatal Late Preterm Steroids (ALPS) study administered steroids to women with singleton pregnancies at 34 to 36 5/7 weeks at high risk for preterm birth and found decreased risk of neonatal respiratory morbidity with steroid administration (Gyamfi-Bannerman et al., 2016). The ACOG and the Society for Maternal Fetal Medicine (SMFM) support steroid administration per the ALPS protocol for women who have not received prior courses of steroids. The SMFM and ACOG recommend against use of tocolytics in this context (ACOG, 2016b, 2016c; SMFM, 2016). In the study protocol, patients receiving steroids were administered 12 mg of betamethasone 24 hours apart and then "treated clinically according to local practice"; whether there is a clinical benefit associated with delaying delivery beyond 24 hours after steroid administration is unclear.

CONTROVERSIES IN PPROM MANAGEMENT

Cerclage and PPROM

Management of women who present with PPROM with a cerclage is controversial, and data to guide management are limited (Pergialiotis et al., 2015). One review found that in the setting of PPROM and cerclage, women who did not have cerclage removed were significantly more likely to have at least 48 hours of latency but were at significantly higher risk for maternal chorioamnionitis and neonatal death from sepsis. This led the authors to conclude that for PPROM at less than 23 weeks or greater than or equal to 32 weeks, cerclage should be removed immediately. For patients greater than or equal to 23 to less than 32 weeks, the authors recommend cerclage should either be removed immediately or after a 48-hour course of steroids (Giraldo-Isaza & Berghella, 2011). Another review on the same subject found the quality of data to be poor and not useful in guiding management. The review article demonstrated that studies were retrospective, used varying outcome measures, did not perform adjusted analyses, and were mostly performed before the current era of standard

PPROM management (steroids and antibiotic administration; Walsh, Allen, Colford, & Allen, 2010).

Herpes Simplex Virus and PPROM

Management of PPROM in the setting of active HSV infection is controversial. Increased risk of fetal HSV infection with expectant management must be weighed against risks of prematurity from earlier delivery. Because the viral load and risk of neonatal HSV is lower with recurrent infections, expectant management may be warranted in these patients. Data are limited in women with primary HSV outbreaks and PPROM (Ehsanipoor & Major, 2011). There are no clear recommendations for timing of delivery with either recurrent or primary HSV infections. In the setting of expectant management, it is reasonable to administer acyclovir or valacyclovir to patients with active lesions and PPROM to decrease virus activity; however, it is unclear if there is fetal or neonatal benefit from antiviral therapy.

Tocolytics in the Setting of PPROM

The use of tocolytics in the setting of PPROM is also controversial. A Cochrane meta-analysis demonstrated an increased risk of chorioamnionitis with tocolysis in the setting of PPROM. Latency was extended in this analysis with tocolysis; however, neonatal outcomes were not improved. These studies were performed prior to universal administration of corticosteroids and antibiotics. The authors concluded that there is insufficient evidence to support tocolytic therapy for women with PPROM (Mackeen, Seibel-Seamon, Grimes-Dennis, Baxter, & Berghella, 2011). In a survey study of maternal-fetal medicine specialists, the majority of respondents reported using tocolytics in PPROM to gain time for antenatal steroid administration (Ramsey et al., 2004). Tocolysis beyond the 48 hours required for steroid administration is not recommended.

Continuation of 17-Hydroxyprogesterone

Many women who present with PPROM at less than 34 weeks may have a prior history of prior preterm birth and may be receiving 17-hydroxyprogesterone (17P). While researchers have hypothesized that 17P may work by an anti-inflammatory mechanism, no evidence exists that receiving 17P in the setting of PPROM increases maternal or neonatal infectious morbidity. No benefit to continuing 17P in the setting of PPROM has been established. Random allocation

CLINICAL PEARLS

- PPROM is defined as spontaneous rupture of the membranes prior to labor at less than 37 weeks gestational age.
- PPROM causes one-third of preterm births, and timely diagnosis and treatment are necessary to optimize care.
- Important gestational-age dependent interventions may include antibiotics to increase latency, corticosteroid administration to reduce risk for neonatal morbidity, and magnesium for fetal neuroprotection.

of women with PPROM to 17P did not demonstrate any benefit (Combs et al., 2015). Currently there is insufficient evidence to recommend for or against continuing 17P in the setting of PPROM in women less than or equal to 34 weeks gestational age.

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Trauma in Pregnancy 16

Roxanne Vrees

Trauma is estimated to complicate 1 in 12 pregnancies and is the leading cause of nonobstetric maternal death in the United States (Mendez-Figueroa, Dahlke, Vrees, & Rouse, 2013). The incidence of trauma increases as pregnancy progresses, which has both maternal and fetal implications. Potential maternal injuries include contusions, sprains and strains, fractures, dislocations, and poisoning, as well as life-threatening injuries. In addition to almost 1 million deaths each year, maternal trauma is associated with an increased incidence of spontaneous abortion, preterm birth, preterm premature rupture of membranes, uterine rupture, unplanned cesarean delivery, placental abruption, and fetal demise (Mendez-Figueroa et al., 2013). The gestational age at the time of injury, the type and severity of the injury, and the injury mechanism are all important considerations that impact treatment course as well as maternal and fetal outcomes. This chapter will focus primarily on noncatastrophic trauma in viable pregnancies, along with a brief discussion of catastrophic trauma including pelvic fractures, burns, electrical injuries, and maternal cardiopulmonary arrest. Exhibit 16.1 provides a general overview of the classification of trauma during pregnancy. A comprehensive review of catastrophic trauma in the pregnant patient is beyond the scope of this section.

MECHANISMS OF INJURY

The vast majority of trauma in pregnancy can be attributed to unintentional injuries, with motor vehicle collisions (MVC) being the most common cause. The incidence rate for MVCs during pregnancy is estimated to be 207 cases per 100,000 pregnancies, with close to 90% of women involved in MVCs receiving some form of medical care during pregnancy (Kvamstrand, Milsom, Lekander, Druid, & Jacobsson, 2008; Whitehead, 2011). Furthermore, MVCs are a leading cause of mortality with rates of 1.4 maternal deaths and 3.7 fetal deaths per 100,000 pregnancies, respectively (Kvamstrand et al., 2008).

While the incidence and occurrence for most mechanisms of injury are equally distributed throughout pregnancy, falls are far more common during winter months and beyond 20 weeks gestation due to pelvic laxity, weight gain, and subsequent postural imbalance. Current estimates from population-based studies suggest that one in four women will fall at least once during pregnancy (Dunning et al., 2003). A population-based prospective study evaluating pregnant women hospitalized following a fall revealed a four-fold increase in preterm

EXHIBIT 16.1

Classification of Trauma

Noncatastrophic Trauma

- Low impact motor vehicle collision without air bag deployment
- Minor abdominal, head, neck, or back injuries without pain
- Mechanical fall without physical injuries
- Physical assault without physical injuries
- Poisoning and drug overdoses
- Victims not in major trauma category

Catastrophic Trauma

- Cardiac or respiratory arrest
- High impact motor vehicle collision with air bag deployment
- Direct abdominal, head, neck, or back injury with associated pain
- Unresponsive or loss of consciousness
- Maternal burns involving greater than 40% body surface area
- Motor vehicle vs. pedestrian
- Penetrating injuries
- Unstable vital signs (BP <80/40 or HR <50 or >140 or fetal heart rate <110 or >160)

BP, blood pressure; HR, heart rate.

Source: Courtesy of Women & Infants Emergency Obstetrics and Gynecology Division, Providence, RI.

labor, an eight-fold increase in placental abruption, and a two-fold increase in non-reassuring fetal heart rate patterns, when compared to a similarly matched control group (Schiff, 2008). Whether the primary mechanism of injury is a MVC or a mechanical fall, blunt trauma resulting in subsequent placental abruption is a common concern related to the mechanical strain placed on the gravid uterus. Abruptio placentae complicates up to 40% of pregnancies with major injuries and 3% of minor trauma with direct uterine force (Brown, 2009). Two proposed mechanisms for placental abruption in the literature are the shearing force from initial impact and the contrecoup effect that results from negative pressure within the uterus (Mendez-Figueroa et al., 2013). The premature separation of the placenta from the uterine wall results in decreased uterine blood flow, which can lead to significant fetal hypoxia and acidemia. In the most severe cases, fetal death can occur.

While uncommon, pelvic fractures in the setting of pregnancy carry a particularly high maternal and fetal morbidity given the propensity for massive intraperitoneal hemorrhage and subsequent hypovolemic shock (Mirza, Devine, & Gaddipati, 2010). Not surprisingly, both maternal and fetal outcomes are dependent on the degree and extent of the injury. In general, women who sustain minor pelvic fractures in the third trimester of pregnancy can safely attempt vaginal birth (American College of Obstetricians and Gynecologists [ACOG], 1998). The indicators that may prohibit a successful vaginal delivery include fractures that are extensive, severely dislocated, or unstable. Vaginal birth was successful in 75% of women who had suffered pelvic fractures during the latter portion of their pregnancy (Leggon, Wood, & Indeck, 2002).

Penetrating trauma is a relatively rare occurrence during pregnancy and accounts for 9% of all trauma-related pregnancy admissions (Petrone et al., 2011). The vast majority of penetrating injuries are due to gunshots from handguns and, to a lesser extent, stab wounds from knife-related injuries. Maternal mortality is rare, occurring in less than 5% of penetrating trauma cases, and is directly related to the size of the gravid uterus in relation to other intra-abdominal organs (Leggon et al., 2002; Mirza et al., 2010). In contrast, increased hospital stay, postoperative complications, and direct fetal injury are by far more common following penetrating trauma with reported fetal mortality rates as high as 73% (Petrone et al., 2011). The management following penetrating injury is ultimately determined by the entrance location. Injury to the maternal bowel is likely with upper abdominal penetrating injuries, while lower abdominal wounds are more likely to injure the uterus and/or fetus. Of note, the appearance of the entrance wound is not predictive of the extent of internal injury (Petrone et al., 2011).

The current literature on burn injuries occurring during pregnancy is based on case reports or case series. Burns during pregnancy may occur from either electrical or thermal causes. Regardless of the cause of the burn, the pregnant state, maternal age, and trimester of pregnancy do not alter maternal survival rates. Outcomes, however, are largely dependent on the depth of the burn and total body surface area involved. When greater than 40% of the total body surface area is involved, maternal and fetal mortality rates approach 100%, largely due to sepsis (Chama & Na'Aya, 2002). Maternal and fetal mortality are also increased when direct inhalation injury occurs due to significant airway compromise and subsequent maternal and fetal hypoxia (Karimi, Momeni, & Rahbar, 2009). While data on electrical injuries during pregnancy is limited, injuries vary according to type and voltage of current, as well as its path through the body. Significant maternal injuries are uncommon but can result due to direct effects of the heat generated by the current in conjunction with associated trauma. Minor electrical shock, such as from a home appliance, does not appear to impact fetal birth weight, mode of delivery, or gestational age at the time of delivery (Einarson, Bailey, Inocencion, Ormond, & Koren, 1997).

Intentional trauma also poses significant maternal and fetal risks during pregnancy. Intimate partner violence (IPV) is the most common form of intentional trauma with prevalence rates ranging from 1% to 57% during pregnancy (Mendez-Figueroa et al., 2013). Overall, the management of domestic and sexual violence is similar to that of blunt trauma unless gunshot and/or stab wounds are involved. Sexual assault is often an underreported yet critical component to consider when a pregnant woman is also a trauma patient. Acute traumatic injuries following assault range from minor trauma to more significant injuries, including maternal and fetal death. Pregnant women who are verbally abused are more likely to deliver low-birth-weight infants, while those who are physically abused have higher rates of neonatal deaths (Yost, Bloom, McIntire, & Leveno, 2005). The overall risk of physical injury increases for women who are rape victims by a known assailant, when a weapon is involved, when the perpetrator is under the influence of drugs or alcohol, or the assault occurs in the victim's or perpetrator's home (ACOG, 2011).

INITIAL TRIAGE

Optimal management of the pregnant trauma victim often requires a multidisciplinary approach. While diagnostic and treatment algorithms for the

EXHIBIT 16.2

Key Questions to Elicit Following Motor Vehicle Accidents or Falls

Primary

- Was there any head or direct abdominal trauma?
- Did you have loss of consciousness?
- How fast were you traveling?
- Were you restrained, driver or passenger?
- Any air bag deployment?

Secondary

- When is your due date?
- Do you have any contractions, vaginal bleeding, or leakage of fluid?
- Can you feel the baby move?

Source: Courtesy of Women & Infants Emergency Obstetrics and Gynecology Division, Providence, RI.

management of catastrophic versus noncatastrophic trauma will vary, fetal outcomes following trauma in pregnancy are directly correlated with early and aggressive maternal resuscitation. Accordingly, a primary management goal when caring for any pregnant trauma victim is maternal stabilization. Following a motor vehicle accident or fall, in a pregnant woman who is stable, initial key questions to elicit are listed in Exhibit 16.2.

According to the National Center for Injury Prevention and Control, pregnant women greater than 20 weeks gestation must be transported to a medical center capable of performing a prompt and thorough trauma evaluation alongside management of potentially life-threatening injuries (Centers for Disease Control and Prevention, 2011).

PHYSICAL EXAMINATION AND INITIAL MANAGEMENT

Both the impact and management of blunt abdominal trauma on a developing fetus are largely dependent on gestational age at the time of injury. For example, in pregnancies during the first trimester, direct fetal or placental injury is unlikely given the protection afforded by the maternal bony pelvis (ACOG, 1998). Furthermore, in any nonviable fetus, prolonged fetal monitoring is not indicated. The only appropriate fetal intervention is expectant management. In addition to gestational age, critical factors to consider include the degree of maternal injury and mechanism of injury. Exhibit 16.3 provides guidelines for clinical management of noncatastrophic blunt abdominal trauma.

The primary goals in the initial assessment and management of an injured pregnant woman are essentially identical to those in the nonpregnant population. First steps include a vital sign assessment and a targeted trauma history, alongside stabilization and transfer to a facility with the appropriate level of care. Aortocaval compression, which can occur from supine positioning of the pregnant patient, can result in decreased venous return from the lower extremities with a subsequent drop in maternal systolic blood pressure of up to 30 mmHg and a 30% decrease in stroke volume (Rudloff, 2007). Prevention of supine hypotensive syndrome via left lateral uterine displacement is therefore essential to optimize maternal and fetal hemodynamics.

EXHIBIT 16.3

Guidelines for Clinical Management of Noncatastrophic Blunt Abdominal Trauma

1. Assess maternal vital signs and triage according to emergency severity index
2. Perform intimate partner violence screening and safety assessment
3. Document fetal heart tones
4. Perform basic blood work—CBC, type and screen, hold tube, KB at provider discretion if Rh negative
5. Obtain targeted history (include date and time of event, last menstrual period, due date)
6. Provide medical evaluation by a licensed provider with treatment of injuries as clinically indicated
7. Monitor poisoning and/or toxin exposures as appropriate based on the toxin involved and gestation age. All carbon monoxide exposures should be evaluated with both a carbon monoxide (CO) level as well as determination of maternal acid–base status and assessment for signs/symptoms of CO poisoning
8. Fetal evaluation:
   a. Gestational age greater than 24 weeks by estimated date of delivery or fetal biometry
      - 4 hours of continuous fetal monitoring with tocodynamometry
      - Prolonged monitoring indicated if greater than six contractions in any given hour, uterine tenderness, nonreassuring fetal heart tracing, vaginal bleeding, preterm labor, ruptured membranes, high impact trauma, or severe maternal injuries
   b. Gestational age less than 24 weeks by estimated date of delivery or fetal biometry
      - Fetal heart rate documented by Doppler or real time ultrasound
      - Tocometer if high concern for abruption by history or physical examination
      - Fetal monitoring for periviable gestational age 23 to 23.6 weeks at institution/provider discretion
9. Administer Rh immune globulin if Rh negative
10. Discharge to home if stable maternal and fetal status
11. Admit for 24 hours of monitoring if greater than six contractions/hour or nonreassuring fetal heart tracing as noted previously
12. Perform admission labs: coagulation studies, type, and cross if active bleeding and maintain large bore IV access
13. Consider steroids for fetal lung maturity if delivery is possible and gestational age is less than 36 weeks and 6 days completed

CBC, complete blood count; KB, Kleihauer–Betke; IV, intravenous.

Sources: Adapted from ACOG (1998); Brown (2009); Dahmus and Sibai (1993); and Muench and Canterino (2004).

Clinical findings suggestive of a catastrophic trauma prompt immediate maternal stabilization and initiation of resuscitative measures. It is critical to note that a variety of both anatomic and physiologic changes occur in normal pregnancy; these are shown in Table 16.1. These changes can both mask and

TABLE 16.1 Changes in Normal Pregnancy That May Affect Trauma Management

AFFECTED VALUE OR SYSTEM	CHANGE DURING NORMAL PREGNANCY
Systolic blood pressure	Decreased by an average of 5 to 15 mmHg
Diastolic blood pressure	Decreased by 5 to 15 mmHg
Electrocardiogram	Flat or inverted T waves in leads III, V1, and V2; Q waves in leads III and AVF
Blood volume	Increased by 3% to 50%
White blood cell count	May be increased; range: 5,000 to 25,000/mm^3
Fibrinogen	Increased; range: 264 to 615/dL
D-dimer	Frequently positive
Respiratory rate	Increased by 40% to 50%
Oxygen consumption	Increased by 15% to 20% at rest
Partial pressure of oxygen	Increased; range 100 to 108 mmHg
Partial pressure of carbon dioxide	Decreased; range 27 to 32 mmHg
Bicarbonate	Decreased; range: 19 to 25 mEq/L
Base excess	Present; range: 3 to 4 mEq/L
Blood urea nitrogen	Decreased; range: 3 to 3.5 mg/dL
Serum creatinine	Decreased; range: 0.6 to 0.7 mg/dL
Alkaline phosphatase	Increased because of placental production; range: 60 to 140 IU/L
Kidneys	Mild hydronephrosis
Gastrointestinal tract	Decreased gastric emptying, decreased motility, and increased risk of aspiration
Musculoskeletal system	Widened symphysis pubis and sacroiliac joints, which may lead to misleading of radiologic studies
Diaphragm	Higher position in pregnancy; consequently, chest tubes would need to be placed in one or two interspaces higher
Peritoneum	Small amounts of intraperitoneal fluid are normally present

AVF, augmented vector foot.

Source: Adapted from Grossman (2004).

mimic injury in the setting of trauma. In fact, pregnant women who are involved in catastrophic trauma may have no initial symptoms or altered vital signs due to the previously mentioned physiologic changes in pregnancy. A clear understanding of these changes is imperative to optimal management of a pregnant trauma victim. An investigation for possible intraperitoneal bleeding is indicated in the setting of altered level of consciousness, unexplained shock, significant thoracic injuries, and multiple, major orthopedic injuries.

The physical examination following noncatastrophic trauma includes an assessment of the pregnant woman's general appearance; heart, lung, and abdominal examination; assessment of extremities; and a targeted pelvic examination. The pelvic examination may facilitate potential diagnoses such as preterm labor and placental abruption. Fetal assessment is also crucial when the fetus has been determined to be a viable gestation.

A team consisting of both trauma experts and obstetricians will ideally be available to collaboratively manage cases of catastrophic trauma. The primary survey focuses on establishing maternal cardiopulmonary stability: airway, breathing, and circulation. The initial evaluation should also include examination and stabilization of the cervical spine. Since maternal blood pressure and heart rate are not reliable predictors of blood volume, early and aggressive intravenous fluid resuscitation with consideration of red blood cell transfusion is critical, unless the injuries are minor. It is recommended that vasopressors be avoided unless absolutely necessary for maternal stabilization, as these medications are associated with fetal compromise resulting from diminished uterine blood flow. Physiologic changes in the respiratory system such as a decreased functional residual capacity in conjunction with increased oxygen consumption renders the pregnant trauma victim more vulnerable to hypoxia. Supplemental oxygen and consideration for early intubation in the absence of adequate ventilation is essential. In addition, the elevated level of the diaphragm during pregnancy has implications for chest tube placement and emergency thoracotomy. These procedures are generally performed one or two intercostal spaces higher than in the nonpregnant patient (Rudloff, 2007).

After initial stabilization, it is appropriate to evaluate other maternal injuries. This consists of obtaining a complete history, including a focused obstetric history, performing a targeted physical examination, and monitoring the fetus. The first step in assessing any penetrating injury in the pregnant female regardless of the type or location is to adequately expose the body. Careful and thorough inspection of the entire body facilitates evaluation and timely management of what may be multiple injuries. Clinical management will ultimately depend on the entrance location of the wound and gestational age. Operative management is often utilized for entrance wounds above the fundus due to the increased likelihood of visceral injuries. Conversely, more conservative options such as ultrasound, diagnostic laparoscopy, serial abdominal exams, and diagnostic peritoneal lavage are reserved for those injuries that occur below the uterine fundus. Moreover, the decision to proceed with surgical intervention is dependent on numerous factors including the type and location of the injury, uterine size, fetal status, and maternal vital signs. Aggressive fluid replacement, respiratory support, and initial wound care are the emergency management goals in pregnant burn victims in conjunction with fetal monitoring, when appropriate. In addition, all patients with evidence of smoke inhalation require evaluation for carbon monoxide poisoning. Ultimately, both maternal and fetal outcomes are drastically improved when a multidisciplinary team approach is utilized and thus early transport to a facility capable of evaluating and treating trauma, obstetrical, and neonatal emergencies is critical. In accordance with the National Center for Injury Control and Prevention guidelines, women suffering penetrating trauma, significant burns, or electrical injuries require transfer to a tertiary care setting with the appropriate trauma and intensive care unit personnel available (CDC, 2011). Uterine rupture, although a rare event, complicates less than 1% of all trauma-related injuries. Although there is a higher incidence of rupture in the presence of pelvic fractures or a prior cesarean section, uterine rupture can also occur in the absence of obvious risk factors (Aghababian, 2011). Of note, findings of both uterine rupture and abruptio placentae are quite similar and often include abdominal pain and tenderness, signs of hypovolemia, and nonreassuring fetal status (see Figure 16.1). In addition to the standard secondary survey, assessment of the injured pregnant patient includes performing a pelvic examination to assess for vaginal bleeding, ruptured membranes, and signs or symptoms of labor. Fetal monitoring will

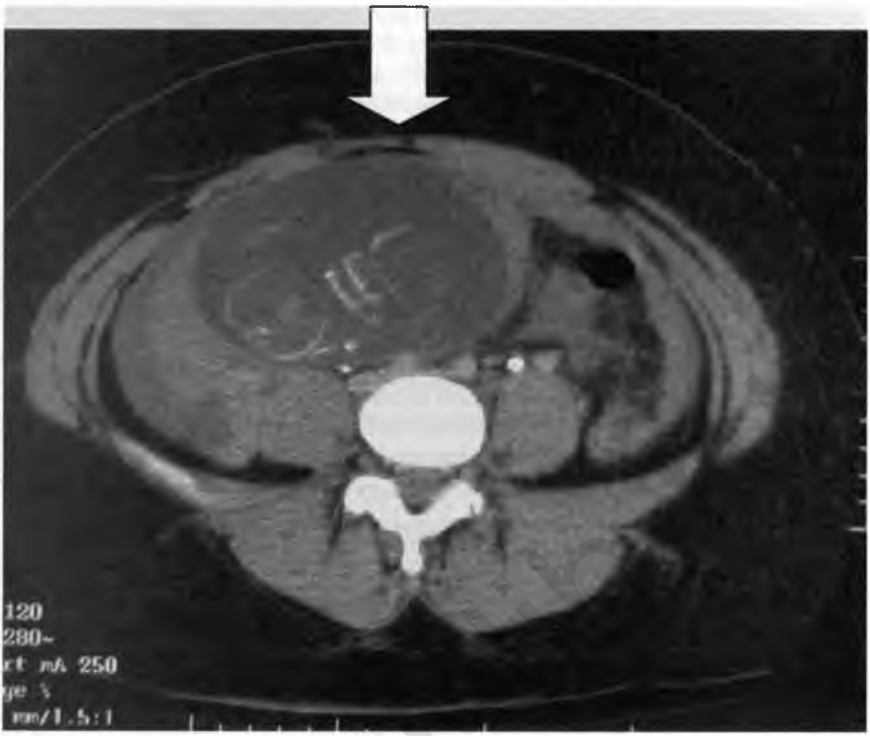

Figure 16.1 Uterine rupture post trauma

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

evaluate for the presence of contractions and any abnormal fetal heart rate pattern. Administration of appropriate medications including narcotics and tetanus immunoglobulin and toxoid are safe and appropriate in pregnancy, when indicated.

Maternal death is most often due to either head injury or hemorrhagic shock. The most common causes of fetal death are maternal shock and/or death followed by abruptio placentae and direct fetal injury. The risk of fetal, neonatal, and infant death is largely dependent on the gestational age at the time of delivery (El-Kady, Gilbert, Towner, & Smith, 2004).

Initial fetal assessment following trauma includes an accurate determination of gestational age, when possible, in conjunction with immediate auscultation of fetal heart tones. If fetal heart tones are absent, resuscitation of the fetus should not be attempted prior to stabilization of the mother. There were no fetal survivors in a series of 441 pregnant trauma patients when fetal heart tones were absent on initial evaluation (J. A. Morris et al., 1996). Fetal heart tones are auscultated by Doppler. At the same time, the gestational age can be estimated by fundal height, history, Leopold's maneuvers, or ultrasound. Determining fetal viability is the most crucial step following documentation of fetal heart tones, noting that this definition is subject to institutional variation. Ultrasound remains the most accurate method for determining gestational age and placental location. However, its clinical utility is limited by both availability and clinical expertise. All decisions regarding fetal viability are made on the basis of the best gestational age available. Figure 16.2 provides a general algorithm for the management of catastrophic trauma.

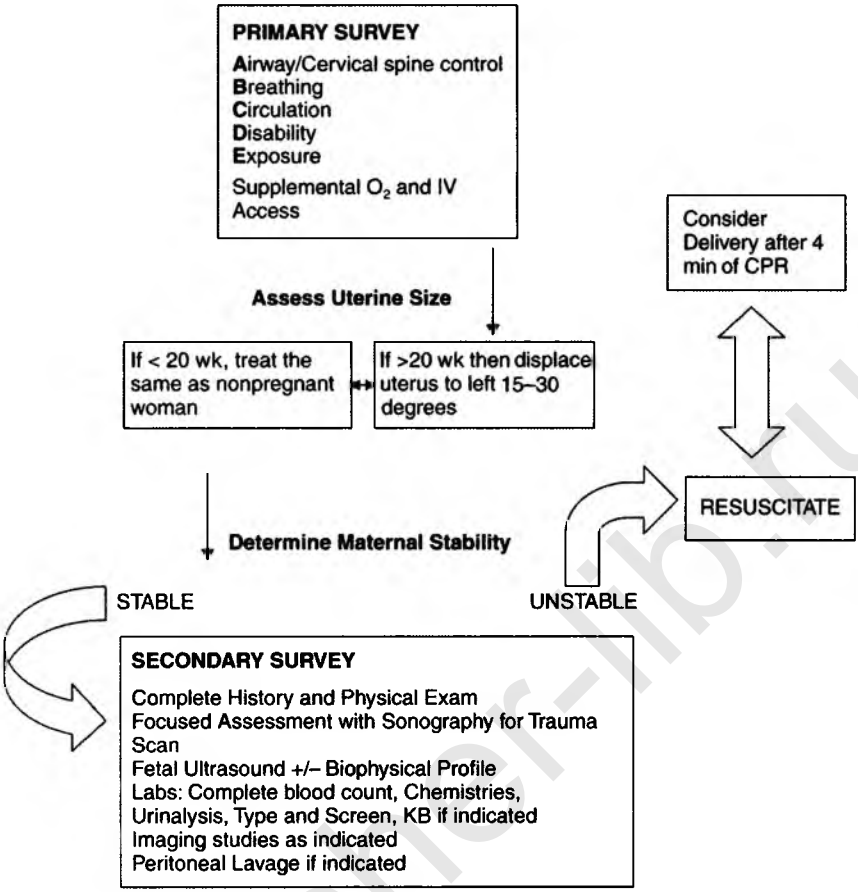

Figure 16.2 Algorithm for the management of catastrophic trauma

CPR, cardiopulmonary resuscitation; IV, intravenous; KB, Kleihauer–Betke.
Sources: Adapted from Muench and Canterino (2007).

LABORATORY AND IMAGING STUDIES

Although the initial trauma assessment for pregnant women will follow nonpregnant guidelines, it is imperative to confirm pregnancy status at the forefront of the evaluation. In addition to pregnancy confirmation, a type and screen is obtained to determine maternal blood type. In an asymptomatic mother with reassuring fetal status and a minor trauma, no further laboratory evaluation is warranted. In cases of catastrophic trauma or when maternal injuries are present, additional blood work should include a complete blood cell count, type and screen, and a coagulation profile. Fetomaternal hemorrhage (FMH) is the transplacental hemorrhage of fetal blood into the maternal circulation and is a potential complication following trauma. There is no real correlation between the severity of trauma, gestational age and frequency, and/or volume of FMH. Complications include maternal isoimmunization, fetal and neonatal anemia, fetal cardiac arrhythmias, or even fetal death. FMH can be detected by the Kleihauer–Betke (KB) acid elution technique performed on maternal blood. Unfortunately, the sensitivity of the KB test is relatively low, and there is no direct

correlation between KB testing and prediction of adverse perinatal outcomes (Trivedi et al., 2012). Thus, routine KB testing is not a standard component in the evaluation of all trauma victims. All Rh-negative mothers who present with a history of abdominal trauma should receive one 300 mcg prophylactic dose of Rh immune globulin within 72 hours of the traumatic event. One vial of 300 mcg protects against 30 mL of fetal blood (15 mL of fetal red blood cells). For women in the first trimester, a 50-mcg dose, when available, is sufficient. Presently, the main clinical utility of the KB test in the Rh-negative population is to determine the appropriate dose of Rh immune globulin needed to prevent Rh sensitization.

In conjunction with fetal monitoring, obstetric ultrasound is a critical tool in both maternal and fetal evaluation following trauma. Ultrasound provides invaluable information such as gestational age, fetal presentation, placental location, amniotic fluid indices, and fetal well-being via biophysical testing. In addition, focused assessment with sonography for trauma (FAST) is both a safe and effective means of detecting free fluid in the abdominal cavity, which indicates the possibility of internal injuries. Placental abruption is ultimately a clinical diagnosis, since signs suggestive of utero-placental hematomas are seen in only a minority of cases. Computed tomography also has a role in the evaluation of pregnant trauma victims with suspected intra-abdominal injuries; however, the risks associated with radiation exposure must be weighed against potential benefits of the study.

CLINICAL MANAGEMENT AND FOLLOW-UP

In viable pregnancies, it is recommended that fetal monitoring be initiated as soon as possible following maternal trauma but not until the mother's condition has been stabilized. Overall, fetal monitoring is most useful for determining reassuring fetal status and for guiding appropriate discharge home. Urgent cesarean delivery is an appropriate intervention in pregnancies considered to be viable, if signs of nonreassuring fetal status, such as prolonged bradycardia or repetitive decelerations, persist in an otherwise adequately resuscitated mother.

The ideal duration of fetal monitoring remains unclear with recommendations ranging from 4 to 48 hours (Mirza et al., 2010). Placental abruption and preterm labor are the most common and feared complications following maternal blunt abdominal trauma. Placental abruption has been reported to occur up to 24 hours following maternal trauma but has never been reported when less than one contraction is present in any 10-minute interval over a 4-hour period (J. A. Morris et al., 1996). The most commonly used fetal monitoring algorithm is continuous monitoring for a total of 4 hours following any maternal trauma, even in the absence of obvious signs or symptoms of abdominal injury. At the completion of 4 hours, fetal monitoring can be discontinued if uterine contractions are less frequent than 1 in 10 minutes, the fetal heart tracing is overall reassuring, and there is no maternal abdominal pain or vaginal bleeding. If contractions persist at a frequency of greater than or equal to 6 per hour during any portion of the 4 hours, then admission to an obstetric facility for a full 24 hours of monitoring is indicated. Additional indications for prolonged fetal monitoring include fetal tachycardia, significant uterine tenderness, nonreassuring fetal heart tracing, spontaneous rupture of membranes following trauma, significant maternal injuries, or a high-risk mechanism of injury (e.g., high-speed collision with air bag deployment). Interestingly, despite the current standard for extensive fetal evaluation following minor trauma in pregnancy, none of the commonly used objective measures adequately predict adverse outcomes (Cahill et al., 2008). Recommendations including shorter duration for fetal monitoring, along with fewer laboratory studies, may be adjusted in the future based on additional research.

Fetal vasculature is particularly sensitive to catecholamines, and the survival of the fetus following trauma is largely dependent on maintenance of adequate uterine perfusion and delivery of oxygen. Once hypovolemic shock ensues, the fetus has likely suffered significant compromise and the possibility of preserving the pregnancy at that point is merely 20% (Desjardins, 2003).

Pregnant women presenting in cardiac arrest are managed according to advanced cardiac life support (ACLS) guidelines. Although chest compressions are more difficult than in the nonpregnant individual due to reduced chest wall compliance and the presence of the gravid uterus, there are no guidelines for cardiopulmonary resuscitation (CPR) specific to pregnancy. Thus, closed-chest CPR is routinely performed on pregnant women in the supine position. Urgent cesarean delivery has traditionally been considered appropriate in the setting of imminent maternal death, following unsuccessful CPR or a stable mother with a nonreassuring fetal heart rate tracing (S. Morris & Stacey, 2003). Fetal survival is not likely if greater than 15 to 20 minutes have transpired since the loss of maternal vital signs. One review suggests that optimum infant and maternal survival are obtained when cesarean delivery is initiated within 4 minutes of maternal cardiac arrest and the fetus is delivered within 5 minutes (KatzBalderson, & DeFreest, 2005). Notably, ineffective resuscitation efforts may become effective following delivery as a result of decreased fetal-placental mass and improved cardiac return to the heart. However, in clinical practice, it is operationally difficult to complete a perimortem cesarean delivery within 5 minutes unless preparations are made at the onset of maternal arrest. Other studies challenge the traditional 4- to 5-minute rule, suggesting that the term *perimortem cesarean delivery* be renamed, "resuscitative hysterotomy" (Grossman, 2004). This nomenclature transitions the focus from a fetocentric to a maternal-fetal protocol with emphasis placed on the improved maternal hemodynamics following delivery of the fetus. Specifically, following maternal arrest, if the gestational age is known to be 20 to 24 weeks or greater or the uterus is palpable/visible above the umbilicus, preparation should be made for emergency cesarean delivery simultaneous with standard ACLS.

CLINICAL PEARLS

- The vast majority of trauma in pregnancy can be attributed to unintentional injuries, with motor vehicle conditions being the most common.
- IPV is the most common form of intentional trauma.
- In viable pregnancies, it is recommended that fetal monitoring be initiated as soon as possible following trauma but not until the mother's condition has been stabilized.

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Preeclampsia With Severe Features, Eclampsia, and Hypertensive Issues

17

Agatha S. Critchfield and Asha J. Heard

Acute hypertension in pregnancy is a severe obstetric complication that requires immediate evaluation and treatment. It can occur in the context of a variety of disorders of pregnancy and is associated with significant maternal and fetal morbidity and potential mortality. Hypertension in pregnancy can occur along a spectrum as noted in Table 17.1.

The spectrum of pregnancy-related hypertensive disorders frequently presenting with acute changes in blood pressure control will be presented. The common presenting symptomatology, the initial steps in maternal/fetal evaluation (history, physical examination, and laboratory evaluation), and management in the obstetric triage setting will be covered. In addition, other possible etiologies of acute hypertension, preeclampsia with severe features, and possible imitators of HELLP (**h**emolysis, **e**levated liver enzymes, and **l**ow **p**latelets) syndrome will be discussed.

DEFINITIONS

Hypertension in pregnancy, otherwise known as gestational hypertension (GHTN), is defined as a systolic blood pressure level of 140 mmHg or greater and a diastolic blood pressure level of 90 mmHg or greater (National High Blood Pressure Education Program Working Group, 2000). *Severe* hypertension is defined as persistent systolic blood pressure of 160 mmHg or greater or diastolic blood pressure of 110 mmHg or greater. Severe hypertension is associated with a significantly higher rate of potentially catastrophic maternal and fetal events, including maternal stroke or other central nervous complications, and placental abruption with subsequent fetal compromise (Magee & von Dadelszen, 2009). Of note, elevated systolic blood pressure has been more strongly associated with maternal cerebral vascular accident than diastolic blood pressure (Martin et al., 2005).

As many as 25% of women with GHTN will go on to develop *preeclampsia* (Saudan, Brown, Buddle, & Jones, 1998), which is defined as persistent hypertension diagnosed after 20 weeks gestation with the addition of proteinuria *or* evidence of end-organ damage, or both. Preeclampsia occurs in 3% to 10% of all pregnancies (Haddad & Sibai, 2009) and is a disorder of largely unknown etiology that is likely associated with abnormal placentation and subsequent wide-reaching

TABLE 17.1 Pregnancy-Induced Hypertension Spectrum

DISORDER	DEFINITION
GHTN	Persistent hypertension without proteinuria noted in previously normotensive patient after 20 weeks gestation
Preeclampsia	Persistent hypertension after 20 weeks gestation with either proteinuria or end-organ dysfunction, or both. See Exhibit 17.1 for laboratory evidence of end-organ damage and signs of preeclampsia with *severe features*
Chronic hypertension	Hypertension predating the pregnancy/noted prior to 20 weeks gestation
Eclampsia	Occurrence of seizures not attributable to other causes in patient with preeclampsia

GHTN, gestational hypertension.

Source: Adapted from ACOG (2013).

EXHIBIT 17.1

Laboratory Abnormalities in Preeclampsia and Diagnosis of Preeclampsia With Severe Features

Preeclampsia is considered to have severe features if one or more of the following is present:

1. Systolic blood pressure ≥160 or diastolic blood pressure ≥110 on two occasions at least 4 hr apart when patient is on bed rest
2. New onset cerebral or visual disturbances
3. Pulmonary edema
4. Epigastric or right upper quadrant pain
5. Impaired liver function (aspartate aminotransferase [AST] or alanine aminotransferase [ALT] twice normal concentration)
6. Thrombocytopenia (platelets <100,000/mcL)
7. Progressive renal insufficiency (serum creatinine >1.1 mg/dL or a doubling of baseline serum creatinine)

Source: Adapted from ACOG (2013).

vascular and endothelial dysfunction (American College of Obstetricians and Gynecologists [ACOG], 2013). Preeclampsia is noted to have *severe features* if a variety of signs or symptoms indicating evolving endothelial dysfunction are present (see Exhibit 17.1; ACOG, 2013). Potential fetal effects of hypertensive disorders in pregnancy include placental dysfunction manifested as poor fetal growth, oligohydramnios, nonreactive fetal heart rate testing, abruption, and intrauterine fetal demise.

Further on the spectrum of hypertensive disorders of pregnancy is *eclampsia* (occurrence of seizures not attributable to other causes in a patient with preeclampsia). In addition, preeclampsia can be accompanied by significant end-organ damage and coagulopathy, as evidenced by the frequent presentation

EXHIBIT 17.2

Maternal Risk Factors for Preeclampsia

1. Nulliparity
2. Teen pregnancy
3. Advanced maternal age
4. History of prior preeclampsia
5. Obesity
6. Pregestational diabetes
7. Thrombophilias
8. Chronic hypertension
9. Renal disease
10. Multiple gestations

Source: Adapted from Roberts (2013) and Sibai (2005).

of preeclampsia with *HELLP syndrome*. While HELLP syndrome can present without evidence of hypertension and/or proteinuria (Roberts, 2013), it is considered in this chapter due to the shared pathophysiologic changes and frequent presentation in the context of severe preeclampsia.

Chronic hypertension is defined as hypertension predating the pregnancy or noted prior to 20 weeks gestation. Another clinical entity to be considered is *preeclampsia* (with or without severe features) *superimposed on preexisting chronic hypertension* (sometimes referred to simply as *superimposed preeclampsia*). Unfortunately, superimposed preeclampsia poses a significant diagnostic conundrum as women affected by chronic hypertension often have some element of baseline renal dysfunction and resultant proteinuria, in addition to elevated blood pressures. However, it is known that maternal and fetal prognosis in the setting of superimposed disease is worse than with other disease processes alone (Roberts, 2013). Therefore, clinicians must be vigilant of any increase in blood pressure or worsening of baseline proteinuria in pregnant women with previously diagnosed chronic hypertension and have a high index of suspicion for superimposed preeclampsia. Maternal risk factors for the development of preeclampsia are noted in Exhibit 17.2.

While the spectrum of hypertensive disorders in pregnancy is often referred to collectively as "pregnancy-induced hypertension," this is not an endorsed term and only disorder-specific terms should be used.

PRESENTING SYMPTOMATOLOGY

Considering the pervasive endothelial dysfunction present in preeclampsia/eclampsia, it is not surprising that the presenting symptomatology often relates to a multitude of organ systems suffering from poor vascular perfusion. Cerebral symptoms most commonly include a persistent headache but can also include dizziness, tinnitus, fever, drowsiness, changes in respiratory rate, and tachycardia. Visual symptoms often present as diplopia, scotoma, blurred vision, and vision loss. Gastrointestinal symptoms are common and usually present with nausea, vomiting, and possible epigastric pain but can also include hematemesis. Renal symptoms may include oliguria, anuria, or hematuria. In addition, many

pregnant women will note an increase in edema (extremities, facial). Some women with severe features of the disease who suffer from cardiopulmonary compromise and resultant pulmonary edema will report significant shortness of breath. While many of these symptoms are possible, certain symptoms are considered more ominous and indicative of *preeclampsia with severe features*. These include those signs of hepatic capsular distension (which can present as epigastric pain), dyspnea that is secondary to pulmonary edema, headache indicative of poor cerebral perfusion (and possible impending eclampsia), and retinal artery edema and spasm causing visual changes (Roberts, 2013).

HISTORY AND DATA COLLECTION

The gravid woman presenting to an obstetric triage setting with hypertension warrants immediate evaluation. While initial history and data collection are obtained simultaneously, steps must be taken by the care team to begin treatment of severe range blood pressures and, if present, eclamptic seizure activity. In addition, fetal status must be evaluated as soon as possible with either a modified biophysical profile (mBPP) or biophysical profile (BPP).

Maternal history includes a pertinent history of present illness focusing on classic preeclampsia symptomatology. Maternal past obstetric history (including prior preeclampsia/eclampsia), as well as history of preexisting hypertension or other medical/surgical conditions, must be obtained.

Maternal blood pressure needs to be evaluated with an appropriately sized cuff (length 1.5 times the circumference of the upper arm) to minimize inaccurate readings. Ideally, the blood pressure is obtained after a rest period of 10 minutes, without exposure to caffeine or tobacco for 30 minutes. The blood pressure is obtained with a woman sitting upright; however, it can also be evaluated with the patient lying in the left lateral position with the brachial artery at heart level (Magee et al., 2008). While some electronic devices are acceptable, in general mercury sphygmomanometry (manual blood pressure cuff) is preferred due to increased accuracy (Magee & Von Dadelszen, 2009).

PHYSICAL EXAMINATION

While initial steps toward the treatment of the hypertensive emergency begin and laboratory evaluations are obtained, a thorough physical examination is performed. Classic physical examination findings of preeclampsia, while not diagnostic, include edema, hyperreflexia, and clonus. Retinal artery changes (due to localized retinal vascular narrowing and segmental spasm) occur in 50% of patients with preeclampsia (Roberts, 2013). Other less common and significantly more ominous findings on physical examination include ascites and hydrothorax (associated with marked edema, increased neck vein distension, and rales on pulmonary examination) consistent with pulmonary edema/congestive heart failure, hepatic enlargement and tenderness indicative of hepatic capsular distension, and petechiae, bruising, or bleeding associated with disseminated intravascular coagulation (DIC).

A complete physical examination is performed, including cardiovascular, pulmonary, abdominal, ophthalmologic, neurologic, skin, and extremity evaluation. A cervical examination is also performed to evaluate the Bishop's score for cervical readiness and possible delivery planning. The fetal status is evaluated as soon as possible using external fetal monitoring and by ultrasound evaluation.

Laboratory studies include complete blood count (CBC), creatinine, liver function tests, uric acid, lactate dehydrogenase (LDH), coagulation profile, urinalysis, and urine protein:creatinine ratio. Consideration can be given to sending a urine toxicology screen as sympathomimetic drugs such as amphetamines can elevate blood pressure.

The diagnosis of preeclampsia does not require the presence of proteinuria, though proteinuria is common. Proteinuria is defined as 1+ or greater protein on a urine dip or greater than 300 mg protein/24-hour period noted on a 24-hour urine collection specimen. Proper collection of a 24-hour urine specimen involves discarding the first void of the day followed by complete collection for 24 subsequent hours with an adequate volume of urine obtained. Adequacy is determined by 24-hour urine creatinine excretion equal to 15 to 20 mg/kg prepregnancy body weight. Recently, obstetric providers have adopted the use of the urine spot protein:creatinine ratio, which is a favored method of proteinuria evaluation in the nonpregnant population (Eknoyan et al., 2003) and has gained support in the medical literature as a valid way to evaluate proteinuria in the pregnant population (ACOG, 2013; Côté et al., 2008; Neithardt, Dooley, & Borensztajn, 2002; Papanna, Mann, Kouides, & Glantz, 2008).

Common abnormalities noted on laboratory analysis include evidence of hemoconcentration (elevated hematocrit), hemolysis (thrombocytopenia, elevated LDH), renal compromise (elevated creatinine), hepatic damage (elevated liver function tests), coagulopathy (elevated prothrombin time [PT], elevated international normalized ratio [INR], elevated partial thromboplastin time [PTT], low fibrinogen), and elevated uric acid. Approximately 20% of patients with preeclampsia with severe features will have HELLP syndrome with laboratory findings as noted in Table 17.2 (Sibai et al., 1993). Frequent laboratory reevaluation in the situation of markedly abnormal maternal labs, changing clinical status, or expectant management of severe preeclampsia needs to be considered.

There are no specific imaging studies required in the context of maternal hypertensive emergencies. While the exact incidence of cerebral hemorrhage in nonfatal eclampsia is unknown, it has been reported that 50% of reversible, pregnancy-related ischemic strokes do occur in the context of preeclampsia (Zeeman, 2009). If persistent neurologic changes suspicious for maternal intracranial pathology after resolution of seizure activity are noted, CT imaging of the head is indicated. If pulmonary edema is suspected, an urgent chest radiograph is

TABLE 17.2 Criteria for the Diagnosis of HELLP Syndrome and Corresponding Laboratory Findings

Hemolytic anemia	Schistocytes on peripheral smear LDH ≥600 IU/L Bilirubin ≥1.2 mg/dL Haptoglobin ≤25 mg/dL
Elevated liver enzymes	AST ≥70 IU/L
Low platelets	Platelet count <100,000 cells/mcL

AST, aspartate aminotransferase; LDH, lactate dehydrogenase.

Source: Adapted from Sibai et al. (1993).

warranted. If congestive heart failure is suspected, maternal echocardiogram can be obtained once the maternal and fetal status is stabilized.

Considering the high risk for fetal morbidity including abruption, growth restriction, and placental insufficiency, fetal evaluation is necessary. Initial fetal testing with nonstress test (NST) and/or BPP is initiated as soon as the clinical situation allows. In addition, ultrasound evaluation for fetal growth, amniotic fluid volume, and umbilical artery systolic-to-diastolic ratios are recommended in the setting of preeclampsia (Maulik, Mundy, Heitmann, & Maulik, 2010).

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of hypertensive emergencies in the obstetric population is broad and must consider both obstetric and nonobstetric etiologies. As previously discussed, pregnancy-specific disorders such as GHTN, preeclampsia, and HELLP syndrome must be at the top of all obstetric triage providers' differential list. In addition, consideration must be given to an exacerbation of chronic hypertension with or without superimposed preeclampsia. When a woman presents with findings consistent with severe preeclampsia/HELLP syndrome, it is critical to keep in mind the variety of other disorders that can present in a similar manner. These include, but are not limited to, acute fatty liver of pregnancy (AFLP) and the thrombotic microangiopathies (including thrombotic thrombocytopenic purpura and hemolytic uremic syndrome) or a systemic lupus erythematosus flare (Sibai, 2009).

Other less common but still possible nonobstetric etiologies for hypertensive emergencies in the obstetric triage setting include withdrawal from antihypertensive medication (most pertinent to those women with chronic hypertension), renal artery stenosis, increased adrenergic activity secondary to pheochromocytoma, autonomic dysfunction (e.g., spinal cord injury, Guillain–Barré), or the use of sympathomimetic drugs such as cocaine or amphetamines.

CLINICAL MANAGEMENT

It is essential to initiate prompt treatment of persistent severe range blood pressures to decrease the risk of adverse vascular events—particularly maternal stroke or other central nervous system complications (Magee et al., 2008). The goal of blood pressure management is to expeditiously lower mean arterial blood pressure by no more than 25% initially, with the ultimate goal of lowering and maintaining the blood pressure at less than 160/105 mmHg (Magee & von Dadelszen, 2009). Common parenteral medications used in the obstetric setting are noted in Table 17.3.

Labetalol is a beta-blocker that also has some alpha-blocking activity. It is avoided in those women with asthma, cardiac disease, or active abuse of sympathomimetic drugs (cocaine, amphetamines). A reasonable initial dose of labetalol is 10 to 20 mg given once intravenously (IV). If the desired effect is not obtained within 10 minutes, repeated doses may be given to a maximum of 300 mg total. Labetalol can also be used as a continuous IV drip. Hydralazine is a vasodilator that can be given in 5 to 10 mg IV increments every 20 to 30 minutes by *slow push* as needed to a total maximum dose of 20 mg. Of note, hydralazine can cause maternal hypotension if not given slowly. The most common oral agent used in the acute setting is nifedipine, which is a calcium channel blocker that comes in short, intermediate, and long-acting forms. The short-acting form of nifedipine can be given in the acute setting when, for example, IV

TABLE 17.3 Treatment of Acute Hypertension in Pregnancy

MEDICATION	MECHANISM OF ACTION	DOSE (MG)	ROUTE	FREQUENCY (MIN)	24-HOUR MAXIMUM DOSE (MG)	CAUTION/ CONTRAINDICATIONS
Labetalol	Beta-blocker (has some alpha-blocking activity)	10–20→40→80→80	IV	10	300	Asthma, sympathomimetic drugs (cocaine), and cardiac disease
Hydralazine	Vasodilator	5–10	IV	20–30	20	Must give by slow IV push. Otherwise possible maternal hypotension
Nifedipine*	Ca^{2+} channel blocker	10	PO	30	120	Cardiac disease. Concurrent use of magnesium sulfate

IV, intravenous; PO, per os (orally).

*Not FDA approved for use.

Source: Adapted from Roberts (2013).

access has yet to be obtained. Of note, the use of short-acting nifedipine in the treatment of acute hypertension is an off-label (non-FDA approved) use. It is used with caution in women with a history of cardiac disease. While concurrent use of magnesium sulfate and nifedipine is generally considered safe, careful monitoring is advised as both medications act as calcium antagonists (ACOG, 2015). Treatment may be initiated with 10 mg by mouth. This can be repeated every 30 minutes to a maximum total dose of 120 mg/d. For severe refractory hypertension, sodium nitroprusside has been recommended in small doses and for a brief duration (in an intensive care setting only). There is a concern for fetal cyanide toxicity if used for prolonged periods (Sass, Itamoto, Silva, Torloni, & Atallah, 2007).

Another priority in the treatment of severe preeclampsia is the prevention of eclampsia. Though there is no consensus regarding the use of magnesium sulfate for the prevention of seizures in those women with preeclampsia without severe features, there is a significant body of evidence to support the use of magnesium sulfate for the prevention of seizures in patients with severe preeclampsia (Altman et al., 2002; Coetzee, Dommisse, & Anthony, 1998). One common protocol is a 4-g loading dose (in 100 mL fluid) given over 20 minutes, followed by 1 to 2 g per hour as a continuous IV infusion.

For treatment of active seizures, magnesium sulfate is a more effective treatment in the eclamptic population than either phenytoin or diazepam (Eclampsia Trial Collaborative Group, 1995). If treatment with magnesium sulfate has not yet begun, it can be administered with the previously noted regimen. Deep intramuscular (IM) administration in the buttock is acceptable if IV access is yet to be obtained (5 g IM in each buttock). Of note, magnesium sulfate is contraindicated in women with heart block or myocardial damage and must be used with extreme caution in patients with myasthenia gravis or significant renal disease. For women experiencing seizures despite magnesium sulfate treatment, a repeat 2 g magnesium bolus (IV) can be considered. In addition, diazepam (5–10 mg IV every 5–10 min, maximum 20 mg) or lorazepam (4 mg slow IV push, may repeat times 1 after 10 min) can also be administered. Of note, lorazepam has a longer duration of action though it can take up to 2 minutes to take effect. Protection of the airway to prevent aspiration and prevention of maternal injury during seizure activity is important to consider. Fetal bradycardia will often occur during maternal seizure activity and most often resolves with maternal stabilization.

Providers must also be aware of the potential for magnesium sulfate toxicity. Signs and symptoms include ECG changes, loss of deep tendon reflexes, respiratory suppression, and the possibility for cardiovascular collapse. Treatment of magnesium sulfate toxicity is calcium gluconate 1 g IV and cardiopulmonary support. Most providers recommend frequent evaluation of patient status while on magnesium sulfate to evaluate for toxicity. This includes evaluation of the cardiopulmonary status (cardiac and pulmonary exam, reviewing fluid intake/output, oxygen saturation) and deep tendon reflexes. Provider evaluation every 3 to 4 hours in a stable woman may be appropriate. Many providers would consider evaluation of serum magnesium levels and subsequent titration of magnesium doses in those women who are at high risk for magnesium sulfate toxicity (i.e., those with poor renal function).

Overall, when considering the decision to deliver a woman with preeclampsia, the provider must balance maternal and fetal risks. In general, continued close observation of a woman with preeclampsia without severe features is appropriate in the context of stable maternal and fetal status, though most providers would recommend delivery at 37 weeks gestation in this

situation. In general, inpatient management of all women with preeclampsia with twice weekly laboratory evaluation and daily fetal testing is recommended. However, consideration can be given to outpatient management of women with preeclampsia who are asymptomatic, have reassuring laboratory evaluation and fetal testing, and who are compliant with care. If the woman is deemed a candidate for outpatient management, weekly prenatal visits with twice weekly fetal testing are warranted.

The decision to expectantly manage those women with preeclampsia with severe features and/or HELLP syndrome remote from term (less than 32 weeks gestation) to achieve steroid administration has received recent support but should only be attempted under the care of an obstetrician comfortable with this high-risk scenario, in a tertiary care setting (Sibai & Barton, 2007). Indications for *immediate* delivery regardless of gestational age include uncontrolled severe hypertension despite maximum doses of two antihypertensive agents, eclampsia, pulmonary edema, abruption, oliguria (<0.5 mL/kg/hr), persistent headache, vision changes, epigastric/right upper quadrant pain, rapid deterioration of HELLP syndrome, platelets less than 100,0000/mcL, creatinine greater than 1.4 mg/dL, or nonreactive fetal testing (Sibai, 2009). If no indication for immediate delivery exists, women can be admitted to labor and delivery for further fetal and maternal monitoring, magnesium sulfate administration, repeat laboratory evaluation, and steroid administration for fetal lung maturity (dexamethasone 6 mg IM every 12 hr times four doses or betamethasone 12 mg IM every 24 hr for two doses). Those who are very stable may be candidates for expectant management beyond 48 hours, though the general recommendation is for delivery by 34 weeks gestation in the setting of severe preeclampsia (Sibai & Barton, 2007). Of note, even in those women with an indication for expedited delivery, induction of labor can be attempted if no other contraindications exist. The presence of preeclampsia/eclampsia is not necessarily an indication for delivery by cesarean section.

CLINICAL PEARLS

- Acute hypertension in pregnancy is a severe obstetric complication that requires immediate evaluation and treatment.
- The diagnosis of preeclampsia does not require the presence of proteinuria, though proteinuria is common.
- When a woman presents with findings consistent with severe preeclampsia/HELLP syndrome, it is wise to keep in mind the variety of other disorders that can present in a similar manner.

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Labor Evaluation 18

Elisabeth D. Howard

The process of childbirth at term is normally initiated by regular uterine contractions, spontaneous rupture of membranes, or both (Cunningham, Leveno, & Bloom, 2014). Safe, thorough evaluation of the pregnant woman at term who presents to an obstetric triage setting requires knowledge of the necessary components of maternal and fetal assessment, including history, physical examination, and clinical management. This chapter presents a review of clinical management of the main presenting concerns of women at term, including premature rupture of membranes (PROM), latent labor, active labor, and imminent delivery.

PROM AT TERM

The incidence of PROM at term is 8% to 10% of all pregnancies (American College of Obstetricians and Gynecologists [ACOG], 2007) and refers to spontaneous rupture of membranes at term (≥37 weeks of gestation) occurring before the onset of labor (Cunningham et al., 2014; Hannah et al., 1996). The management of PROM at term remains somewhat controversial and is based primarily on results from the Term PROM Study (1996). Managed expectantly, 95% of women with PROM will labor and deliver within 72 hours (Hannah et al., 1996). More recent data from the ACOG (2007) recommend induction of labor for women with term or near-term PROM upon presentation, whereas the position of the American College of Nurse Midwives (ACNM, 2008) suggests that with appropriate counseling and informed consent, under specific conditions and absence of risk factors, selected patients may be offered expectant management as a safe alternative to induction of labor. This is predicated on the preference of the woman and provider evaluation (Cunningham et al., 2014; Dare et al., 2006).

PRESENTING SYMPTOMATOLOGY

A history of a sudden gush of fluid or continued trickling of fluid is suggestive, but not confirmatory evidence, of ruptured membranes. Time of leakage, color of fluid (i.e., blood tinged, meconium stained), consistency, and odor are important to ascertain, including recent intercourse. Associated cramping, contractions, and presence of fetal movement need to be noted.

HISTORY AND PHYSICAL EXAMINATION

Ruptured membranes are confirmed by a sterile speculum examination and the visualization of a pool of amniotic fluid in the vaginal vault or observed leakage of fluid from the cervical os. If there is scant fluid present in the vaginal vault, a swab may be taken. It is critical to obtain fluid from the vaginal vault rather than the cervical os, where mucus may be present and confound findings. Vaginal secretions are normally slightly acidic, whereas amniotic fluid is basic, thus turning nitrazine paper dark blue. By itself, this finding is nonspecific, as red blood cells and semen can also turn nitrazine paper dark blue. Additionally, the fluid should be dried on a slide and studied under a microscope. Dried amniotic fluid forms crystals (ferning) on a microscope slide, whereas vaginal secretions do not. Cervical dilation and effacement are estimated visually only during the sterile speculum examination (Cunningham et al., 2014).

Gestational age is determined by standard parameters. Maternal vital signs including blood pressure, temperature, and pulse are assessed. In addition, abdominal examination is performed to determine fetal presentation, lie, estimated fetal weight, and presence or absence of contractions. The fetal heart rate (FHR) may be evaluated with a fetoscope, Doppler, or an external fetal monitor for baseline FHR, variability, and presence or absence of decelerations and accelerations. It is critical that confirmation of fetal presentation be obtained. Group B Streptococcus (GBS) status will need to be determined.

DIFFERENTIAL DIAGNOSIS

If spontaneous rupture of membranes is not confirmed by examination, other possibilities need to be considered. These include normal leukorrhea of pregnancy, loss of mucus plug, involuntary loss of urine, ejaculatory fluid from sexual intercourse, and vaginal infections.

CLINICAL MANAGEMENT

When PROM is confirmed by physical examination, the risks and benefits of both induction of labor and expectant management may be reviewed with the pregnant woman. The maternal risks of ruptured membranes at term are low (Cunningham et al., 2014; Saccone, 2016). The risks to the fetus include ascending infection and umbilical cord compression (ACOG, 2007). In general, these risks may be mitigated with delay of baseline vaginal examination and minimal vaginal examinations (ACNM, 2008).

The largest prospective study to date that has investigated management of PROM is the Term PROM study. This was a multicenter, randomized trial that consisted of over 5,000 women at term with PROM (Hannah et al., 1996). In the expectant management arm of this trial, there was a higher incidence of chorioamnionitis and endometritis (Seaward et al., 1997). The incidence of neonatal infection was not statistically significant in any of the groups. It is recommended that women receive counseling and informed consent about the risks and benefits of induction of labor versus expectant management. According to ACNM (2008), women who select expectant management as a safe alternative to induction of labor must meet the following conditions: a term,

uncomplicated pregnancy, single vertex pregnancy with clear amniotic fluid, absence of identified infection, absence of fever, a Category 1 FHR tracing, and minimization of digital vaginal examinations (including delay of a baseline vaginal examination). Observation of the woman for the onset of spontaneous labor includes documentation of the rationale of care, informed consent/patient counseling, and clinical circumstances (ACNM, 2008).

Visualization and estimation of cervical dilation and length are appropriate for planning for cervical ripening versus Pitocin induction, although no studies have proven the superiority of prostaglandin induction over Pitocin in the setting of PROM. Confirmation of fetal presentation via abdominal examination and ultrasound are crucial in the absence of a digital examination. Although there may be a role for observation after PROM, the most standard recommendation, based on the current evidence with term PROM, is that labor is preferentially induced at the time of presentation (ACOG, 2007; Cunningham et al., 2014; Saccone & Berghella, 2015).

There are times when the woman's stated history of spontaneous rupture is inconsistent with the physical examination findings, yet the history is compelling. If examination results are equivocal, it may be appropriate to repeat the sterile speculum examination in 20 to 30 minutes or longer after the woman has been reclining, to assess for reaccumulation of pooling or ferning, and repeat nitrazine testing.

LATENT LABOR

The first stage of labor comprises both latent and active phases. Labor is a normal physiologic process characterized by sequential and rhythmic changes that result in birth of the newborn. While it is typically a gradual, continuous process that takes place over time, it is divided into first, second, and third stages of labor. This section addresses the diagnosis of the latent phase of the first stage of labor.

The initial phase of labor begins when a woman perceives regular contractions that effect changes in the consistency, position, dilation, and effacement of the cervix (King et al., 2015). This latent phase of labor is complex and is not well understood or well studied. There is a wide range of variation in the duration of the latent phase (Zhand, Landy, et al., 2010). This is partially due to the subjective nature of a patient's perception as to the onset of contractions. In addition, this is the time when the clinician makes the determination between early and false labor (Braxton Hicks contractions).

Clinically, it is crucial to recognize when a woman is still in the latent phase of labor and not yet active because this has several management implications (Greulich & Tarrant, 2007; King et al., 2015). Latent labor admission to a labor unit is associated with higher risk for overuse of multiple labor interventions, such as administration of oxytocics, operative birth for abnormal labor progress, and cesarean delivery (Greulich & Tarrant, 2007; King et al., 2015; Tilden et al., 2016). In addition to these outcomes, the estimated gestational age (EGA) is a critical determinant of neonatal outcome as the data on late-term infants (37–39 weeks EGA) show a higher incidence of morbidity (Parikh et al., 2014). In addition, for women to adequately distinguish latent from active labor, it is helpful to provide detailed and specific guidance. Instruction about comfort measures at home is an important aspect of care that contributes to patient satisfaction (Hosek, Faucher, Lankford, & Alexander, 2014).

PRESENTING SYMPTOMATOLOGY

Women may present with regular contractions that are still infrequent in timing. The contractions may be irregular and the intervals between them long. Discomfort may be chiefly in the lower abdomen and is likely to be relieved by sedation. In latent labor, the contractions, though infrequent, are becoming coordinated and increasing in intensity. Women present in early labor for a variety of reasons, including pain, need for reassurance, and partner's urging (Cheyne et al., 2007). Anxiety and uncertainty are factors that influence the decision to seek care as well as the desire to shift responsibility to the hands of a clinician (Cheyne et al., 2007).

PHYSICAL EXAMINATION

A review of the medical record, including the medical and obstetric histories, is obtained. Additional data include the following: frequency, duration and intensity of contractions, time established, discomfort, any mitigating factors, status of membranes, vaginal bleeding, and leakage of fluid. Maternal coping resources are reviewed, and these include the amount of recent sleep, support persons available, level of hydration, and alimentation. Vital signs, including blood pressure, temperature, and pulse, are noted, as well as an abdominal examination to determine fetal presentation and position. The FHR is evaluated and a cervical examination is performed.

CLINICAL MANAGEMENT

Pregnant women in the latent phase of labor need support, encouragement, and advice if they are discharged from an obstetric triage unit (Greulich & Tarrant, 2007; King et al., 2015; Tilden et al., 2016). Ideally, the discussion of latent labor takes place prenatally, and healthy pregnant women are encouraged to spend the latent phase at home (Greulich & Tarrant, 2007; Tilden et al., 2016). The role of psychologic factors on pain perception is well known (King et al., 2015). Educational interventions may be most effective in decreasing the number of women admitted in early labor (Tilden et al., 2016). Anticipatory guidance and written instructions on the length of latent phase, comfort measures, and guidelines regarding when to call the provider are helpful for the pregnant woman to have (King et al., 2015).

Cognitive pain management techniques such as guided imagery and relaxation techniques decrease anxiety and promote comfort, thereby decreasing the catecholamine response. Encouragement of freedom of movement enhances uterine activity and increases sense of personal control over labor. Sensory stimuli such as music of one's choosing, aromatherapy, touch, acupressure, and hydrotherapy all decrease anxiety, thereby reducing pain and promoting comfort and progress (Janssen, Shroff, & Jaspar, 2012). The therapeutic presence of family, a doula, and a calm physical environment promote comfort and decrease anxiety (King et al., 2015). Overall suggested comfort measures for women in latent labor include tub baths, hydration, alimentation, ambulation, therapeutic touch, encouragement, and support of family (ACNM, 2012; Hanada, Matsuzake, Ota, & Mori, 2015).

It is important to review the risks of early admission including Pitocin augmentation, need for epidural anesthesia, and the potentially higher cesarean section rate. If the gestational age is less than 39 weeks, supportive, rather than active, management is warranted. The opportunity and time for the woman in early labor to ask questions and to be comfortable with the discharge plan of care is vital. In addition, it is essential that discharge documentation explicitly state that she is not in active labor in compliance with the Emergency Medical Treatment and Active Labor Act (EMTALA) guidelines. Table 18.1 reviews nonpharmacologic coping strategies.

If a woman is particularly anxious or fatigued, she may benefit additionally from the following medications for outpatient support and management as noted in Table 18.2.

TABLE 18.1 Nonpharmacologic Coping Strategies for Laboring Women

METHOD	TECHNIQUES	EFFECTS
Cognitive pain management	Childbirth preparation Information Guided imagery	Decreases pain perception Decreases anxiety Promotes comfort
Behavioral	Relaxation • Patterned breathing • Slow, light, and accelerated Positioning and movement • Ambulation • Side lying • Hands and knees • Birthing/exercise ball	Decreases catecholamine response Increases oxygen Enhances uterine blood flow, uterine activity, descent Increases personal control Facilitates mechanisms of labor, fetal descent, fetal position Relieves pressure
Sensory	Music Aromatherapy Touch, massage, effleurage Acupressure Transcutaneous electrical nerve simulation units (TENS) Hot/cold therapy Hydrotherapy • Shower • Tub • Pool	Promotes comfort Decreases anxiety Reduces pain, promotes progress Decreases pain Relieves pain Promotes comfort
Labor support	Therapeutic presence Maintain comfortable environment Encouragement Anticipation of needs	Promotes comfort Decreases anxiety
Physical support	Hydration and nutrition Promotion of rest	Provides energy Promotes progress

TABLE 18.2 Outpatient Therapeutic Rest: Pharmacologic Regimens

MEDICATION	BRAND NAME	DOSE (MG)	COMMENTS
Promethazine	Phenergan	12.5–25	Antiemetic, sedating properties without significant maternal or newborn side effects
Hydroxyzine	Vistaril	50–100 (PO or IM)	Has antianxiety and sedative properties. Maternal sedation is achieved without significant maternal or newborn side effects
Diphenhydramine	Benadryl	50 (PO)	Hypnotic and may assist with rest
Zolpidem	Amblen	5–10 (PO)	Hypnotic and may help with rest

IM, intramuscular; PO, per os (orally).

Source: Adapted from Greulich and Tarrant (2007).

PROLONGED LATENT PHASE

Approximately 5% of women may experience a prolonged latent phase (Cunningham et al., 2014). There are currently no specific diagnostic guidelines to define latent labor; therefore, most clinicians refer to Friedman's (1967) definition of prolonged latent phase as greater than 20 hours in nulliparas and greater than 14 hours in multiparas. Using these parameters, approximately 5% of women may experience a prolonged latent phase (Cunningham et al., 2014). However, one recent study on the natural course of normal labor suggests that active labor begins later than first presumed, at 6 cm rather than 4 cm (Zhang, Landy, et al., 2010). In addition, when the position of the fetus is occiput posterior, the duration of the latent phase is often prolonged (Simkin, 2010; Simkin & Ancheta, 2011). These are often the type of labor patients seen multiple times for latent labor phase in obstetric triage units. It is essential to assess and treat exhaustion. Options in addition to therapeutic rest include active management with uterotonics, amniotomy, or both (Nachum, Garmi, Kadan, Shaley, & Salim, 2010).

There are times when women may benefit from inpatient support services, particularly when they are fatigued and have exhausted existing coping resources (Austin & Calderon, 1999; King et al., 2015). The clinical management options include therapeutic rest, uterotonic drugs or amniotomy, and induction/augmentation of labor (Nachum et al., 2010). In general, a woman with an unfavorable cervix may benefit from relief measures and therapeutic rest in an inpatient setting. Morphine may be administered subcutaneously (15–20 mg) or intramuscularly (10 mg; Anderson, 2011). Approximately 85% of women provided therapeutic rest will progress to the active phase of labor, 10% will have diminished contractions, and 5% will have a persistent dysfunctional pattern (Greulich & Tarrant, 2007; Nachum et al., 2010). Women with prolonged latent phase who are greater than 41 weeks gestation, have a favorable cervix, and desire labor stimulation, or have contraindications to expectant management, should be offered Pitocin. The favorability of the cervix is determined by the Bishop's score, which includes a digital examination ascertaining cervical dilatation, effacement, position, and consistency of the cervix and station. Each component is assigned a numeric value. In general, a Bishop's score of 6 or greater is considered favorable in a multiparous woman and 8 or greater is favorable in a nulliparous woman (Cunningham et al., 2014). For information on determining the Bishop's score, refer to Table 18.3.

TABLE 18.3 Assessment of Cervical Ripeness (The Bishop's Score)

PARAMETER/ SCORE	0	1	2	3
Position	Posterior	Intermediate	Anterior	—
Consistency	Firm	Intermediate	Soft	—
Effacement	0%–30%	31%–50%	51%–80%	>80%
Dilation	0 cm	1–2 cm	3–4 cm	>5 cm
Fetal station	–3	–2	–1, 0	+1, +2

Source: Adapted from Bishop (1964).

ACTIVE LABOR

Whereas slow changes in cervical effacement, dilation, and station characterize latent labor, the active phase is associated with a faster rate of dilation, generally beginning at 5 to 6 cm (Hanley, 2016; Zhange, Troendle, et al., 2010). The EMTALA comes into play in an obstetric triage or emergency setting when transfer becomes necessary. For example, in an actively laboring woman, the decision to transfer is based on the clinical assessment that there is adequate time to effect a safe transfer to another hospital before delivery.

On the basis of the older labor curves, average duration of active labor in healthy women is reported as 7.7 hours for nulliparas and 5.6 hours for multiparas (Albers, 1999). There is new evidence, however, on the natural progress of labor to suggest that for primigravidas, this active phase actually begins at 5 cm, and in multiparous women, it begins at 6 cm (Zhang, Troendle, et al., 2010).

PRESENTING SYMPTOMATOLOGY

Women presenting in active labor often give a history of contractions occurring at regular time intervals that are gradually shortening. The discomfort may be located in the back or abdomen. The intensity will increase over time, and the discomfort will not be stopped by attempts at relaxation. Most notably, the cervix will efface and dilate over time. It is crucial to inquire about the presence of fetal movement, any leakage of fluid, or vaginal bleeding experienced. Ultimately, labor is a clinical diagnosis, determined by history, cervical change by examination, and uncomfortable uterine contractions.

PHYSICAL EXAMINATION AND CLINICAL MANAGEMENT

The goals of the initial physical examination are to establish maternal coping/pain control and baseline cervical status, review the prenatal record, assess for presence of GBS colonization, and evaluate vital signs. A woman with regular uterine contractions who has demonstrated cervical change or is at least 5 to 6 cm is considered to be in active labor (Zhang, Landy, et al., 2010). Contemporary review of labor patterns suggest that active labor starts at 6 cm (Zhang, Landy, et al., 2010). Attempts to define the norms and limits of labor duration have yielded variable results because labor is difficult to measure systematically

(Neal et al., 2010). Clinical decision making takes into account maternal coping, contraction pattern, fetal well-being, and cervical dilation.

LABORATORY TESTS

A complete blood count (CBC) and blood typing are ordered on actively laboring women. Women who do not have a documented human immunodeficiency virus (HIV) need a rapid HIV drawn, as well as a hepatitis B screening performed if not noted in the medical record. Women with a history of herpes simplex virus are assessed for evidence of prodromal symptoms in addition to an evaluation via sterile speculum examination to visualize for any lesions. Additional laboratory tests will be dependent on maternal history (e.g., diabetes, hypertension) and changes in maternal–fetal status. The GBS status is noted, and, if appropriate, GBS prophylaxis is initiated as noted in Figure 18.1.

IMMINENT BIRTH

MANAGING A DELIVERY IN THE OBSTETRIC TRIAGE/ EMERGENCY SETTING

Most normal births occur with excellent outcomes, even when the birth occurs outside of a fully equipped labor and delivery unit. Imminent delivery of the newborn requires an understanding of the second stage of labor and the mechanisms of delivery. The second stage of labor begins when the cervix has reached full dilation and is completed with expulsion of the infant. Safe management of uncomplicated birth is a core competency for practitioners working in the emergency department (Wilbeck, Phillippi, & Schorn, 2014).

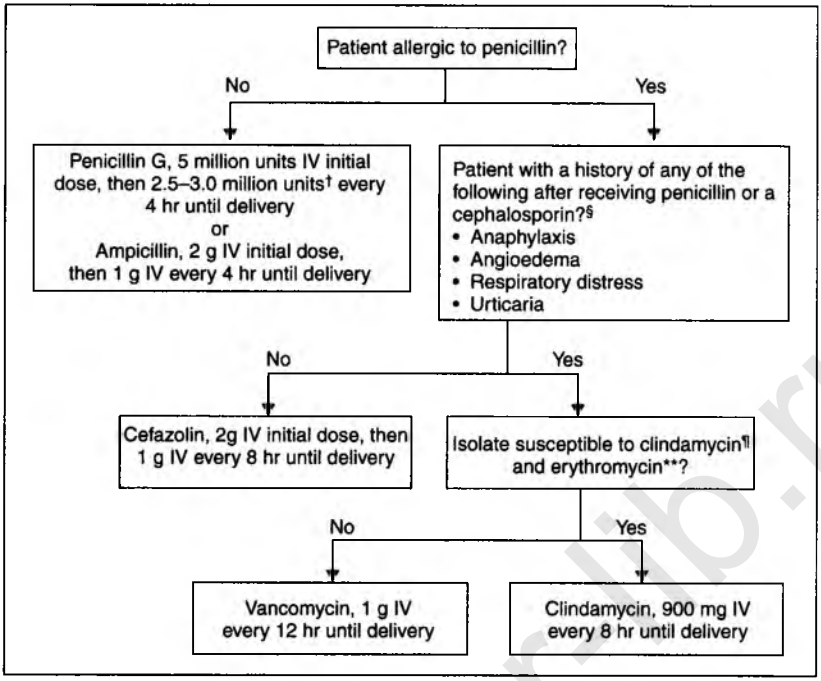
PRESENTING SYMPTOMATOLOGY

There are common factors that may cause rapid or precipitous delivery, including multiparity and spontaneous rupture of membranes. Signs of imminent delivery include maternal urge to push, involuntary bearing down, separation of labia, bulging perineum, passage of stool, and the maternal declaration that the "baby is coming."

CLINICAL MANAGEMENT

If there is reason to believe that delivery is imminent and there will not be time to transfer the patient, help is requested. The most critical information to ascertain includes the following: due date, number of current pregnancy, whether prenatal care has been received, and any health or pregnancy-related problems. The equipment needed includes gloves, gown, goggles, blankets, bulb syringe, sterile clamps, and sterile scissors. It is important to support the birthing woman by remaining calm and giving gentle, directive, concise communication in addition to reassurance. An additional provider is designated to obtain fetal heart tones. It is critical to keep birth safe by positioning the woman in either a semi-Fowler's or side-lying position and keeping the room controlled. Universal precautions must be observed at all times. A pediatric provider is called to participate. If membranes are ruptured, presence of meconium is noted.

CDC RECOMMENDED REGIMENS FOR INTRAPARTUM ANTIBIOTIC PROPHYLAXIS FOR PREVENTION OF EARLY-ONSET GROUP B STREPTOCOCCAL (GBS) DISEASE*



Abbreviation: IV = intravenously.

* Broader spectrum agents, including an agent active against GBS, might be necessary for treatment of chorioamnionitis

† Doses ranging from 2.5 to 3.0 million units are acceptable for the doses administered every 4 hours following the initial dose. The choice of dose within that range should be guided by which formulations of penicillin G are readily available to reduce the need for pharmacies to specially prepare doses.

§ Penicillin-allergic patients with a history of anaphylaxis, angioedema, respiratory distress, or urticaria following administration of penicillin or a cefazolin for GBS intrapartum prophylaxis. For penicillin-allergic patients who do not have a history of those reactions, cefazolin is the preferred agent because pharmacologic data suggest it achieves effective intraamniotic concentrations. Vancomycin and clindamycin should be reserved for pencillin-allergic women at high risk for anaphylaxis.

¶ If laboratory facilities are adequate, clindamycin and erythromycin susceptibility testing (Box 3) should be performed on prenatal GBS isolates from penicillin-allergic women at high risk for anaphylaxis. if no susceptibility testing is performed, or the results are not available at the time of labor, vancomycin is the preferred agent for GBS intrapartum prophylaxis for penicillin-allergic women at high risk for anaphylaxis.

** Resistance to erythromycin is often but not always associated with clindamycin resistance. If an isolate is resistant to erythromycin, it might have inducible resistance to clindamycin, even if it appears susceptible to clindamycin. If a GBS isolate is susceptible to clindamycin, resistant to erythromycin, and testing for inducible clindamycin resistance has been performed and is negative (no inducible resistance), then clindamycin can be used for GBS intrapartum prophylaxis instead of vancomycin.

Figure 18.1 Centers for Disease Control and Prevention Guidelines for Group B Streptococcus prophylaxis (CDC, 2010).

The birth is controlled by providing a calm environment and assisting the mother with gentle breathing. The delivery of the fetal head may be controlled with flexion of the infant's head with the nondominant hand, allowing controlled extension of the head and supporting the perineum with the opposite hand. As

the fetal head extends, a nuchal cord is assessed and, if present, gently reduced. As the infant delivers, if the bed makes it difficult to clear the shoulders, then place a bed pan or blanket roll under the woman's buttocks or realign the woman to a lateral position.

Immediate care of the newborn includes keeping the infant warm via skin-to-skin contact with the mother, drying, stimulating, and clearing the airway. The umbilical cord may be cut and clamped following delivery and the Apgar scores assigned.

It is critical that the obstetric triage unit have a coordinated simulation drill in place for deliveries that take place before transfer to the labor floor. Simulation improves learning outcomes and increases competence (Wilbeck et al., 2014). Simulations, in addition to practice drills and team training, can ensure that imminent birth can take place in a calm, safe environment. In practice, high-quality patient care occurs in a coordinated team with providers with complementary skill sets (Wilbeck et al., 2014).

CLINICAL PEARLS

- Best practices for PROM include delaying a baseline exam, obtaining an ultrasound for fetal position, identifying GBS status, and evaluation of the FHR.
- Recent studies on the natural course of labor suggests that active labor begins later than was first presumed, at 6 cm rather than 4 cm.
- Obstetric triage units and emergency rooms located remotely from a labor and delivery unit must perform simulated drills to prepare for imminent and emergent births.

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19 *Severe Medical Complications in Pregnancy*

Lucia Larson and Karen Rosene-Montella

Pregnant women with potentially serious medical illnesses are a challenge to the clinician. Women can develop new medical illnesses coincidental to pregnancy or may have underlying medical disease that worsens with the physiologic changes of pregnancy. Women are increasingly delaying pregnancy until older ages which are associated with more medical complications. An approach to evaluating the pregnant woman with potentially serious medical illness in the obstetric triage unit is outlined. Topics addressed include headache, shortness of breath (SOB) and pulmonary disease, chest pain, and cardiovascular disorders, as well as selected causes of abdominal pain.

HEADACHE

Headache is a common complaint in pregnancy and the majority of women presenting to obstetric triage have migraine, tension-type headaches, or headaches related to preeclampsia. Other serious and potential life-threatening causes of headaches that must be diagnosed and treated promptly are noted in Table 19.1.

Though most headaches caused by preeclampsia do not cause neurologic impairment or death, a subset of women with preeclampsia will have associated subarachnoid hemorrhage, intracerebral bleeding, or posterior reversible encephalopathy syndrome (PRES). The risk for subarachnoid hemorrhage from rupture of cerebral aneurysms and arteriovenous malformations is increased in pregnant women. The gravida is also at risk for cerebral vein thrombosis and benign increased intracranial hypertension (pseudotumor cerebri). A tumor can also present as a headache during pregnancy.

Migraine headaches often worsen in the beginning of pregnancy, paralleling the hormonal changes of the early pregnancy, and are described as headaches with characteristics similar to prepregnancy headaches. An aura, unilateral throbbing, or nausea and vomiting are all suggestive of a migraine headache. Triggering factors such as certain foods (nuts, aged cheeses, and caffeine), change in sleep pattern, or stress may be identified. Since many women eliminate caffeine intake with pregnancy, caffeine withdrawal may trigger headaches early in pregnancy. Tension-type headaches are typically tight, squeezing headaches that worsen later in the day and are not associated with aura, visual or other neurologic signs or symptoms, or nausea or vomiting. Warning signs that may suggest more serious causes of headache include sudden onset (thunderclap), new or

TABLE 19.1 Selected Causes of Headache in Pregnant Women Presenting to Obstetric Triage/Emergency Department

CAUSE OF HEADACHE	DISTINGUISHING FEATURES	COMMENTS	TREATMENT
Most common			
Tension type	Bilateral, nonthrobbing, steady, mild to moderate pain. Not worsened by physical activity	May be associated with muscular tenderness. Medication may have been discontinued	Acetaminophen (preferred analgesic)
Migraine	Unilateral, throbbing headache, associated with nausea, vomiting, photophobia, or phonophobia. May be preceded by aura (typically visual but may have other neurologic manifestation)	Patients may be able to identify specific triggers. Migraine frequency typically decreases as pregnancy progresses but worsens postpartum. Medication may have been discontinued	Acetaminophen (can be combined with beverage containing caffeine), metoclopramide, prochlorperazine, IV magnesium
Most serious			
Preeclampsia/ eclampsia • Intracerebral bleed • Subarachnoid bleed • Cerebral edema and ischemia • PRES	May have abnormal preeclampsia labs. Headache will be migraine-like in nature and may be associated with focal neurologic signs and symptoms. Seizures may occur	Head CT and/or brain MRI can be useful	Careful blood pressure control, caution with fluids, delivery when appropriate
Subarachnoid hemorrhage • Cerebral aneurysm • AVM • Preeclampsia/ eclampsia	Sudden-onset thunderclap headache. With sentinel bleed, headache can improve, but with continued bleeding, declining mental status develops	Rupture of aneurysm and AVM increased in pregnancy. Noncontrast head CT best to identify blood. MRI to identify specific lesions. Not 100% diagnostic, so LP to identify blood in CSF required in patient with sudden-onset headache and negative imaging. Associated with high mortality	
Cerebral vein thrombosis	Variable presentation: only headache that may be mild to sudden-onset and severe. May worsen with reclining or Valsalva. Have focal signs and symptoms, seizures, or declining mental status	Diagnosis requires MRI with venous imaging (MRI/MRV). Increased incidence in pregnancy. May be associated with hypercoagulable states	Treatment usually entails anticoagulation with LMWH

CAUSE OF HEADACHE	DISTINGUISHING FEATURES	COMMENTS	TREATMENT
Pseudotumor cerebri	Headache can be migraine or tension or have associated visual symptoms, such as photopsia or diplopia. May have pulsatile tinnitus. Papilledema present and may have visual field cut and/or 6th nerve palsy	MRI should be obtained to rule out lesion. LP reveals elevated opening pressure. Performing formal visual fields is critical to monitor optic nerve involvement as vision loss is a serious complication	Acetazolamide, steroids, or serial LPs to decrease opening pressure
Tumor: meningioma, malignancy	Headaches may be focal, worse in the morning and improve during the day, progressive, and associated with nausea. Focal neurologic signs and symptoms develop	CT scan or MRI	
Meningitis	Global severe headache in ill patient presenting with fever and nuchal rigidity. Altered mental status common in acute bacterial meningitis	Emergent lumbar puncture diagnostic. Head CT before LP is only necessary if there is concern for mass lesion as suggested by focal neurologic findings on exam	Antibiotics as soon as possible and should include ampicillin for *Listeria* coverage in pregnant women. Typical regimen is vancomycin, a third-generation cephalosporin, plus ampicillin
Pituitary apoplexy	Sudden-onset headache associated with ophthalmoplegia and change in mental status	Caused by sudden hemorrhage or infarct in pituitary gland with pituitary adenoma. Macroadenomas increase in size in pregnancy	
Other causes worth considering			
Rebound headaches	Occurs in patients with headache who have been taking analgesics more than 2–3 days per week. Headaches develop with awakening and occur daily		Stop offending agent. Administer prophylaxis for underlying headache disorder
OSA	Morning headaches, associated daytime somnolence, snoring	Can develop in pregnancy and may be related to weight gain and/or edema of upper airways	

AVM, arteriovenous malformation; CSF, cerebrospinal fluid; IV, intravenous; LMWH, low-molecular-weight heparin; LP, lumbar puncture; MRV, magnetic resonance venography; MRI, magnetic resonance imaging; OSA, obstructive sleep apnea; PRES, posterior reversible encephalopathy syndrome.

different type of headache, worsening upon awakening in the morning or waking up at night, onset with exertion, association with neurologic impairment, or fever. Further investigations for patients with these concerning features may include CT of head, magnetic resonance imaging/angiography/venography (MRI/MRA/MRV) of the brain, and lumbar puncture (Mitsikostas et al., 2016; Skliut & Jamieson, 2016). In addition, victims of domestic violence may present with chronic complaints including headaches.

When migraine or severe tension headache is not relieved by acetaminophen alone, the addition of caffeine (such as coffee or a cola drink) and/or metoclopramide or prochlorperazine may be helpful. Narcotics are frequently suboptimally effective and are associated with rebound headaches (Goadsby, Goldberg, & Silberstein, 2008), although they can be helpful in the acute setting. Intravenous (IV) magnesium (1–2 g) is useful for relief of acute migraines in nonpregnant women, and it is reasonable to assume it may be effective and safe during pregnancy. If acute treatment does not provide adequate control of headache, prophylactic medication such as riboflavin, beta-blockers, and tricyclic antidepressants are an option (R. E. Wells, Turner, Lee, Bishop, & Strauss, 2016).

RESPIRATORY ISSUES

Shortness of Breath

Dyspnea is a common complaint in normal pregnancy experienced by up to 50% of women. However, pathologic cardiopulmonary causes are essential to distinguish, as noted in Table 19.2.

The pregnant woman with dyspnea of pregnancy has symptoms at rest but not with exertion and may describe the need to "take deep breaths" or frequent "sighs." They may also be SOB while talking on the telephone. These women are thought to be particularly sensitive to the normal increased tidal volume of pregnancy. Deconditioning or SOB associated with progressing pregnancy and weight gain may cause dyspnea on exertion, but the history and physical exam are otherwise reassuring. The presence of wheezing, chest tightness, cough, or nocturnal awakening suggests asthma as a cause of dyspnea.

A history of pulmonary or cardiac disease predating pregnancy suggests the possibility of worsening disease or an inability to tolerate pregnancy-related physiologic changes. Shortness of breath that presents at the peak of blood volume (28–32 weeks) may be due to underlying cardiac disease exacerbated by increased volume. Associated symptoms that suggest concerning underlying pathology include fever, cough, chest tightness or chest pain, orthopnea (though this can be present in normal pregnant women secondary to the elevated diaphragm), and paroxysmal nocturnal dyspnea (PND). Physical examination findings mandating a more extensive workup for underlying cardiopulmonary disease include increased respiratory rate, decreased pulse oximetry at rest or with exertion, tachycardia, abnormal lung exam, elevated jugular venous pulsation (JVP), and loud murmurs or gallops on cardiac exam. An initial workup includes a complete blood count (CBC), shielded anterior–posterior (AP) and lateral chest x-rays (CXR), and an EKG. Evaluation for pulmonary embolism (PE) with chest CT pulmonary angiogram (CTPA) and lower-extremity Doppler or ventilation perfusion scan (VQ scan), underlying structural heart abnormalities with an echocardiogram, or other lung pathology with pulmonary function tests may be indicated.

TABLE 19.2 Selected Causes of Shortness of Breath in Pregnant Women Presenting to Obstetric Triage/Emergency Department

ETIOLOGY	FEATURES	COMMENTS
Dyspnea of pregnancy	Experience of "air hunger" or the need to take a deep breath. Patients note the need to "catch their breath" while talking on the phone. There are no symptoms or physical exam findings suggestive of underlying cardiac or pulmonary disease	Thought to be caused by awareness of the increased ventilation in pregnancy. Begins early in pregnancy, at an average of 18 weeks gestation. Tends to improve later in pregnancy
Asthma	Complaints of chest tightness, dyspnea, and nocturnal awakening. Cough is common. May identify triggers such as cigarette smoke, gastroesophageal reflux, or sinusitis. Exam reveals wheezing	Pulmonary function tests and peak flow measurements useful. CXR is normal, if obtained. Treatment includes beta-agonists and steroids per the National Asthma Guideline Recommendations (National Asthma Education and Prevention Program, 2007)
Pneumonia	Cough, fever, and SOB are typical presenting features. Physical exam reveals evidence of lung consolidation	CXR reveals pneumonia. Most gravidas with pneumonia require admission to monitor for progression and to ensure oxygen saturations remain above 95%
PE	Variable presentation, which may include SOB, dizziness, sudden-onset pleuritic chest pain, hemoptysis, and palpitations. Exam may or may not reveal tachycardia, hypotension, hypoxia, pleural rub, or evidence of lower-extremity DVT	EKG may reveal sinus tachycardia of right heart strain but often normal. CXR may be normal. CTPA done in combination with lower-extremity Doppler or VQ scanning is diagnostic. D-dimers are -not validated in pregnancy. Treatment is anticoagulation with LMWH or unfractionated heparin. Patients may require IVC filter if near term, unable to tolerate anticoagulants, have failed anticoagulants, or have large clot burden
Pulmonary edema	SOB associated with crackles on lung exam. Look for underlying disorder associated with pulmonary edema such as preeclampsia, sepsis or pyelonephritis, abnormal cardiac exam if associated underlying cardiac disease is present	May respond readily to diuresis with furosemide and treatment of underlying precipitating disorder. Physiologic changes that predispose to pulmonary edema include increased blood volume and lower oncotic pressure. With preeclampsia, there is associated endothelial damage and further lowering of oncotic pressure. If there is infection, there may be increased effects of endotoxin
Pulmonary hypertension	Progressive SOB, which may or may not be associated with chest pain and syncope. Cardiac exam may reveal persistent S2 splitting, and there may be evidence of right-sided heart failure on exam in severe cases	EKG may reveal right heart strain. Echo may reveal elevated pulmonary artery pressures, but cardiac catheterization is necessary for accurate measurement. Search for secondary causes including PE is crucial. Pulmonary hypertension has a very high mortality in pregnancy

(continued)

TABLE 19.2 Selected Causes of Shortness of Breath in Pregnant Women Presenting to Obstetric Triage/Emergency Department (*continued*)

ETIOLOGY	FEATURES	COMMENTS
Valvular heart disease	Progressive SOB with cough, orthopnea, PND, and exertional symptoms suggest cardiac disease. May have elevated JVP, cardiac murmur and gallop, crackles on lung exam, and lower-extremity edema	Cardiac echo is diagnostic. The physiologic demands of pregnancy may unmask previously well-compensated valvular heart disease
Peripartum cardiomyopathy	In addition to progressive dyspnea, cough, orthopnea, and PND, patients may present with palpitations or syncope secondary to an arrhythmia. Exam reveals elevated JVP, displaced point of maximal impulse, gallop, crackles on lung exam, and edema	Cardiac echo reveals ventricular dysfunction. Presents later in pregnancy, and no other causes of cardiomyopathy are identified. Preeclampsia must be differentiated. Causes of death include arrhythmia, thromboembolic disease, and progressive heart failure
MI	Classic presentation includes substernal chest tightness that radiates to left shoulder/arm and jaw and is associated with SOB, nausea, vomiting, and diaphoresis. Atypical presentations are common in women, so high index of suspicion is necessary	EKG and cardiac enzymes are used for diagnosis. Women may not have traditional risk factors such as diabetes, hypertension, hyperlipidemia, and smoking. Mechanism may be coronary artery dissection, thrombosis in a normal coronary artery, or vasospasm, in addition to coronary artery disease. Cocaine should be considered

CTPA, computerized tomography pulmonary arteriogram; CXR, chest radiograph; DVT, deep venous thrombosis; EKG, electrocardiogram; IVC, inferior vena cava; JVP, jugular venous pressure; LMWH, low-molecular-weight heparin; MI, myocardial ischemia/infarct; PE, pulmonary embolism; PND, paroxysmal nocturnal dyspnea; SOB, shortness of breath; VQ, ventilation perfusion scan.

Pulmonary Embolism

PE in pregnancy is a leading cause of maternal death in developed nations (Zeitlin & Mohangoo, 2008). Factors contributing to the increased risk of thrombosis in pregnancy include venodilation secondary to hormonal and mechanical factors, increase in prothrombotic and decrease in fibrinolytic factors, and venous trauma at labor and delivery. Risk factors for thrombosis in pregnancy include history of thrombophilia, smoking, elevated body mass index, antepartum immobilization, age, parity, cesarean delivery, preeclampsia, and assisted reproductive techniques (Jacobson, Skejeldestad, & Sandset, 2008; James, Jamison, Brancazio, & Myers, 2006; van Walraven et al., 2003).

There is no one clinical sign or symptom that is consistently seen in gravidas with PE, and a high index of suspicion is needed to prevent missing this potentially fatal diagnosis. Women may or may not present with chest pain, SOB, tachypnea, tachycardia, hypoxia, or abnormal chest x-ray or EKG. In one study, over half of the pregnant women with documented PE had normal pO_2 on arterial blood gas and normal A–a gradients (Powrie et al., 1998). In the nonpregnant population, the Wells criteria (P. S. Wells et al., 2000) and Geneva criteria (Le Gal et al., 2006) are useful clinical decision tools for determining

the probability of PE, but elements of these tools, such as heart rate, are altered by pregnancy physiology. Furthermore, the use of D-dimers is hampered by increasing levels as gestation progresses and cannot be considered reliable to rule out PE in the gravida without further studies (Konkle, 2015).

Because these tools have not been validated in pregnancy, diagnostic imaging is the cornerstone for the diagnosis of PE in pregnant women. The initial evaluation includes a CXR that may reveal an alternate diagnosis with minimal radiation exposure. PE can then be definitively diagnosed with either a VQ scan or CTPA. An advantage of the CTPA is the potential to identify an alternate diagnosis with lower fetal radiation exposure. However, the risk for maternal breast cancer may be increased because CTPA exposes the maternal breasts to as much as 2 to 5 rads of radiation (Miller, Chalhoub, & Bourjeily, 2011). Some centers use breast shields to mitigate this risk. In addition, CTPA is more likely to be technically limited in pregnancy because the increased blood volume and cardiac output affect the arrival of contrast to the pulmonary artery. The VQ scan has a strong negative predictive value for PE, and fetal radiation exposure is still well within the acceptable range. Some clinicians prefer it to CTPA, particularly for women who have had previous CT scans or who are otherwise at increased risk for breast cancer. Local expertise in interpreting the results of VQ or CTPA is also a driving force in determining the best test to order. In the pregnant woman with symptoms of PE and findings suggestive of a lower-extremity deep vein thrombosis (DVT), a lower-extremity Doppler ultrasound is a reasonable first test. If a DVT is identified, PE can be presumed and therapeutic anticoagulation is indicated regardless.

The mortality of untreated PE is 30%, and death can occur from a recurrent PE within several hours of the initial event. Since anticoagulation decreases mortality to 2% to 8%, it is crucial to begin treatment quickly (Kearon et al., 2008). In women with a high suspicion for PE and low risk for bleeding, anticoagulation is begun immediately so as not to delay for the results of testing. Stable women with a potential alternative diagnosis in whom testing is performed quickly can be treated after the results of investigations are known. The preferred initial treatment for PE is low-molecular-weight heparin (LMWH) because of its proven mortality benefits, associated decreased recurrence of thrombosis, better bioavailability, ease of administration, and decreased risk of heparin-induced thrombocytopenia (Greer, 2015). Intravenous unfractionated heparin still has an important role for use in women at high risk for bleeding; near delivery; with significant hypotension, obesity, or renal insufficiency; or in whom thrombolytics may be considered.

Although the use of thrombolytics has been reported in pregnancy with a risk of bleeding similar to that of nonpregnant women, thrombolytics are most likely to be beneficial in the hemodynamically unstable gravida with refractory hypoxemia (Leonhardt, Gaul, Nietsch, Buerke, & Schleussner, 2006). Inferior vena cava (IVC) filters may be considered for use in pregnant women with PE who have contraindications to anticoagulation or in whom a large clot burden has been identified in the lower extremities or pelvis, which could potentially cause a fatal recurrent PE (Harris, Velineni, & Davies, 2016).

Asthma

Asthma is a common medical condition in pregnancy, affecting approximately 3.7% to 8.4% of pregnancies in the United States (Kwon, Belanger, & Bracken, 2003). Though asthma does not necessarily worsen in pregnancy, approximately one third of women will develop asthma exacerbations during gestation.

Exacerbations are more likely to occur in women who have more severe asthma before pregnancy (Schatz et al., 2003). Factors specific to pregnancy that may contribute to exacerbations include hormonal changes, noncompliance with medications, increased gastroesophageal reflux, and possible triggering by rhinitis of pregnancy.

Gravidas with an asthma exacerbation may present with SOB, wheezing, cough, and/or chest tightness. Physical exam may reveal increased respiratory and heart rate, hypoxia, wheezing, and decreased air flow. Use of accessory muscles of respiration and paradoxical breathing portend respiratory failure. Peak flows are helpful to determine severity of exacerbation if performed with proper technique. Though pulse oximetry determines oxygenation, an arterial blood gas is necessary in women suspected of having more serious exacerbations to assess maternal $PaCO_2$. In pregnancy, the normal maternal PaO_2 is 100 to 105 mmHg and average $PaCO_2$ is 30 mmHg. For fetal well-being, it is necessary to maintain the pregnant woman's oxygenation saturation greater than 95% or the maternal pO_2 at not less than 70 mmHg of oxygen. The pregnant asthmatic with a $PaCO_2$ of 35 mmHg is already retaining CO_2 and signifies impending respiratory failure. Because of the increased rates of aspiration and failed intubation in pregnancy, it is critical to anticipate the potential need for intubation in advance so that equipment and experienced personnel are prepared.

Supplemental oxygen, short-acting beta-agonists (SABA), and steroids are used for treatment of acute asthma exacerbations in pregnant women as they are in the nonpregnant population (Dombrowski et al., 2008; National Asthma Education and Prevention Program, 2007). Albuterol can be administered by nebulizer or metered dose inhaler and is initially given every 20 minutes for three doses followed by hourly doses as needed. Women who do not respond quickly to SABA or who are already taking steroids require the addition of methylprednisolone or prednisone. Ipratropium is added for severe exacerbations. Chest radiograph is indicated if there is concern about an underlying pulmonary process such as pneumonia. Women can be discharged with close outpatient follow-up if the peak expiratory flow rate is greater than or equal to 70% of predicted, there is a sustained response 60 minutes after the last treatment, no supplemental oxygen is required to keep oxygen saturation greater than 95% at rest or with exertion, there is no distress, and physical exam is normal. A low threshold for admission in pregnancy is prudent if there are any concerning symptoms because pregnant women have less respiratory reserve and higher oxygen saturation requirements than do nonpregnant women.

CARDIAC AND VASCULAR ISSUES

Chest Pain

The causes of chest pain in pregnancy range from benign and self-limiting to potentially life threatening. An initial history and physical exam help to narrow the differential. Often, the clinician is able to tell patients what the pain "isn't" with more certainty than what the pain "is." It can be reassuring that once the life-threatening causes are eliminated, it is unlikely that the cause of the chest pain will be harmful to either the pregnant woman or fetus and will likely resolve quickly. Many causes of chest pain are also causes of SOB, and the evaluation for these disorders overlap. The most serious causes of chest pain that must not be missed include PE, myocardial ischemia, and aortic dissection. Table 19.3 provides an overview of key points for chest pain in pregnancy.

TABLE 19.3 Selected Causes of Chest Pain in the Pregnant Women Presenting to Obstetric Triage/Emergency Department

ETIOLOGY	FEATURES	COMMENTS
Musculoskeletal	Tenderness found on palpation. Pain associated with movements. May have bruising or swelling noted associated with trauma	Careful questioning about domestic violence, which increases during pregnancy, is indicated as women may be reluctant to disclose. Exam may reveal chest wall tenderness
GERD	Retrosternal burning pain often associated with food intake. Squeezing may represent esophageal spasm	Common in pregnancy secondary to decreased lower esophageal tone and delayed gastric emptying. Antireflux measures, antacids, metoclopramide, and ranitidine are helpful. Omeprazole may be considered if measures are inadequate
Pericarditis	Pain typically improves with sitting up and leaning forward. Often sharp and pleuritic in nature	EKG evolves and can show PR depression, widespread ST elevation, and T-wave inversions. Cardiac echocardiograph may show pericardial effusion. Elevated troponin and CPK signals associated with myocarditis
MI (see Table 18.2)	SOB, nausea, vomiting, and diaphoresis are classic associated symptoms of MI. Women often present with atypical symptoms, so high index of suspicion is necessary	EKG, cardiac enzymes are initial workup. Cardiac echocardiograph may be useful. Pregnant women with myocardial ischemia may have traditional risk factors for coronary artery disease but risk factors may be absent in those with coronary artery dissection, thrombosis within a normal coronary artery, and vasospasm, all of which occur as a cause of MI in pregnancy. Cocaine should also be considered
Aortic dissection	Acute onset of severe tearing or ripping pain in chest that may radiate to back. Associated signs and symptoms may be seen from involvement of branches of the aorta. These include stroke, myocardial infarction, paraplegia, and loss of pulses. New aortic insufficiency may be heard on cardiac exam and discrepancy of 20 mgHg between arms may be noted	Life-threatening emergency. CXR may show widened mediastinum or aorta. EKG may be normal or show ischemia. CT scan, MRI, or transesophageal echo diagnostic are used. Increased incidence occurs in pregnancy. Associated with Marfan's and Turner's syndromes and coarctation of the aorta. Also bicuspid aortic valve, Ehlers–Danlos syndrome, vasculitis, trauma, and crack cocaine

(*continued*)

TABLE 19.3 Selected Causes of Chest Pain in the Pregnant Women Presenting to Obstetric Triage/Emergency Department (*continued*)

ETIOLOGY	FEATURES	COMMENTS
PE (see Table 18.2)	Sudden onset of chest pain that is classically pleuritic but may be constant. May be associated with SOB, hemoptysis, or palpitation but presentation is variable and requires high index of suspicion. Exam may or may not reveal tachycardia, hypotension, hypoxia, pleural rub, or evidence of lower-extremity DVT	EKG most likely to reveal sinus tachycardia. It may also show right heart strain, but more often it is normal. Chest x-ray may be normal. CTPA done in combination with lower-extremity Dopplers or VQ scanning is diagnostic. D-dimers are not validated for the diagnosis of venous thromboembolism in pregnancy (Miller et al., 2011)
Pneumonia	Cough, fever, and SOB are typical presenting features. May have history of antecedent viral illness. Physical exam reveals evidence of lung consolidation	Chest x-ray reveals pneumonia. Most gravidas with pneumonia require admission to monitor for progression and to ensure oxygen saturations remain above 95%
Pneumothorax	Abrupt onset of pleuritic chest pain and SOB. Decreased breath sounds may be noted on affected side. Patient may have a previous history of pneumothorax. Smoking is a risk factor	Upright chest x-ray diagnostic. Tension pneumothorax is associated with hypoxia, tachycardia, and hypotension and requires immediate aspiration
Herpes zoster	Pain may be described as burning, stabbing, or throbbing and can precede the vesicular rash. Hypoesthesia in the dermatomal distribution is sometimes present	Rash may develop as long as 30 days after pain
Preeclampsia/ eclampsia/ HELLP/acute fatty liver of pregnancy	Not typically associated with chest pain, but it can occur	Rarely preeclampsia/eclampsia is associated with MI. Pain originating in the liver can occasionally be felt as chest or epigastric pain

CPK, creatinine phosphokinase; CTPA, computerized tomography pulmonary arteriogram; CXR, chest radiograph; DVT, deep venous thrombosis; EKG, electrocardiogram; GERD, gastroesophageal reflux disease; HELLP, hemolysis, elevated liver enzymes, and low platelets; MI, myocardial ischemia/infarct; PE, pulmonary embolism; SOB, shortness of breath; VQ, ventilation perfusion scan.

Myocardial Ischemia and Infarction

The risk for myocardial infarct (MI) is increased by three- to fourfold in pregnancy as compared with the nonpregnant state (James, Jamison, Bisswas, et al., 2006). Pregnant women with myocardial ischemia may present with classic substernal chest tightness associated with dyspnea, nausea, and diaphoresis, but they can also present atypically. Therefore, a high index of suspicion is needed. Risk factors for MI in pregnancy include maternal age over 35, hypertension, diabetes mellitus, obesity, eclampsia, and severe preeclampsia (Ladner, Danielsen, & Gilbert, 2005). In one study of the coronary arteries of 103 women with MI in pregnancy, only 40% were found to have atherosclerotic disease whereas 27% had coronary artery dissection, 8% had thrombus in a normal coronary artery, 2%

had spasm, 2% had emboli, and 13% were found to be normal (Roth & Elkayam, 2008). Initial treatment includes oxygen, aspirin, beta-blockers, heparin, and nitrates (Elkayam et al., 2014; McGregor, Barron, & Rosene-Montella, 2015). Cardiac catheterization is preferred to thrombolysis because of the increased incidence of coronary artery dissection.

Vascular Issues

Pregnant women have an increased risk for arterial dissections, which is thought to be related to the hormonal and hemodynamic changes of pregnancy. Examples include the increased incidence of cerebral aneurysm rupture and coronary artery dissection. In addition, women with Marfan's syndrome and dilated aortic roots greater than 4.0 to 4.5 cm are at very high risk of aortic dissection. Beta-blockers are used in these women to decrease shear forces on the vasculature. The pain associated with aortic dissection is typically described as a severe tearing pain radiating to the back. Not only does Ehlers–Danlos type IV have a high maternal mortality secondary to arterial rupture, but there is also a significant risk of bowel perforation and uterine rupture in pregnancy. Splenic artery aneurysms are more likely to occur in women and are not necessarily associated with portal hypertension. Splenic artery rupture is more likely to happen in the third trimester and is associated with high maternal and fetal mortality. Early diagnosis with ultrasound or CT scan with prompt intervention may be lifesaving. The diagnosis needs consideration in any pregnant woman presenting with severe upper abdominal pain, especially if hemodynamically unstable (Sadat, Dar, Walsh, & Varty, 2008).

Palpitations

Pregnant women commonly report palpitations. The majority are not due to serious medical causes; however, recognizing those who have serious arrhythmias is crucial. A previous history of cardiac disease, such as congenital heart disease, increases the likelihood of finding an arrhythmia requiring intervention. Supraventricular arrhythmias are more common but ventricular arrhythmias also occur with increased frequency in pregnancy. The history of a sudden-onset rapid rhythm with sudden termination is suggestive of supraventricular tachycardia, whereas a slow resolution is more suggestive of sinus tachycardia. A rapid irregular rhythm suggests atrial fibrillation. A dangerous ventricular arrhythmia may present with presyncope or sudden syncope, and it is particularly concerning if there is a family history of premature or sudden death. Underlying cardiac disease may manifest with an abnormal rate and heart sounds. The cardiac monitor and 12-lead EKG may reveal the rhythm abnormality but may be normal if the symptoms have resolved. Abnormalities on the EKG may be suggestive of underlying cardiac disease or a bypass tract or reveal a prolonged QT interval that is associated with ventricular arrhythmia. Women at risk for serious arrhythmia require admission to a telemetry unit even if symptoms have resolved and the EKG is normal. Those at low risk may be further evaluated with an outpatient holter monitor or event monitor. An echocardiogram is necessary to assess for structural heart abnormalities in women with true arrhythmia. Most of the medications used to treat nonpregnant women can be used safely in pregnancy. Direct current (DC) cardioversion can be used when indicated (Adamson & Nelson-Piercy, 2007). Table 19.4 summarizes the causes of palpitations in pregnant women.

TABLE 19.4 Causes of Palpitations in Pregnant Women Presenting to Obstetric Triage

ARRHYTHMIA	FEATURES	COMMENTS
Sinus tachycardia	Often asymptomatic but in the symptomatic patient gradually improves with treatment of underlying disorder	Look for underlying causes including anemia, pulmonary embolism, thyroid disease, infection/sepsis, hypotension, fever, hypoxia, dehydration, myocardial ischemia, heart failure, drugs, pain, pheochromocytoma, anxiety
Supraventricular tachycardia, including Wolfe–Parkinson–White (WPW) syndrome	Sudden onset of rapid regular rhythm that may or may not be associated with presyncope/syncope, chest pain, and SOB	Vagal maneuvers should be tried first; IV adenosine, beta-blockers, and calcium channel blockers can be used. DC cardioversion can be used if indicated
Atrial fibrillation or flutter	Rapid irregularly irregular rhythm that may or may not be associated with presyncope/syncope, chest pain, and SOB	Beta-blockers, calcium channel blockers, digoxin, and procainamide can be used safely. Amiodarone should be avoided if possible because of concern for the fetal thyroid. Anticoagulation with LMWH may be appropriate in some cases to prevent thromboembolic disease. Consider underlying precipitating causes such as PE, thyroid disease, and infection
Ventricular tachycardia	Rapid rhythm associated with syncope/presyncope, chest pain, and/or SOB	DC cardioversion if indicated. Lidocaine preferred to amiodarone secondary to concern for fetal thyroid function

DC, direct current; IV, intravenous; LMWH, low-molecular-weight heparin; SOB, shortness of breath.

SELECTED CAUSES OF ABDOMINAL PAIN

Cholelithiasis, appendicitis, and bowel obstruction in pregnancy are covered elsewhere in this book. However, selected causes of abdominal pain that are less common but important or unusual will be discussed here. Epigastric pain that radiates to the back, improves with leaning forward, and is associated with nausea and vomiting is typical of pancreatitis. Specific pregnancy-associated causes of pancreatitis include cholelithiasis and hypertriglyceridemia. Abnormal laboratory tests in these cases include elevated amylase and lipase; ultrasound may be helpful to identify gallstones, inflammation, or a pancreatic pseudocyst. Thrombosis of mesenteric, pelvic, and hepatic vessels also occurs in pregnancy. Typically, this pain is difficult to localize, but helpful diagnostic tests include

abdominal/pelvic CT scan or MRI taken with images to evaluate the arteries and veins. An elevated lactic acid is ominous, signaling bowel ischemia. Women who note the sudden onset of pain associated with trauma, cough, or sudden movement may have a rectus sheath hematoma. Physical exam reveals tenderness on palpation, and ultrasound is helpful for diagnosis. The mechanical changes of pregnancy are likely responsible for the predisposition to rectus sheath hematoma, but hypertension and anticoagulation are also risk factors. The sudden onset of abdominal pain in association with hypovolemic shock may be caused by aneurysm rupture, but spontaneous hemoperitoneum has also been reported from bleeding of superficial veins of the uterus or parametrium (Brosens, Fusi, & Brosens, 2009). A history of endometriosis and nulliparity appear to be risk factors. Though not necessarily a primary abdominal disorder, diabetic ketoacidosis (DKA) can present with abdominal pain that may be associated with nausea, vomiting, polyuria, polydipsia, and altered mental status. Glucose is typically elevated, but a significant number of pregnant women with DKA present with glucose less than 200. Chemistries reveal an elevated anion gap, elevated creatinine, and positive serum ketones. Immediate hydration, IV insulin, correction of electrolyte abnormalities, and a search for the underlying cause of DKA are imperative to decrease maternal and fetal morbidity and mortality.

The clinician caring for the pregnant woman presenting to the obstetric triage unit or emergency room with medical illness must consider a broad differential of disorders including those that occur coincidental to pregnancy, those that may be affected by the pregnant state, and those unique to pregnancy itself. The management of pregnant women with severe medical illness often requires an interdisciplinary team, which includes the obstetrician/maternal–fetal medicine physician, obstetric internist, surgeon, and other subspecialists.

CLINICAL PEARLS

- The management of pregnant women with severe medical illness requires an interdisciplinary team consisting of an obstetrician/maternal–fetal medicine specialist, obstetric internist, surgeon, and other subspecialists who can best balance the risks and benefits of diagnostic strategies and treatment interventions.
- When migraine or severe tension headache is not relieved by acetaminophen alone, the addition of caffeine and/or metoclopramide or prochlorperazine may be helpful.
- The risk for MI is increased by three- to fourfold in pregnancy. These women with myocardial ischemia may present with classic substernal chest tightness associated with dyspnea, nausea, and diaphoresis; they can also present atypically, so a high index of suspicion is needed.

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Vaginal Bleeding in Pregnancy

Robyn A. Gray

Throughout pregnancy, vaginal bleeding can cause adverse maternal, fetal, and neonatal outcomes. Although vaginal bleeding is more common in early pregnancy, during the latter half it complicates approximately 5% of pregnancies. The major causes of antepartum bleeding include "bloody show" associated with labor or cervical insufficiency, placental abruption (30%), placenta previa (20%), uterine rupture, and vasa previa (<0.5%; Clark, 2004).

Vaginal bleeding is a common presenting complaint to emergency departments, and especially to an obstetric triage unit. Expeditious and thorough evaluation of vaginal bleeding during pregnancy in the acute setting is crucial to overall maternal and fetal well-being. This review will focus on the major causes of vaginal bleeding in the second and third trimester, specifically beyond viability (gestational age of at least 23 weeks 0 days), as well as the approach to diagnosis and management.

HISTORY AND DATA COLLECTION

The same history is obtained for any woman presenting with second- or third-trimester bleeding. This includes specific focus on the current pregnancy, and particular focus on any risk factors that point to abruption or abnormal placentation. Questions to consider include: how much bleeding has occurred, is there a prior ultrasound or diagnosis to account for bleeding, has there been any recent sexual intercourse, and is the woman experiencing symptoms of significant blood loss such as lightheadedness. The prenatal record can be reviewed for blood type and Rh status (for Rh immune globulin, as needed), hemoglobin and/or hematocrit, and all ultrasound findings with focus on placental location. The amount of blood loss prior to presentation can be estimated by a pad count, as well as the amount and size of clots. Prior episodes of bleeding and hospitalization need to be elicited and noted. Evaluation of pain includes a description of quality, onset, location, severity, and radiation, as well as understanding the relationship between onset of pain and bleeding.

PLACENTAL ABRUPTION

Placental abruption, decidual hemorrhage leading to the premature separation of the placenta from the uterine wall, most often due to rupture of maternal vessels prior to delivery of the fetus, complicates 1% of pregnancies

EXHIBIT 20.1

Complications Associated With Placental Abruption

Fetal

- Growth restriction (chronic abruption)
- Preterm delivery, and associated morbidity
- Perinatal mortality
- Fetal hypoxemia or asphyxia

Maternal

- Hypovolemia secondary to blood loss
- Blood transfusion
- Disseminated intravascular coagulopathy (DIC)
- Cesarean hysterectomy, and associated morbidity
- Renal failure
- Acute respiratory distress syndrome (ARDS)
- Multisystem organ failure (MOF)
- Death

Source: Adapted from Oyelese and Ananth (2006).

(Oyelese & Ananth, 2006). Placental abruption can place the mother and fetus at significant risk for poor outcomes, as shown in Exhibit 20.1. The hematoma that results can be small and self-limited, or may be larger and continue to expand. The hematoma functions to limit the exchange of gases and nutrients to the fetus; therefore, the risks to the fetus are dependent upon the severity of abruption and gestational age at delivery.

PRESENTING SYMPTOMATOLOGY

Classically, pregnant women with placental abruption will present with vaginal bleeding and abdominal pain. The vaginal bleeding can be acute and heavy, or it can be chronic with intermittent acute episodes of bleeding. Often, pregnant women will have vague complaints of spotting, mild abdominal pain/cramping, and/or back pain. Less than 5% of abruptions will present with leaking of fluid in addition to vaginal bleeding (Ananth, Oyelese, Yeo, Pradhan, & Vintzileos, 2005). Women can present with simply pain and no bleeding in the setting of a concealed abruption. In rare circumstances, a patient can have such a large concealed abruption that he or she presents with mental status changes due to acute anemia. Concealed abruptions comprise approximately 10% to 20% of all placental abruptions (Oyelese & Ananth, 2006). Some women present for evaluation due to concerns surrounding an injury; for example, fall, motor vehicle accident, or physical assault. Symptoms of abruption may evolve during the period of monitoring for these injuries. Risk factors for placental abruption are outlined in Exhibit 20.2.

PHYSICAL EXAMINATION

Pallor, hypotension, mental status changes, and/or tachycardia may be indicative of orthostatic changes and a severe hemorrhage, and must prompt an

EXHIBIT 20.2

Risk Factors for Placental Abruption

Nonmodifiable

- Trauma
- Preterm premature rupture of membranes/spontaneous rupture of membranes
- Multifetal gestation
- Hydramnios
- Abnormal placentation (placenta previa, uterine anomaly, leiomyomata)
- Chorioamnionitis
- Chronic hypertension
- Preeclampsia/Eclampsia
- History of abruption
- Inherited thrombophilia

Modifiable

- Cocaine
- Cigarette smoking

Sources: Adapted from Ananth, Oyelese, Srinivas, Yeo, and Vintzileos (2004) and Pariente et al. (2011).

expeditious, focused physical examination. If ultrasound records are easily located, confirmation of placental location is noted prior to performing a digital examination. If not available, bedside ultrasound can be performed to assess for placenta previa. Careful abdominal examination is done to assess uterine tone, as a large abruption may present with a firm uterus, contracted with increased tone. The pelvic exam includes visualization of external genitalia, noting lesions, lacerations, masses, or hematoma. On speculum examination, the volume of blood in the vaginal vault is quantified and the cervical os visualized to determine dilatation and presence of active bleeding, as well as polyps or cervicitis. The amount of vaginal bleeding has not been shown to correlate well with the degree of placental separation (Clark, 2004). Therefore, it is not recommended to base potential maternal and fetal outcome on bleeding alone. If bleeding is light, continuation of the examination will include a wet mount to rule out bacterial vaginosis, trichomoniasis, and candidiasis as possible causes of vaginal bleeding.

Continuous external fetal monitoring is necessary with vaginal bleeding in any pregnancy beyond viability. Contractions in the setting of an abruption are classically high frequency and low in amplitude. Tachysystole, defined as more than five contractions in 10 minutes averaged over a 30-minute period, or an elevated resting uterine tone may be seen if an abruption is in progress. An abnormal uterine contraction pattern can point to a diagnosis of a concealed abruption in the women with severe abdominal pain and absent to mild vaginal bleeding.

LABORATORY AND IMAGING STUDIES

In the setting of vaginal bleeding, immediate assessment of blood type, antibody screen, and a complete blood count (CBC) are performed. A urine drug screen may be indicated, as cocaine is a risk factor. When there is concern for hemorrhage or disseminated intravascular coagulopathy (DIC), coagulation studies can

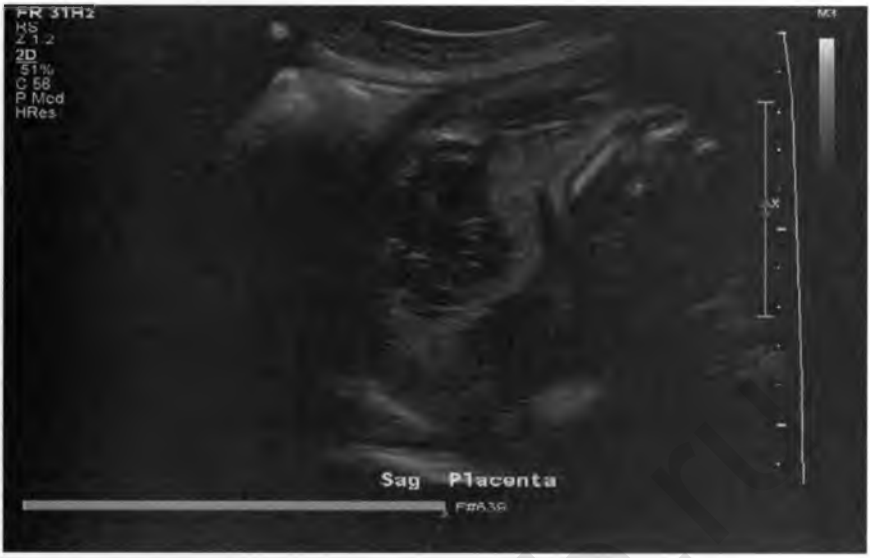

Figure 20.1 Ultrasound of abruption with retroplacental hematoma

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

be obtained, including prothrombin time (PT), partial thrombin time (PTT), International Normalized Ratio (INR), and fibrinogen. Kleihauer–Betke (KB) can be ordered for pregnant women who are Rh(D) immune globulin negative. Obtaining a KB has shown to be unhelpful in diagnosis and management, as the test results do not correlate either with the diagnosis, or neonatal outcomes (Oyelese & Ananth, 2006). However, a KB can be useful in determining the correct dose of Rh immune globulin.

If vaginal bleeding is thought to be an abruption secondary to preeclampsia, then, additionally, a creatinine and liver function test including serum glutamic-oxaloacetic transaminase (AST/SGOT) and serum glutamic pyruvic transaminase (ALT/SGPT), as well as urine protein:creatinine ratio, can be ordered.

If the patient or fetus are unstable, a bedside ultrasound can be utilized, whereas a more complete or formal ultrasound can be pursued if required. Although ultrasound for abruption has a low sensitivity, when noted, it is highly predictive of abruption (Oyelese et al., 2004). Ultrasound has shown to have a 100% positive predictive value when a retroplacental hematoma was noted; however, only 25% of cases have these findings (Glantz & Purnell, 2002). Figure 20.1 shows the irregular, heterogeneous area behind the placenta consistent with a placental abruption (retroplacental hematoma). Ultrasound can provide additional valuable information, including placental location, fetal presentation, fetal biometry, and assessment of amniotic fluid. This information may be integral in adding data to the management plan.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of vaginal bleeding after viability can be divided into obstetric and nonobstetric causes. Exhibit 20.3 notes nonobstetric causes only. The leading causes of vaginal bleeding in pregnancy include placenta previa,

EXHIBIT 20.3

Nonobstetric Causes of Vaginal Bleeding

Gynecologic

- Vaginal laceration
- Cervical trauma
- Infectious
- Vaginitis
- Cervicitis (trichomoniasis, bacterial vaginosis)
- Sexually transmitted (chlamydia, gonorrhea)
- Postcoital
- Cervical polyps
- Malignancy

Urinary

- Urinary tract infection
- Nephrolithiasis

Rectal

- Hemorrhoids
- Fissures
- Crohn's disease
- Ulcerative colitis
- Infectious colitis
- Malignancy

Medical

- Thrombophilia
- Anticoagulation

Source: Adapted from Hoffman (2008).

abruptio placenta, preterm labor, cervical insufficiency, placenta accreta, vasa previa, and uterine rupture. Urinary and rectal sources of bleeding must be considered in women presenting to an emergency setting with the complaint of vaginal bleeding. The differential diagnosis includes urinary tract infections, nephrolithiasis, hemorrhoids, and rectal fissures.

CLINICAL MANAGEMENT AND FOLLOW-UP

Acute Obstetric Hemorrhage

All pregnant women presenting with vaginal bleeding must be assessed for clinical stability. If hemodynamically unstable, immediate therapy must be initiated to stabilize vital signs. First steps include intravascular fluid resuscitation with two large bore intravenous lines, replacement of blood products, coagulation factors (fresh frozen plasma, cryoprecipitate, platelets), and delivery by surgical intervention when gestational age is greater than 34 weeks (Reed, Cypher, & Shields, 2008). Even when gestational age is less than 34 weeks, maternal or fetal instability warrants immediate delivery, often by cesarean section, prior to completion of antenatal corticosteroids.

The approach to placental abruption will vary depending on the type of bleeding at the time of presentation. An area of debate exists over tocolysis in the setting of abruption. Tocolysis is generally contraindicated. One possible indication for administration of tocolysis is to prolong pregnancy, thus allowing for fetal lung maturation.

Occasionally women will present with contractions and pain only, with a presumed diagnosis of preterm labor. It is crucial to maintain a high index of suspicion for abruption with even minor bleeding in the setting of uterine contractions and abdominal pain. Given that 10% to 20% of abruptions are concealed, this demonstrates how the amount of bleeding may not equal the extent of placental separation (Clark, 2004; Oyelese & Ananth, 2006). Close maternal and fetal monitoring are indicated in these scenarios.

When gestational age is between 34 weeks 0 days and 36 weeks 6 days, and secondary issues arise due to chronic abruption—for example, severe fetal growth restriction (FGR)—plans need to be made for delivery. It is reasonable to attempt vaginal delivery if mother and fetus are stable. When women are not in labor and are clinically stable, induction can be considered. According to the Antenatal Late Preterm Steroids (ALPS) Trial (Gyamfi-Bannerman et al., 2016), when delivery is planned, it is reasonable to administer betamethasone in the late preterm unless delivery is anticipated in the next 12 hours, due to labor, active bleeding, or any other contraindications to receive betamethasone. However, delivery by cesarean section at any time during induction for maternal or fetal compromise must be expeditious. In the presence of coagulopathy, a cesarean section carries high maternal morbidity; therefore, correction of any coagulopathy with aggressive transfusion of red blood cells, fresh frozen plasma, cryoprecipitate, and platelets while moving toward cesarean section is crucial.

If the gestational age is between 23 and 34 weeks, and active bleeding has ceased with reassuring fetal testing, expectant management is acceptable. Corticosteroids are administered for lung maturity secondary to increased risk of preterm delivery with chronic abruption. Routine fetal surveillance with serial growth scans and biophysical profiles (BPP) or nonstress tests (NST) can be performed as either inpatient or outpatient management. Delivery occurs in these cases between 37 and 38 weeks gestation, due to increased risk for stillbirth (Oyelese et al., 2004).

With chronic abruption, women can present with intermittent episodes of vaginal bleeding, noted as acute abruption on chronic abruption. In these settings, it is reasonable to consider giving corticosteroids for gestational age between 34 weeks 0 days and 36 weeks and 6 days, according to ALPS data. A rescue course of antenatal corticosteroids can be administered if gestational age is less than 32 weeks 6 days, previous steroid course is greater than 2 weeks prior, and delivery is anticipated within 7 days (American Congress of Obstetricians and Gynecologists [ACOG], 2011; Garite, Kurtzman, Maurel, & Clark, 2009). A multicenter randomized placebo-controlled trial showed improved neonatal outcome with rescue steroids without apparent increased risk (Garite et al., 2009).

When fetal demise has occurred due to placental abruption, vaginal delivery is the optimal route of delivery with close monitoring of maternal vital signs, blood loss, and laboratory values. Cesarean delivery is indicated when there is maternal compromise or if vaginal delivery is contraindicated for reasons such as previous classical cesarean section, though second-trimester induction can be considered (Rouzi, 2003).

PRESENTING SYMPTOMATOLOGY

The classic presentation of placenta previa is sudden, painless vaginal bleeding in approximately 80% of pregnant women. An additional 10% to 20% of women will present with bleeding in the setting of uterine contractions. Symptomatic vaginal bleeding occurs before 30 weeks in roughly one-third of pregnancies, another third between 30 and 36 weeks, and 10% will reach term without any episodes of bleeding (Silver et al., 2006).

PHYSICAL EXAMINATION

The physical examination should be similar to that of placental abruption and will initially focus on any signs of significant blood loss such as pallor, hypotension, mental status changes, and/or tachycardia. If placental location is unknown or immediate documentation is unavailable, bimanual exam is delayed. Immediate bedside ultrasound can be performed in these cases. Digital examinations may exacerbate bleeding in the case of placenta previa and cause an emergent, life-threatening hemorrhage; thus, they are not performed on women with placenta previa. Continuous external fetal monitoring is appropriate in the setting of vaginal bleeding beyond viability. Exhibit 20.4 lists risk factors for placenta previa.

LABORATORY AND IMAGING STUDIES

The initial blood work includes type and screen, CBC, and a hold tube. When bleeding is clinically significant, a crossmatch for packed red blood cells is added. When concern for hemorrhage or DIC is high, coagulation studies are obtained.

EXHIBIT 20.4

Risk Factors for Placenta Previa

- Endometrial scarring
- Prior cesarean section (associated risk of accreta)
  - Unscarred uterus, 1%–5%
  - One previous cesarean section, 11%–25%
  - Two previous cesarean sections, 35%–47%
  - Three previous cesarean sections, 40%
  - Four plus previous cesarean sections, 50%–70%
- Uterine surgery (e.g., myomectomy, uterine septum resection)
- Increased number of prior curettages
- Increased parity
- Maternal smoking
- Multiple gestation
- Infertility treatments
- Advanced maternal age

Sources: Adapted from Faiz and Ananth (2003); Rosenberg, Pariente, Sergienko, Wiznitzer, and Sheiner (2011); and Silver et al. (2006).

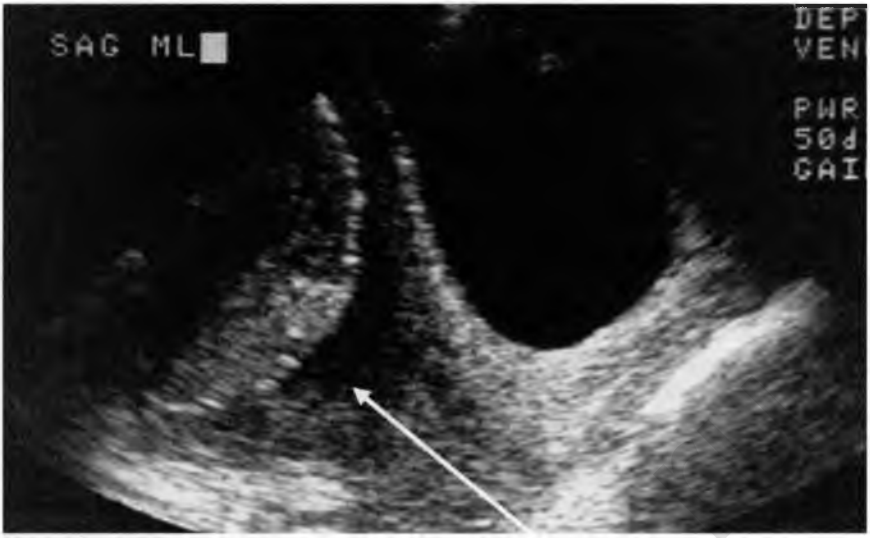

Figure 20.2 Ultrasound of placenta previa, complete. Arrow showing placenta covering entire cervix

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

Ultrasound imaging is essential for the evaluation of placental location. Transabdominal ultrasound for initial assessment of placental location in the obstetric triage setting for initial presentation of vaginal bleeding can be performed, though it has several limitations. A posterior, placenta previa at term can be difficult to visualize, especially when the fetal head is low in the maternal pelvis. Similarly, a complete noncentral previa displaced laterally may be difficult to visualize. When the findings are uncertain and vaginal bleeding is minimal, transperineal or transvaginal ultrasound is performed to define placental position. Figure 20.2 shows the placenta completely covering the internal os, consistent with a complete placenta previa. Figure 20.3 shows the placental edge extends to the level of the internal os, consistent with the diagnosis of marginal previa.

MRI has limited utility in diagnosis of placenta previa due to high cost, limited availability, and established accuracy of transvaginal ultrasound. There is some potential benefit to MRI in setting of a questionable posterior placenta or to assist in the diagnosis of a placenta accreta in the setting of a placenta previa.

CLINICAL MANAGEMENT AND FOLLOW-UP

When pregnant women with a bleed from a placenta previa are hemodynamically stable and have reassuring fetal testing, immediate delivery may not be necessary. Reed et al. (2008) determined that 50% can be managed with supportive care and the pregnancy may be prolonged for up to 4 weeks. A randomized controlled trial by Wing, Paul, and Millar (1996) looked at expectant management comparing safety and costs for inpatient versus outpatient management. The data conclude no significant differences in safety outcomes for outpatient management of placenta previa diagnosed before 37 weeks, with significant cost savings.

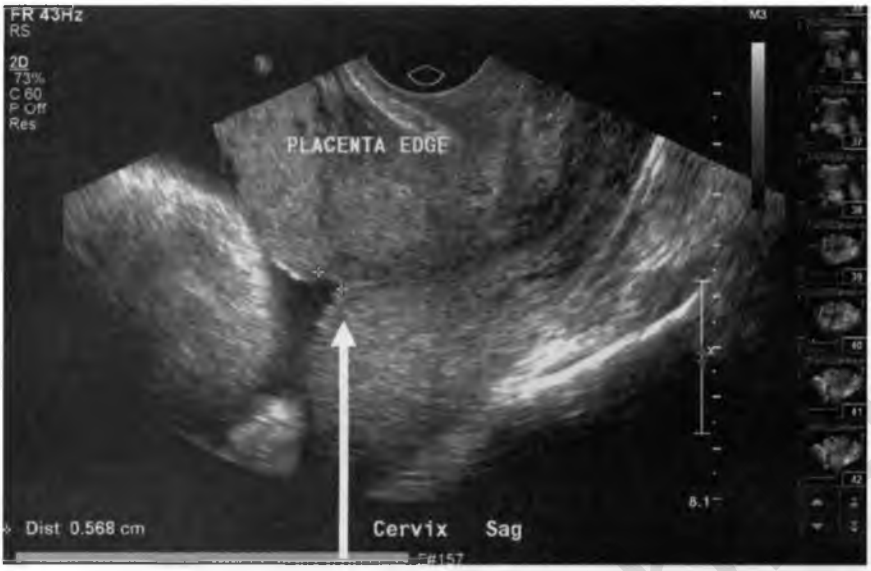

Figure 20.3 Ultrasound of placenta previa, marginal. Arrow showing placenta edge from internal os of cervical canal

Source: Courtesy of Department of Radiology, Women & Infants Hospital.

If delivery is anticipated in the first 12 hours from presentation, and gestational age is less than 31 weeks and 6 days, it is recommended to begin magnesium sulfate for fetal neuroprotection against cerebral palsy (Rouse et al., 2008). Recent systematic reviews and meta-analysis of antenatal administration of magnesium sulfate for prevention of cerebral palsy have supported the use of magnesium with few exclusions: intrauterine fetal demise, fetus with lethal anomalies, and maternal contraindications—for example, myasthenia gravis and renal failure (Conde-Agudelo & Romero, 2009; Reeves, Gibbs, & Clark, 2011).

The current recommendations for management of asymptomatic and/or stable symptomatic placenta previa involve pelvic rest and serial ultrasounds for growth and placental location every 4 weeks. Recent data suggest that placenta previa does not increase the risk of FGR, regardless of type of previa (Harper, Odibo, Macones, Crane, & Cahill, 2010). There are no data to support antepartum testing in asymptomatic patients, but it may be indicated with other coexisting conditions of pregnancy such as intrauterine growth restriction, preterm premature rupture of membranes, preterm labor, and medical comorbidities (e.g., hypertensive disorders, diabetes, gestational diabetes).

VASA PREVIA

Vasa previa is rare, with a prevalence of 1 in 500 to 1:6,000 deliveries (Swank et al., 2016) and difficult to diagnose. Pregnant women with increased risk factors for vasa previa include those with a history of a resolved placenta previa or the rare patient in whom an accessory placenta can be identified on ultrasound. A comparison of women diagnosed antenatally with vasa previa to those undiagnosed until presentation with vaginal bleeding, labor, or spontaneous rupture of membranes showed neonatal survival rates of 97% and 44%, respectively (Oyelese et al., 2004). Given that most cases will present with acute hemorrhage

and fetal tracing abnormalities (classically sinusoidal pattern), emergent cesarean delivery is indicated to prevent the fetus from exsanguinating. Any woman presenting with brisk vaginal bleeding in the setting of ruptured membranes must have an ultrasound evaluation to distinguish placenta previa from vasa previa, when clinically stable. Table 20.1 shows recommendations for clinical management of pregnant women with vasa previa.

Figure 20.4A illustrates how difficult it may be to diagnose a vasa previa. When color Doppler is applied, as in Figure 20.4B, the diagnosis becomes more obvious.

TABLE 20.1 Vasa Previa Management Considerations

CONSIDERATION	MANAGEMENT	LEVEL OF EVIDENCE
Low lying placenta	Evaluation of cord insertion	II-2B
Velamentous insertion, Bilobate/succenturiate placenta, or vaginal bleeding	Transvaginal ultrasound to evaluate internal cervical os	II-2B
Vasa previa suspected	Transvaginal ultrasound with Doppler flow	II-2B
Antenatal diagnosis	Elective cesarean section	II-1A
Preterm delivery	Antenatal corticosteroids between 28 and 32 weeks	II-2B
Preterm delivery	Inpatient management between 30 and 32 weeks until delivery	II-2B
Bleeding or PROM	Urgent cesarean section	III-B
Antenatal diagnosis	Transfer to tertiary care facility	II-3B

PROM, premature rupture of membranes.

Source: Adapted from Gagnon et al. (2009).

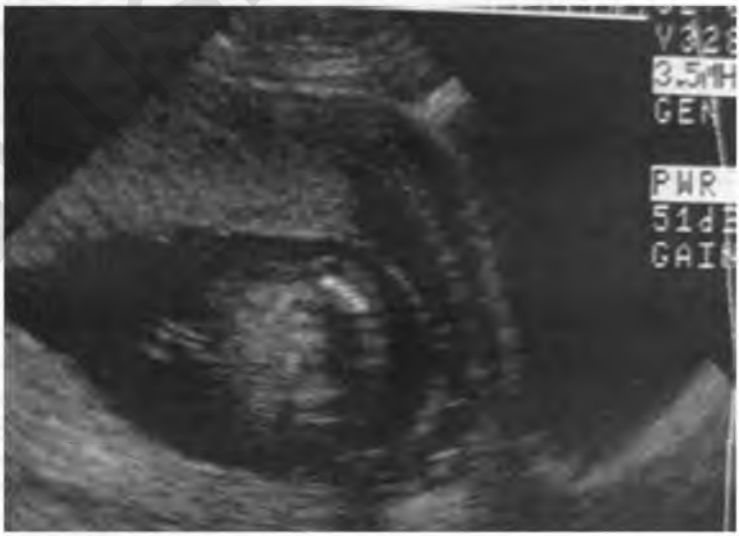

Figure 20.4A Ultrasound of vasa previa

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

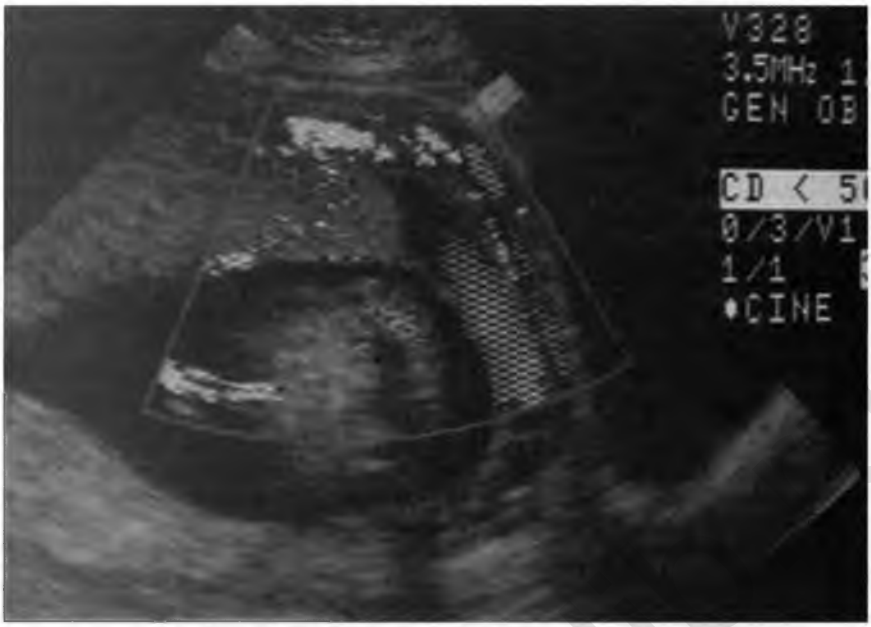

Figure 20.4B Ultrasound of vasa previa, Doppler flow

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

CLINICAL PEARLS

- The major causes of antepartum bleeding include "bloody show" associated with labor or cervical insufficiency, placental abruption (30%), placenta previa (20%), uterine rupture, and vasa previa (<0.5%).
- The possibility of concealed abruption exists in the setting of abdominal pain and lack of bleeding.
- Symptomatic vaginal bleeding occurs before 30 weeks in roughly one-third of pregnancies, another third between 30 and 36 weeks, and 10% will reach term without any episodes of bleeding.

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21 Common General Surgical Emergencies in Pregnancy

Chelsy Caren and David Edmonson

Abdominal discomfort is a common presenting complaint in pregnancy, and often has a benign, physiologic cause. However, severe pain, or pain associated with peritoneal signs on physical examination, is not considered to be normal in pregnancy. The differential diagnosis of such pain in a pregnant woman is extensive, as shown in Table 21.1, and includes both obstetric and nonobstetric conditions.

Emergent general abdominal surgery is performed in approximately 0.2% of pregnant women, most commonly for acute appendicitis, acute cholecystitis, and bowel obstruction (Gilo, Amini, & Landy, 2009). Following a brief discussion of general surgical considerations during pregnancy, each of these conditions is reviewed in detail.

GENERAL SURGICAL CONSIDERATIONS DURING PREGNANCY

Several considerations need to be taken into account during the evaluation, diagnosis, and treatment of a pregnant woman for any disorder that may require emergent surgical intervention. Foremost are the anatomic and physiologic changes that take place in a woman's body as a result of being pregnant. These changes may alter the presentation of a given disease or make a certain diagnosis more or less likely. Obstetric complications, when present, may have an effect on these factors as well. In addition, the well-being of the fetus must be addressed throughout the encounter as well as during any surgery that is deemed necessary. This can be challenging, especially as a delay in diagnosis or treatment can jeopardize the health or life of the mother, fetus, or both.

Physiologic Leukocytosis of Pregnancy

A complete discussion of the pregnancy-induced anatomic and physiologic changes can be found in most general obstetric texts. The changes that are relevant to the evaluation of each surgical condition reviewed in this chapter are highlighted in the respective discussions. However, the physiologic leukocytosis of pregnancy deserves special mention, as knowledge of this change

TABLE 21.1 Differential Diagnoses for Acute Abdominal Pain in Pregnancy by Location

RUQ:	LUQ:
Severe preeclampsia/HELLP syndrome +/– hepatic distension/rupture	Splenomegaly
AFLP	Splenic infarction, abscess or rupture
Acute hepatitis (viral or toxic)	Ruptured splenic artery aneurysm
Perihepatitis (Fitz-Hugh Curtis syndrome)	Gastritis/perforated gastric ulcer
Biliary colic/acute cholecystitis/cholangitis/ gallstone pancreatitis	Pancreatitis
Budd–Chiari syndrome	Perinephritis/pyelonephritis, pneumonia (LLL)/pleuritis/empyema
Hepatic congestion, tumor or abscess	Pulmonary infarction
Pneumonia (RLL)	Costochondritis/rib fracture
Pleuritis	Herpes zoster
Empyema	Diverticulitis of the jejunum or splenic flexure
Pulmonary infarction	Leiomyoma degeneration
Perforated peptic ulcer	
Appendicitis	
Perinephritis/pyelonephritis	
Costochondritis/rib fracture	
Herpes zoster	
Leiomyoma degeneration	

RLQ:		LLQ:	
Spontaneous/septic abortion	Ectopic pregnancy	Spontaneous/septic abortion	Ectopic pregnancy
Round ligament pain	Placental abruption	Round ligament pain	Placental abruption
Leiomyoma degeneration	Pelvic inflammatory disease	Leiomyoma degeneration	Pelvic inflammatory disease
Uterine rupture	Ruptured uterine artery	Uterine rupture	Ruptured uterine artery
Ruptured ovarian cyst	Ovarian torsion	Diverticulitis	Acute enterocolitis
Acute appendicitis	Torsion of appendix epiploica	Ruptured ovarian cyst	Ovarian torsion
Pyelonephritis	Nephrolithiasis	Pyelonephritis	Nephrolithiasis
Intestinal obstruction	Inguinal hernia	Intestinal obstruction	Inguinal hernia
Psoas abscess	Herpes zoster	Psoas abscess	Herpes zoster
Right-sided, Cecal or Meckel's diverticulitis	Acute enterocolitis	Crohn's disease	Ischemic/ ulcerative colitis
Gallstone disease	Crohn's disease	Mesenteric adenitis	
	Mesenteric adenitis		

EPIGASTRIC:		PERIUMBILICAL:	
Labor (late term)	Chorioamnionitis	Labor (late term)	Chorioamnionitis
Placental abruption	Uterine rupture	Placental abruption	Uterine rupture
Peptic ulcer	Pancreatitis	Early appendicitis	Pancreatitis
Biliary colic/acute cholecystitis	Cholangitis/gallstone pancreatitis	Gastroenteritis	Mesenteric ischemia
Gastroenteritis/ gastritis/GERD	Early appendicitis	Bowel obstruction	Leiomyoma degeneration
Severe preeclampsia/ HELLP syndrome +/– hepatic distension/ rupture	Acute hepatitis (viral or toxic)		
AFLP	Perihepatitis (Fitz-Hugh Curtis syndrome)		

EPIGASTRIC:	PERIUMBILICAL:
Leiomyoma degeneration Ruptured abdominal aortic aneurysm	

MIDLINE LOWER ABDOMINAL:		DIFFUSE OR POORLY LOCALIZED:	
Cystitis	Urinary retention	Spontaneous/septic abortion	Labor
Spontaneous/septic abortion	Labor	Ruptured ectopic pregnancy	Placental abruption
Ectopic pregnancy	Placental abruption	Uterine rupture	Spontaneous rupture of a uterine artery
Uterine rupture	Bowel obstruction	Chorioamnionitis	Ruptured abdominal aortic aneurysm
Ruptured ovarian cyst	Crohn's disease	Early or perforated appendicitis	Bowel obstruction
Ovarian torsion	Enterocolitis	Perforated peptic ulcer	Perforated diverticulitis
Pelvic inflammatory disease	Diverticulitis	Gastroenteritis	Irritable bowel syndrome
Leiomyoma degeneration		Mesenteric adenitis/ischemia	Crohn's disease
		Pancreatitis	Pelvic/hepatic/mesenteric/ovarian vein thrombosis
		Sickle cell crisis	Acute porphyria
		Diabetic coma	Malaria/familial Mediterranean fever
		Tuberculous peritonitis	Heavy metal poisoning
		Food poisoning	Primary peritonitis
		Acute leukemia	

AFLP, acute fatty liver of pregnancy; GERD, gastroesophageal reflux disease, HELLP, hemolysis, elevated liver enzymes and low platelets; LLQ, left lower quadrant; LUQ, left upper quadrant; RLQ, right lower quadrant; RUQ, right upper quadrant.

Sources: Matthews and Hodin (2006); Vandeven et al. (2010).

is relevant to all three conditions and to the evaluation of acute abdominal pain in pregnancy, in general. The normal white cell count in a pregnant woman ranges from 6,000 to 13,0000 cells/mm^3 in the first and second trimesters, up to 16,000 cells/mm^3 by term, and may reach the 20,000 to 30,000 cells/mm^3 range during labor (Vandeven, Adzick, & Krupnick, 2010).This contrasts with the normal nonpregnant white cell count, which ranges from 4,000 to 11,000 cells/mm^3. This fact complicates the interpretation of an elevated white cell count in pregnancy, and may require increased reliance upon other elements in the evaluation of a pregnant woman presenting with acute abdominal pain.

Diagnostic Imaging Considerations

When diagnostic imaging is indicated in a pregnant woman, the safety of fetal radiation exposure must be weighed against the risk to the pregnant woman

or fetus of a delayed diagnosis. In most instances, the latter is greater. The most commonly used diagnostic imaging studies expose the fetus to significantly less than 5 rad of ionizing radiation, below which there is no evidence for an increased risk of pregnancy loss, fetal anomalies, fetal growth restriction, or developmental delay of the child (American Congress of Obstetricians and Gynecologists [ACOG], 2016). For instance, a routine chest radiograph exposes the fetus to less than 1 millirad (mrad), while an abdominal flat plate exposes the fetus to 140 mrad. Both are considered acceptable in pregnancy.

Graded compression ultrasonography (US) is the initial imaging modality of choice in pregnant women. This is because it involves no discernable radiation exposure, employs no contrast agents, and there has been no documentation of any biologic effects to mother or fetus over a long history of use (ACOG, 2016; Long, Long, Lai, & Macura, 2011). In addition, results are rapid, and additional pelvic pathology can be detected.

When US is not sufficient to make an accurate diagnosis, noncontrast magnetic resonance imaging (MRI) is the next recommended study. It utilizes the magnetic properties of tissues to create images, and therefore, like US, involves no fetal exposure to ionizing radiation. Gadolinium, the contrast agent commonly used for MRI, crosses the placenta and is excreted into the amniotic fluid by the fetus. Though no adverse effects to the fetus or to the pregnancy have been reported when administered, data are sparse, and the potentially long half-life of gadolinium once it enters the fetal circulation is concerning. In addition, MRI has been shown to be highly accurate without contrast; therefore, it is not used in pregnancy (Long et al., 2011). In addition, as with US, additional pelvic and lower abdominal pathology can be detected simultaneously.

Although the fetus is exposed to ionizing radiation and iodinated contrast during a computed tomography (CT) scan (approximately 20 mrad for a chest CT with abdomen shielded, 150–200 mrad for an abdominal CT with uterus shielded, and 2 rad for a pelvic CT), protocols that decrease this exposure without affecting performance are available and advocated for pregnant women (Long et al., 2011; Vandeven et al., 2010). Additional pelvic and abdominal pathology can be detected as well, though it can take up to 2 hours to administer oral contrast.

Timing of Surgical Intervention

Urgently indicated surgery is acceptable in a pregnant woman regardless of trimester. Alternatively, elective surgery is best deferred until the postpartum period. Per the most recent ACOG Committee Opinion (ACOG, 2015), indicated but nonurgent surgery in pregnant women is best deferred to the early to mid-second trimester. Erroneous causal associations between the surgery and the frequent adverse pregnancy outcomes seen in the first and third trimesters are thereby avoided. These potential outcomes include spontaneous abortion (33%) and preterm contractions/labor (9%), respectively. In addition, by following these guidelines, the fetus would not be exposed to potentially harmful anesthetic agents during the period of organogenesis. However, it is important to note that standard concentrations of commonly used anesthetic agents have not been shown to have teratogenic effects in humans regardless of gestational age (ACOG, 2011). Furthermore, the gravid uterus may obliterate the operative field in the third trimester and make surgery more technically difficult.

ACOG also recommends that when surgery is required during pregnancy it should be performed at an institution where the fetus can be monitored as appropriate, and where an obstetric provider is available, able to interpret the

results, and able to intervene by performing an emergency cesarean section intraoperatively if indicated. Informed consent for emergent delivery on the part of the pregnant woman is essential when possible. Finally, neonatal and pediatric services are required in the event that the fetus is delivered and is viable (ACOG, 2011).

Route of Surgery

Laparoscopic surgery is considered safe in pregnancy and is therefore a viable alternative to laparotomy for surgical emergencies (Spight, Hunter, & Jobe, 2015; Vandeven et al., 2010). In general, the type of surgery chosen is based upon the skills of the surgeon, the availability of equipment and staff, the gestational age at the time of surgery, and the usual patient characteristics taken into account when planning laparoscopic surgeries on nonpregnant individuals, including body mass index and airway access. Open entry techniques are preferred, and dependent positioning is advised in order to shift the uterus off of the inferior vena cava. Lower insufflation pressures are advocated than those used for nonpregnant women, though it has been shown that the intrauterine pressure created by a pneumoperitoneum of 15 mmHg is much less than that found with mid-pregnancy, nonlaboring uterine contractions (Spight et al., 2015). Overall, despite the fact that some adverse fetal outcomes have been reported with negative diagnostic surgeries (Ito, Ito, Whang, & Tavakkolizadeh, 2012; Liang, Anderssen, Jaffe, & Berger, 2015; McGory et al., 2007), the rates of most complications for common nonobstetric surgeries performed via either laparoscopy or laparotomy in pregnant women are not increased above those in nonpregnant women (Moore et al., 2015; Silvestri et al., 2011; Vandeven et al., 2010).

Fetal Monitoring During Surgery

Hemodynamic stability of the mother during surgery does not necessarily imply adequate placental perfusion or fetal oxygenation. When possible, intraoperative fetal monitoring can identify the need for changes in maternal positioning and/or cardiorespiratory status in order to maintain fetal well-being. Therefore, it is recommended by ACOG that a fetal heart rate be documented for a previable fetus both before and after the procedure. Continuous fetal monitoring is recommended for a viable fetus if all of the previously listed general requirements for surgery during pregnancy apply, and if the surgery itself is amenable to safe interruption or modification in order to allow for an emergent delivery. If all of these conditions are not met, then electronic fetal heart rate and contraction monitoring are advised immediately before and after the procedure, to allow for documentation of fetal well-being as well as the presence or absence of contractions (ACOG, 2011).

Anesthesia

A full discussion of the issues encountered by the anesthesiologist in managing pregnant women is outside the scope of this chapter. Briefly, the risks and benefits of the type of anesthesia and individual medications chosen are carefully weighed in conjunction with current obstetric and pediatric knowledge in preparing for the indicated surgery. When possible, regional anesthesia is

preferred, as it eliminates many of the risks and problems encountered with general anesthesia, including difficult/failed intubation and oxygen desaturation. Aspiration prophylaxis with sodium citrate or other medications is generally administered prior to the procedure regardless of the type of anesthesia chosen. Intravenous, inhalation, and neuromuscular blockade medications are titrated to effect, given the potential for pregnancy to alter patient sensitivity to these agents. And, most importantly, maternal hypotension, possible with any type, is avoided as best as possible in the interest of maintaining uterine blood flow (American Society of Anesthesiologists Task Force on Obstetric Anesthesia [ASATFOA], 2016).

Additional Recommendations

The following additional recommendations are based upon observational studies, expert opinion, the results of trials in nonpregnant individuals, and a knowledge of the anatomic and physiologic changes that occur in a woman's body as a result of being pregnant. A woman 18 to 20 weeks pregnant or more is best positioned at a 15% left lateral tilt to prevent the cardiovascular decompensation that may result from compression of the aorta and inferior vena cava by the uterus is a direct supine position. A wedge placed under the woman's right hip is also acceptable. Antibiotics are administered according to the usual guidelines for the procedure being performed, with attention to and avoidance of medications that have been associated with reported fetal toxicities and teratogenic effects if alternatives are available. Deep venous thrombosis (DVT) prophylaxis with sequential compression devices is implemented during surgery of any type or duration, as pregnancy is a well-known hypercoagulable condition. The decision to use systemic anticoagulants, as usual, is dependent upon the nature of the procedure itself, any additional risk factors of the woman herself (obesity, immobilization, personal or family history, etc.), and the nature of the expected course of recovery.

When surgery is performed prior to 7 to 9 weeks gestation, and a corpus luteum cyst is compromised or removed in the process, progesterone supplementation is indicated up to 9 completed weeks gestational age (Pritts & Atwood, 2002). With surgery at or near viability, tocolytics are not recommended prophylactically, but only for treatment of preterm labor when present. Prophylactic glucocorticoids may be considered for surgeries that occur between 24 and 34 weeks gestation if the underlying process or procedure is thought to place the pregnant woman at increased risk for preterm labor. They are not recommended, however, in cases where an infection has spread systemically, as they may undermine the efforts of the maternal immune system to eliminate the infection.

ACUTE APPENDICITIS

Acute appendicitis is the most common general surgical emergency among pregnant women, and accounts for 25% of nonobstetrical surgery performed during pregnancy (Abbasi, Patenaude, & Abenhaim, 2014). The incidence is approximately 1 in 766 births (Liang et al., 2015), and was previously reported to be on par with the incidence in nonpregnant women. However, a recent cohort study of over 350,000 pregnancies from 1997 to 2012 reported that the diagnosis is actually 35% less likely during pregnancy (Zingone, Sultan, Humes, & West, 2015). The highest rates in pregnant women were found during the second

trimester, and the lowest were during the third trimester. Appendiceal rupture is more likely when surgery is delayed more than 20 to 24 hours from symptom onset (Abbasi et al., 2014; Bickell, Aufses, Rojas, & Bodian, 2006; Yilmaz, Akgun, Bac, & Celik, 2007). Therefore, it is not surprising that rupture is more likely in pregnant women, upon whom reluctance on the part of surgeons to operate is more likely to delay treatment, especially during the third trimester. A timely diagnosis is crucial, given that elevated rates of adverse outcomes, including maternal sepsis and preterm labor, are seen under these circumstances (Abbasi et al., 2014).

PRESENTING SYMPTOMATOLOGY

The classic presentation of acute appendicitis includes a report of vague periumbilical pain thought to be due to luminal obstruction of the appendix by a fecalith or by lymphoid hyperplasia. This is a referred pain relayed by visceral mechanisms as a result of the increased pressure in the appendix. It is followed by anorexia, nausea, and vomiting, also mediated by visceral mechanisms. As the inflammatory process progresses beyond the appendix itself and affects the overlying peritoneum of the right lower quadrant or pelvis, the pain shifts to that region. This is reported to be the most common presenting symptom of appendicitis in pregnancy (Liang et al., 2015; Mourad, Elliot, Erickson, & Lisboa, 2000; Yilmaz et al., 2007). Fever often follows, generally low grade unless the appendix is perforated. Diffuse abdominal pain is also more common with perforation. Additional symptoms that may be present include urinary complaints, diarrhea, or constipation, all owing to the proximity of the bladder and bowel to the inflamed appendix. Though microscopic hematuria, pyuria, or bacteriuria are present in one third to more than one half of patients with acute appendicitis (Yilmaz et al., 2007), a complaint of frank hematuria is rare.

In the pregnant woman, especially with advancing gestational age, the presentation may be less "classic," though perhaps not as much as originally thought. Though the growing uterus shifts the location of the appendix a few centimeters superiorly during the pregnancy, the right lower quadrant pain has been found to be in close proximity to McBurney's point regardless of the gestational age of the pregnancy (Hodjati & Kazerooni, 2003; Mourad et al., 2000). This is in contrast to the classic teaching that the pain is displaced superiorly as well, though some recent smaller studies have reported this to be the case (House, Bourne, Seymour, & Brewer, 2014). In addition, since the uterus lifts the anterior abdominal wall away from the appendix as it grows, thereby preventing direct contact between the area of inflammation and the anterior parietal peritoneum, the presentation of the pain may be significantly less pronounced. Gastrointestinal symptoms may also be more subtle, since the uterus intervenes between the appendix and the bladder and bowel in many cases. Though 58% to 77% of pregnant women with appendicitis report some degree of nausea and vomiting, complaints may consist only of simple indigestion, mild bowel irregularity, or generalized malaise (Vandeven et al., 2010).

HISTORY AND DATA COLLECTION

In addition to the history of the onset and progression of pain and upper gastrointestinal symptoms in a pregnant woman suspected of having acute appendicitis, a complete review of systems is recommended to make an accurate diagnosis. In particular, certain urinary or bowel symptoms may make an alternate

diagnosis more likely, since pregnancy-induced physiologic changes render these organs highly susceptible to compromise. Inquiry regarding pregnancy and fetal status is also crucial, as a history of vaginal bleeding or abdominal trauma coincident with the onset of pain would clearly increase concern for an obstetric etiology for the presenting symptoms.

In pregnancies that have reached fetal viability, fetal heart rate abnormalities may also increase concern for pregnancy-related causes of abdominal pain, though they can occur with nonobstetric etiologies as well.

PHYSICAL EXAMINATION

Pregnant women with acute appendicitis appear variably uncomfortable, depending how early in the process they present for care. A documented low-grade fever and elevated heart rate, in addition to the common presenting complaints, would support a diagnosis of early acute appendicitis. A fever above 39.4°C (103°F) is especially concerning for a perforated appendix.

As previously mentioned, the abdominal examination findings on a pregnant woman with acute appendicitis may be attenuated by the presence of the gravid uterus. Though the point of maximal tenderness in the right lower quadrant is still consistently close to McBurney's point (1.5–2 inches from the anterior superior iliac spine in the direction of the umbilicus), rebound and guarding are inconsistently found (Vandeven et al., 2010). Additional peritoneal signs that are less sensitive and variably influenced by the intervening uterus include Dunphy's sign (increased pain with coughing or movement), Rovsing's sign (pain in the right lower quadrant with palpation of the left lower quadrant, indicative of right-sided peritoneal irritation), the psoas sign (right lower quadrant pain with passive hip extension, indicative of retrocecal appendiceal inflammation), and the obturator sign (right lower quadrant pain with passive flexion of the right hip and knee, followed by internal rotation of the right hip, indicative of internal obturator inflammation, and therefore a "pelvic" appendix). Cervical motion tenderness may be present on pelvic examination, as may pelvic tenderness upon rectal examination, especially in the case of a retrocecal or pelvic appendix.

LABORATORY AND IMAGING STUDIES

While the diagnosis of appendicitis is based primarily upon clinical findings, a complete blood count (CBC) is usually obtained to screen for leukocytosis. A retrospective review of the pregnancies of over 66,000 consecutive deliveries at a single hospital was performed in the late 1990s, during which the mean leukocyte count among expectant mothers with confirmed appendicitis was found to be 16,400 cells/mm^3, compared to 14,000 cells/mm^3 for those found to have a normal appendix (Mourad et al., 2000). A left shift or bandemia in the differential, thought previously to favor appendicitis or another infectious process, was found to be nondiagnostic in the same study. When the overall white count is normal, appendicitis is unlikely, while a white count above 20,000 cells/mm^3 in a nonlaboring patient is concerning for an appendiceal perforation.

As previously mentioned, urinalysis in a woman with appendicitis may show microscopic hematuria or pyuria, and this does not discount the diagnosis. In addition, in the absence of biliary disease, mild elevations in serum

bilirubin (>1.0 mg/dL) have been associated with a perforated appendix (Sand et al., 2009).

Though an experienced examiner may be able to diagnose appendicitis based upon history, physical exam, and laboratory findings alone, imaging is recommended when the diagnosis is not certain. The diagnosis of appendicitis is made by US with 86% sensitivity and 81% specificity (Terasawa, Blackmore, Bent, & Kohlwes, 2004) if a thick-walled, noncompressible, blind-ended tubular structure, with a diameter greater than 6 mm, is present in the right lower quadrant, as shown in Figure 21.1.

If a normal appendix is not clearly visualized by US, which has been reported to be the case up to 97% of the time (Lehnert, Groos, Linnau, & Moshiri, 2012), additional imaging with MRI is advised, where available. In the largest study to date, the sensitivity and specificity of MRI in the detection of appendicitis were 100% and 93%, respectively. A negative predictive value of 100% was also noted (Pedrosa, Lafornara, Pandharipande, Goldsmith, & Rofsky, 2009). The diagnostic finding of an enlarged (>6 mm), fluid-filled appendix is shown in Figure 21.2.

When clinical evaluation and US results are not conclusive, or MRI is not readily available, CT is recommended (Long et al., 2011). CT is available in most institutions and has well-established diagnostic value for appendicitis in the general population, with a sensitivity of 94% and a specificity of 95% (Teresawa, Blackmore, Bent, & Kohlwes, 2004). A meta-analysis of three retrospective studies in pregnant women reported sensitivity of 85.7% and a specificity of 97.4% (Basaran & Basaran, 2009). The main findings suggestive

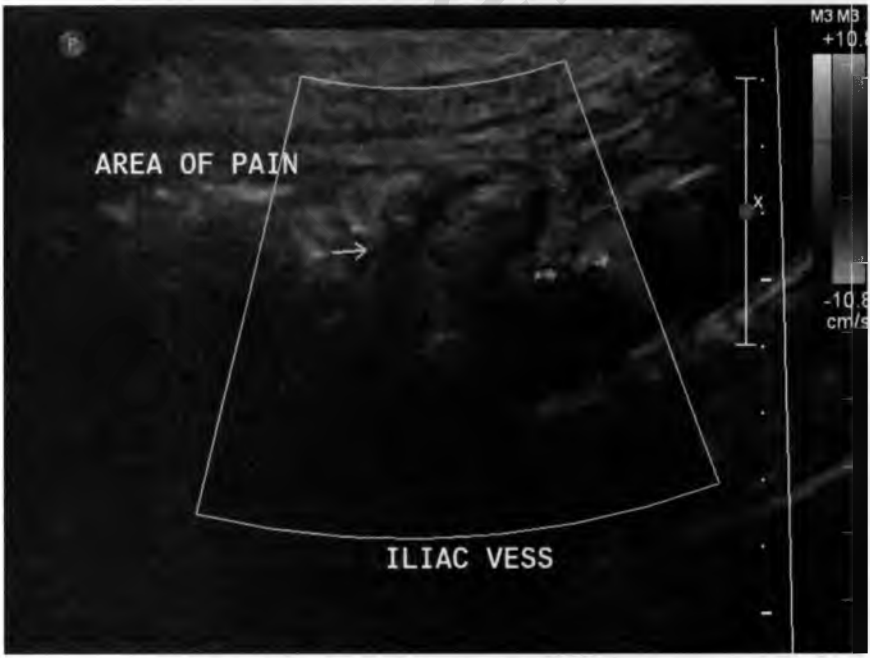

Figure 21.1 Ultrasound appearance of acute appendicitis

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

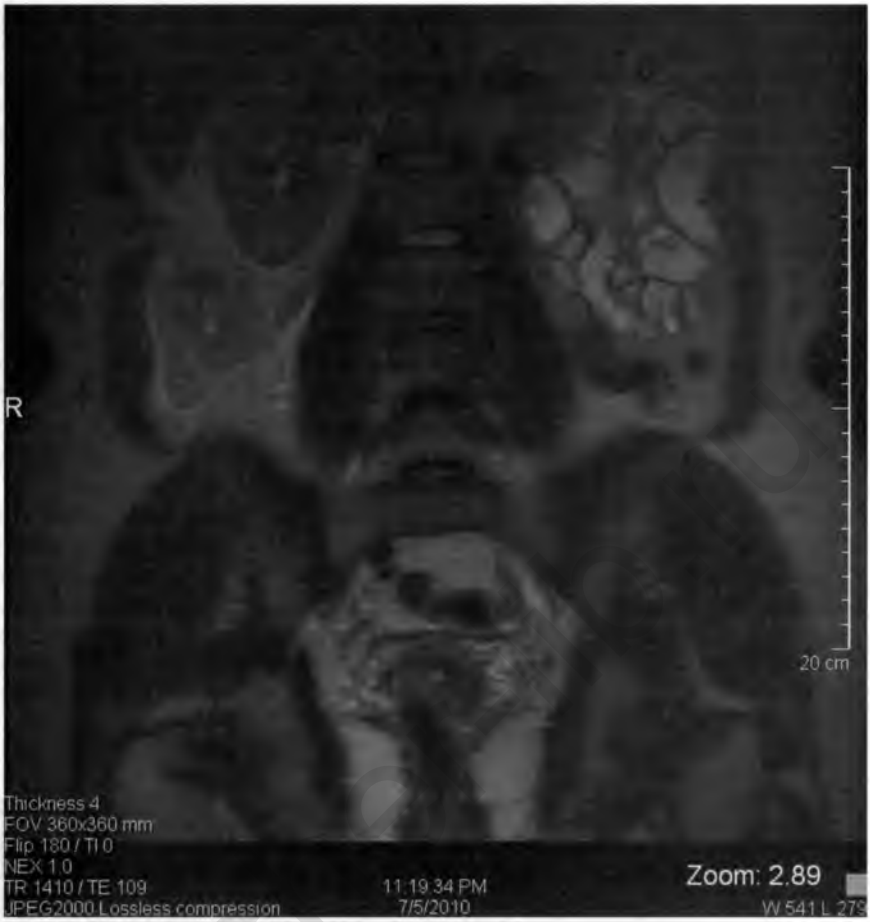

Figure 21.2 MRI appearance of acute appendicitis

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

of appendicitis on CT are an enlarged (>6 mm) nonfilling or occluded tubular structure, inflammation as manifested by appendiceal wall thickening or enhancement, and/or periappendiceal fat stranding in the right lower quadrant, as seen in Figure 21.3.

In addition, in 25% of cases, an appendicolith is visualized (Whitley, Sookur, McLean, & Power, 2009). An appendiceal lumen with air or contrast present on CT essentially rules out the diagnosis, though a nonvisualized appendix does not.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of appendicitis in pregnancy is extensive, as listed in Table 21.2. Cecal and Meckel's diverticulitis deserve special mention, however, as they may present identically to appendicitis. Diagnosis of these conditions is usually the result of imaging studies and/or exploratory surgery to evaluate for appendicitis. Table 21.3 describes peritoneal signs indicative of acute appendicitis.

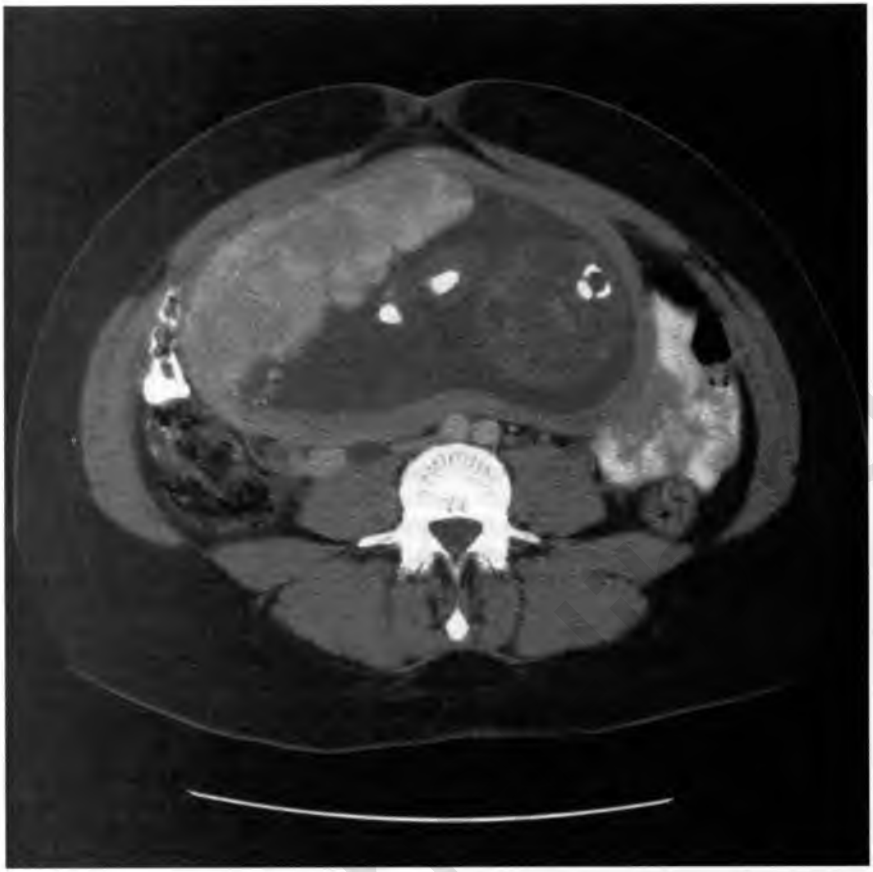

Figure 21.3 CT appearance of acute appendicitis

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

CLINICAL MANAGEMENT AND FOLLOW-UP

When acute appendicitis is strongly suspected or diagnosed by imaging, immediate general surgery consultation is indicated. Due to the high risk of appendiceal perforation with a delay over 20 to 24 hours, an indicated appendectomy should be performed expeditiously regardless of the gestational age of the pregnancy (ACOG, 2011; Bickell et al., 2006; Yilmaz et al., 2007). High rates of adverse maternal and fetal outcomes including maternal sepsis, preterm labor and delivery, and fetal loss are seen when perforation occurs. In equivocal cases, a short period of observation may be recommended. In cases where perforation is known to have already occurred, and the gravida is stable, medical management may be considered by the consulting surgeon (Young, Hamar, Levine, & Roque, 2009). Of note, several recent studies investigating the concept of nonoperative treatment for uncomplicated appendicitis have shown a potential positive outcome for certain subgroups. However, these studies did not evaluate pregnant patients, in whom appendicitis is generally not considered uncomplicated; thus, operative care remains the standard of care for this population (Abbasi et al., 2014; Liang et al., 2015).

TABLE 21.2 Most Common Differential Diagnoses for Acute Appendicitis, Acute Cholecystitis, and Bowel Obstruction in Pregnancy

Acute appendicitis:	Cecal and Meckel's diverticulitis Acute gastroenteritis/mesenteric lymphadenitis, bacterial or viral etiology Inflammatory bowel disease: Crohn's disease/acute terminal ileitis/ulcerative colitis Pyelonephritis Nephrolithiasis Acute cholecystitis/choledocholithiasis/ascending cholangitis/gallstone pancreatitis Bowel obstruction Colonic pseudo-obstruction Ruptured ovarian cysts Ovarian torsion *Obstetrical causes most common in first trimester:* Ruptured ectopic pregnancy Spontaneous or septic abortion Hyperemesis gravidarum Pelvic inflammatory disease *Obstetrical causes most common in second and third trimesters:* Round ligament pain Preterm labor/labor Chorioamnionitis Placental abruption Uterine rupture
Acute cholecystitis:	Choledocholithiasis Ascending cholangitis Gallstone pancreatitis Acute viral hepatitis Peptic ulcer disease Nonbiliary pancreatitis Acute appendicitis Bowel obstruction Paralytic ileus Pyelonephritis Right-sided pneumonia Acute myocardial infarction *Obstetrical causes most common in first trimester:* Hyperemesis gravidarum Fitz-Hugh Curtis syndrome (gonorrhea-induced perihepatitis) *Obstetrical causes most common in second and third trimesters:* Acute fatty liver of pregnancy Severe preeclampsia/HELLP syndrome Preterm labor/labor Placental abruption Uterine rupture Chorioamnionitis
Bowel obstruction:	Paralytic Ileus Colonic pseudo-obstruction Acute appendicitis and corresponding differential diagnoses Acute cholecystitis and corresponding differential diagnoses *Obstetrical causes most common in first trimester:* Ruptured ectopic pregnancy Spontaneous or septic abortion

Bowel obstruction:	Hyperemesis gravidarum
	Pelvic inflammatory disease/Fitz-Hugh Curtis syndrome
	Obstetrical causes most common in second and third trimester:
	Round ligament pain
	Preterm labor/labor
	Placental abruption
	Uterine rupture
	Chorioamnionitis
	Acute fatty liver of pregnancy
	Severe preeclampsia/HELLP syndrome

HELLP, hemolysis, elevated liver enzymes and low platelets.

Sources: Matthews and Hodin (2006); Vandeven et al. (2010).

TABLE 21.3 Peritoneal Signs on Physical Exam Suggestive of Acute Appendicitis

Dunphy's sign	Increased pain with coughing or movement
Rovsing's sign	Pain in the right lower quadrant with palpation of the left lower quadrant, indicative of right-sided peritoneal irritation
Psoas sign	Right lower quadrant pain with passive hip extension, indicative of retrocecal inflammation (likely related to a retrocecal appendicitis)
Obturator sign	Right lower quadrant pain with passive flexion of the right hip and knee followed by internal rotation of the right hip, indicative of internal obturator inflammation (likely related to a pelvic appendicitis)

Source: Adapted from Matthews and Hodin (2006).

In practice, general surgeons have been known to tolerate a higher negative surgical intervention rate in pregnant women, 4% to 50%, as opposed to 10% to 18% in the general population (Gilo et al., 2009; Liang et al., 2015; Yilmaz et al., 2007). Though complication rates are low with these surgeries, fetal loss and preterm labor do occur. The incidence of fetal loss is approximately 4%, essentially the same as that for appendectomy in general, whereas the incidence of preterm labor is actually slightly higher, 10% as opposed to 7% overall (Ito et al., 2012; Liang et al., 2015; McGory et al., 2007). Given that these surgeries are not without risk, experts have advocated for improved diagnostic accuracy in order to reduce fetal loss. Of note, long-term prognosis for women who undergo surgery for acute appendicitis during pregnancy is good, and there does not appear to be an increased risk for infertility or other complications (Viktrup & Hee, 1998).

ACUTE CHOLECYSTITIS

Acute cholecystitis is the second most common indication for general abdominal surgery during pregnancy, and is more common in pregnant than in nonpregnant women. It is usually a result of gallstone disease, occurring when a stone completely obstructs the cystic duct and leads to inflammation of the gallbladder. Additional serious complications of gallstone disease occur when stones enter the common bile duct (choledocholithiasis) and duodenum and result in the

life-threatening emergencies known as ascending cholangitis and gallstone pancreatitis. Though these most serious sequelae of gallstone disease develop in fewer than 10% of symptomatic women, they are associated with a high rate of additional complications such as gangrene (20%) and perforation (2%) of the gallbladder, along with a 15% risk of maternal mortality and a 60% risk of fetal mortality if they are not treated appropriately and in a timely fashion (Vandeven et al., 2010).

Gallstone disease in general is more common in pregnancy due to the elevated circulating estrogen levels, which increase the saturation of bile. Gallstones are found in approximately 4% of gravid women early in pregnancy, and in as many as 12.2% immediately following delivery. However, the incidence of acute cholecystitis in pregnancy is only 0.01% to 0.08% (Ko, Beresford, Schulte, Matsumoto, & Lee, 2005). This relative discrepancy is likely due to the fact that progesterone, also elevated during pregnancy, inhibits gallbladder motility, so that while stones and sludge may form, the contractions of the gallbladder are too weak to cause cystic duct obstruction. After delivery, when progesterone levels drop, obstruction is more likely; in fact, an increased prevalence of acute cholecystitis is also seen during the first year postpartum (Ko et al., 2005).

PRESENTING SYMPTOMATOLOGY

The symptoms of acute cholecystitis are related to the inflammation of the gallbladder, and are similar in pregnant and nonpregnant women. Abdominal pain is usually reported in the right upper quadrant or epigastric region, and may radiate to the back or shoulder. It is often described as severe, crampy or sharp, intermittent or spasmodic, and it generally lasts longer than 4 to 6 hours. Movement usually worsens the pain. Nausea, vomiting, or anorexia may be present. Subjective or documented fever may be reported.

HISTORY AND DATA COLLECTION

When a pregnant woman presents with the previous symptoms, it is crucial to inquire further about the setting in which her abdominal pain began. The pain of both gallstones and acute cholecystitis tends to begin an hour or more following ingestion of fatty food. Pain that begins sooner than 1 hour after eating does not suggest biliary disease. It is also vital to ask about a history of similar episodes in the past that have resolved spontaneously, or a documented history of gallstones. The presence or absence of fever or chills should be elicited as well.

PHYSICAL EXAMINATION

Pregnant and nonpregnant women with acute cholecystitis tend to appear ill. They are often noted to lie quite still on the examining table, as the inflammation of the gallbladder extends to the overlying peritoneum and makes movement more painful. Fever and tachycardia are commonly documented. Jaundice is not typically seen with uncomplicated acute cholecystitis, but is consistent with common bile duct obstruction.

In addition to both voluntary and involuntary guarding, the abdominal exam in acute cholecystitis is usually significant for distinct right upper quadrant tenderness, as a result of the local inflammation there. "Murphy's sign," increased discomfort and/or inspiratory arrest with deep palpation in the

region of the gallbladder fossa, is the physical exam finding pathognomonic for the condition (Vandeven et al., 2010). The inflamed gallbladder is occasionally palpable as a mass, though guarding often masks this finding even in a non-pregnant woman, as can the size of the uterus in the second or third trimester in a pregnant woman. Detection of Murphy's sign, as well as the other common peritoneal signs, varies with maternal habitus and gestational age.

LABORATORY AND IMAGING STUDIES

Laboratory evaluation of a pregnant woman suspected of having acute cholecystitis includes a CBC with differential and liver and pancreatic function testing. As with acute appendicitis, the typically elevated white blood cell count found with acute cholecystitis may be difficult to interpret in light of the normal leukocytosis of pregnancy. An elevated alkaline phosphatase is normally found in pregnancy as well, but significant elevations (two or more times the normal value) of the transaminases or bilirubin levels are consistent with common bile duct obstruction. Slight elevations in serum transaminases and amylase may be seen with uncomplicated cholecystitis, due to the passage of small stones or sludge, while significant elevations of amylase and lipase increase suspicion for gallstone pancreatitis.

Women presenting with the symptoms and clinical findings suggestive of acute cholecystitis in pregnancy often require imaging to confirm the diagnosis. Echogenic shadowing on US as shown in Figure 21.4, indicative of the presence of gallstones, is consistent with but not diagnostic of acute cholecystitis. Gallbladder wall thickening greater than 4 to 5 mm, edema, and pericholecystic

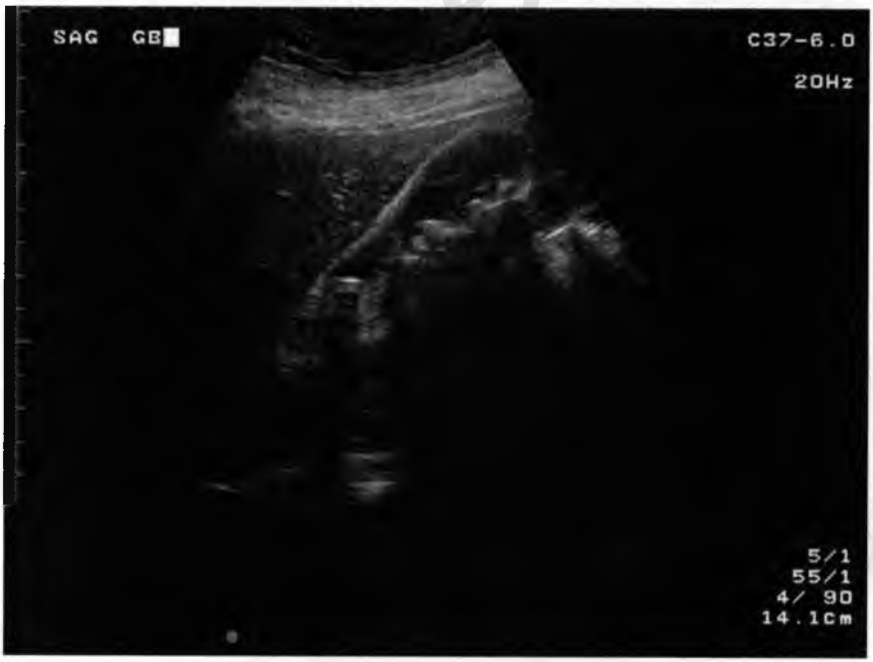

Figure 21.4 Ultrasound appearance of gallstones

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

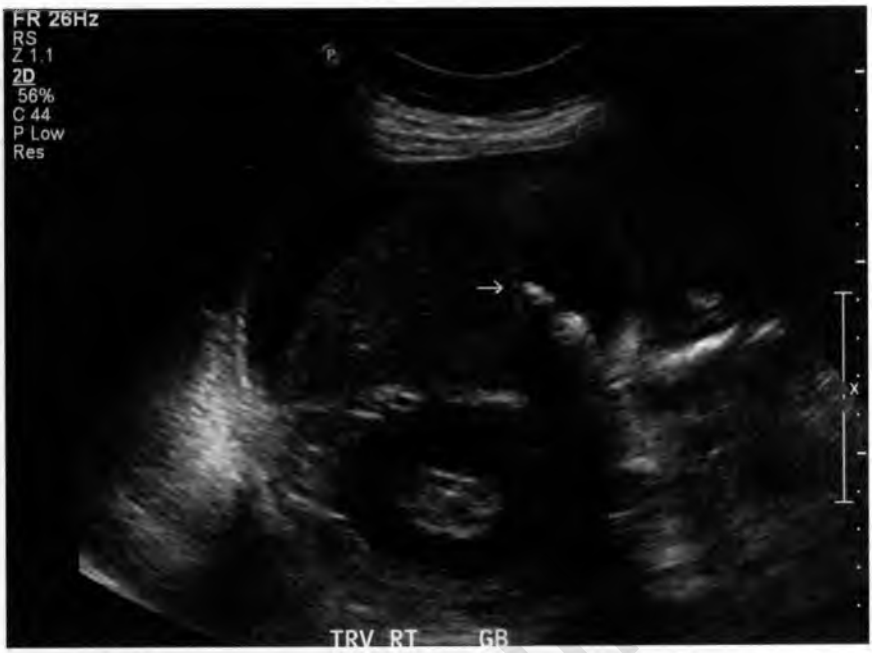

Figure 21.5 Ultrasound appearance of acute cholecystitis

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

fluid are pathognomonic, as shown in Figure 21.5. A "sonographic Murphy's sign," pain with visualized compression of the gallbladder by the ultrasound transducer, confirms the presence of inflammation. US is over 97% accurate in making the diagnosis, though it may not detect small stones or sludge (Vandeven et al., 2010).

Magnetic resonance cholangiography (MRCP) is an imaging modality currently being studied in clinical trials for use in the diagnosis of acute cholecystitis. There are no clear guidelines for its use in pregnancy; however, it is generally considered to be safe, and can be particularly useful in complicated cases, such as when symptomatic choledocholithiasis or gallstone pancreatitis are suspected (Date, Kaushal, & Ramesh, 2008). Endoscopic retrograde cholangiopancreatography (ERCP) is a minimally invasive procedure that has also been proposed for the evaluation of symptomatic choledocholithiasis or gallstone pancreatitis, and can be performed with no direct exposure of the fetus to radiation. The additional benefit of ERCP relative to MRCP is its therapeutic capability. It is possible, during the course of the procedure, to retrieve gallstones from their respective points of obstruction in the common bile duct and thereby alleviate the symptoms of the various gallstone-related disorders (Date et al., 2008; Tham et al., 2003).

DIFFERENTIAL DIAGNOSIS

The most common conditions to consider in the differential diagnosis of acute cholecystitis in pregnancy are listed in Table 21.2. The main competing diagnosis for the presentation of acute cholecystitis is symptomatic cholelithiasis, or biliary colic. Contractions of the gallbladder following a fatty meal push any stones

present up against the entrance to the cystic duct, and cause visceral pain due to the increase in pressure that results inside the gallbladder. As the gallbladder relaxes, the stones commonly fall back, and the pain completely resolves within a few hours. As previously mentioned, the pain of acute cholecystitis does not typically follow this crescendo-decrescendo pattern, but tends to be more constant and severe, lasting longer than 4 to 6 hours. In addition, constitutional symptoms such as fever and malaise are present much more frequently with acute cholecystitis than with biliary colic alone, as is leukocytosis (Gilo et al., 2009).

CLINICAL MANAGEMENT AND FOLLOW-UP

When acute cholecystitis is diagnosed, a general surgical evaluation is warranted in order to determine whether medical or surgical management is indicated. In the past, medical management was the definitive treatment for acute cholecystitis in pregnancy. However, while initial relief of symptoms is common with medical management (85%), recurrence prior to delivery in pregnant women is common, with hospitalization required for management of the relapses 90% of the time (Vandeven et al., 2010). In addition, progression of disease including choledocholithiasis and gallstone pancreatitis may occur with future attacks, and are associated with high rates of maternal and fetal morbidity and mortality (Date et al., 2008; Vandeven et al., 2010).

For these reasons, while conservative management is often enacted initially for both pregnant and nonpregnant individuals, the definitive treatment for acute cholecystitis in both populations is surgery. Surgery has not been shown to increase maternal or fetal morbidity or mortality rates in pregnancy, and can prevent progression of disease (Cohen-Kerem, Railtom, Oren, Lishner, & Koren, 2005; Silvestri et al., 2011). Current recommendations are for cholecystectomy during a pregnant woman's initial hospitalization for acute cholecystitis, generally within 72 hours of presentation and within 24 to 48 hours after antibiotics, hydration, and supportive care have been initiated (Date et al., 2008). Immediate surgery is indicated if the woman appears septic or there is concern for gangrene or perforation of the gallbladder.

Regarding surgical route, the Society of Gastrointestinal and Endoscopic Surgeons (SAGES) published treatment guidelines that state, "Laparoscopic cholecystectomy is the treatment of choice in the pregnant patient with gallbladder disease, regardless of trimester" (SAGES, 2016). Their conclusions agree with a recent systematic review that reported the relative safety of laparoscopic versus open cholecystectomy as well (Nasioudis, Tsilimigras, & Economopoulos, 2016). In addition, as previously mentioned, ERCP has been proposed for both evaluation and treatment of symptomatic choledocholithiasis or gallstone pancreatitis in pregnancy.

BOWEL OBSTRUCTION

The incidence of intestinal obstruction during pregnancy is most recently reported to be 1 in 2,500 to 3,500 deliveries. It was reported to be as low as 1 in 68,000 deliveries in the 1930s (Vandeven et al., 2010). This dramatic rise is related to the growing number of women who undergo surgery for various medical conditions, including the increasingly popular bariatric procedures, prior to becoming pregnant. The intra-abdominal adhesions formed as a result of these operations are the most common cause of intestinal obstruction in

the gravid woman. Obstruction due to intestinal volvulus is less common, though it is more common in pregnancy than in the general population. Intussusception, hernia incarceration, and intestinal carcinoma are even less frequent causes.

There are three stages of pregnancy during which intestinal obstruction is most likely to present. The first is during the fourth to fifth months, when the growing uterus enters the "true" abdominal cavity and begins to stretch any adhesions that exist there. The second is during the eighth to ninth month, when the baby "drops," with a resultant slight decrease in size of the uterus, and the third is after delivery, when the uterine size decreases dramatically. At each of these times, the relationship of the abdominal viscera to the intra-abdominal adhesions is altered by a change in size of the uterus, and obstruction may occur. In cases of volvulus, an already redundant sigmoid colon (most frequently) or mobile cecum is raised out of the pelvis by the growing uterus and twists around its point of fixation. Of note, incarcerated inguinal hernias, the second most common cause of small bowel obstruction (SBO) in the general population, are rare in pregnancy due to the small bowel being similarly elevated out of the pelvis and, therefore, away from the inguinal region.

PRESENTING SYMPTOMATOLOGY

The symptoms of intestinal obstruction in the pregnant woman include abdominal pain and vomiting, just as in the nonpregnant individual. Reports of abdominal distension, however, are less consistent owing to the presence of the gravid uterus. Poorly localized, crampy, paroxysmal upper abdominal pain with frequent emesis is more typical of proximal SBO, while lower abdominal pain with less frequent, and possibly feculent, emesis is consistent with colonic obstruction. Obstipation is more common with distal bowel obstruction (Vandeven et al., 2010).

In addition to the previous gastrointestinal complaints, individuals with bowel obstruction often present with symptoms that are consistent with progressive hypovolemia, the "hallmark" of the condition. Especially with SBO, dilation and bacterial overgrowth occur in the proximal bowel. The resulting edema and loss of absorptive function of the bowel wall then cause fluid sequestration in the bowel lumen and, ultimately, loss of this fluid into the peritoneal cavity. In addition to the fluid losses from vomiting, this results in severe dehydration. Pregnant women may report dizziness, lightheadedness, fatigue, and/or shortness of breath above baseline. They may also note significantly decreased urine output. As the intraluminal pressure increases, perfusion to the bowel may be compromised and necrosis may occur. In this case, diffuse, constant abdominal pain and fever may be reported as well.

HISTORY AND DATA COLLECTION

A history of prior abdominal surgery is essential to obtain in any individual who presents with symptoms concerning for bowel obstruction. In particular, a history of gynecologic pelvic surgery, appendectomy, gastric bypass surgery, or bowel resection, especially when the latter is due to prior obstruction or intra-abdominal malignancy, raises concern for a current obstruction (Kakarla, Dailey, Marino, Shikora, & Chelmow, 2005; Vandeven et al., 2010). A history of Crohn's or other inflammatory bowel disease in a pregnant woman also increases the risk due to the increased prevalence of adhesions with these disorders.

PHYSICAL EXAMINATION

Upon presentation, a pregnant woman with a bowel obstruction may be found to be hypotensive and/or tachycardic owing to dehydration. Oliguria is likely. A fever raises the suspicion for bowel necrosis and/or strangulation.

Abdominal examination includes notation of any surgical scars present, as well as the presence of distension that is not consistent with the woman's gestational age, both of which raise suspicion for bowel obstruction. Auscultation and percussion of the abdomen for the high-pitched, hypoactive, or absent bowel sounds characteristic of obstruction are increasingly difficult as the pregnancy progresses, and findings may not be reliable. Surgical scars are palpated, as are the umbilical, inguinal, and femoral regions, to check for hernias. Peritoneal signs including localized or rebound tenderness and guarding are variable in pregnancy, as previously discussed, and are worrisome when present. Finally, a rectal examination is necessary to search for masses as well as gross or occult blood, which may be consistent with ischemia, intussusception, or neoplasm.

LABORATORY AND IMAGING STUDIES

No laboratory studies are diagnostic of bowel obstruction, though they can be helpful in evaluating the degree of dehydration present. Blood urea nitrogen (BUN), creatinine, and hematocrit elevations reflect poor hydration status. Since creatinine usually decreases during pregnancy, even a normal nonpregnant creatinine level may be considered elevated. Leukocytosis with a left shift may be a sign of bowel ischemia or perforation, as may an elevated serum lactate (sensitivity 90%–100%, specificity 42%–87%; Markogiannakis et al., 2007).

Upright and flat abdominal radiographs are the imaging studies of choice when bowel obstruction is suspected, both in the pregnant and nonpregnant population. Distended loops of bowel with multiple air-fluid levels are generally seen with SBO, as shown in Figure 21.6, but may also be seen with colonic obstruction. A grossly dilated loop may be seen with volvulus. Though these films may be nonspecific or equivocal 30% to 50% of the time with early obstruction (Markogiannakis et al., 2007; Vandeven et al., 2010), serial films that show progressive changes confirm the diagnosis, while air in the colon or rectum makes a complete obstruction less likely. An upright chest film is also helpful to evaluate for free air under the diaphragm, suggestive of perforation, if this is not seen clearly on abdominal film.

When plain abdominal films are not diagnostic, a small bowel series with water-soluble contrast, or a CT scan with dilute barium or water-soluble contrast, may be performed. The former is the gold standard study for determining partial versus complete obstruction, while the latter is superior at detecting closed-loop obstructions and providing information as to the etiology of the obstruction. Although not as informative as CT, ultrasound is more sensitive and specific than plain films and does not expose the fetus to contrast agents, so it may be useful in pregnant women as well.

DIFFERENTIAL DIAGNOSIS

The clinical symptoms and signs of bowel obstruction overlap with those of both acute appendicitis and acute cholecystitis, as shown in Table 21.2. Paralytic ileus and colonic pseudo-obstruction present most similarly to the mechanical bowel obstructions discussed previously. These are functional obstructions due to

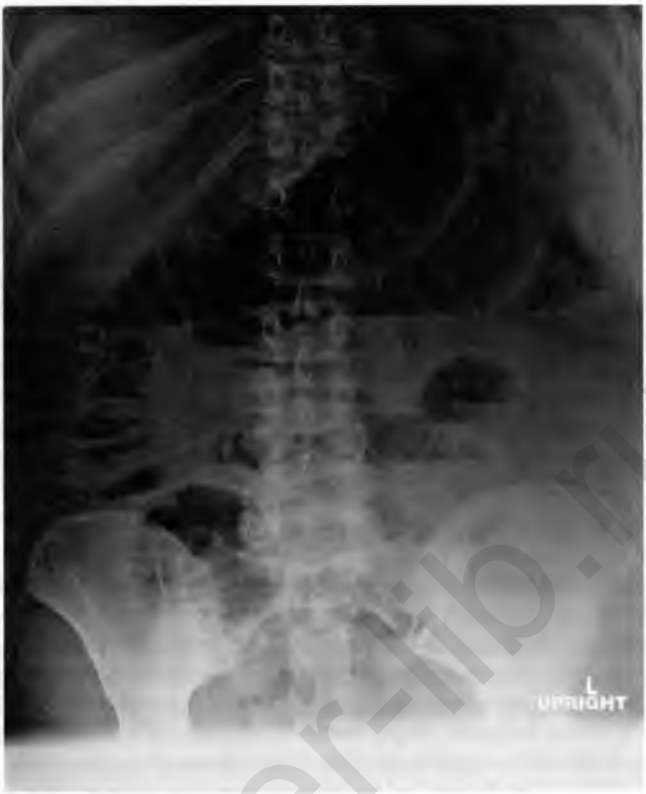

Figure 21.6 Abdominal x-ray of small bowel obstruction

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

underlying alterations in the motility of the gastrointestinal tract, and have many etiologies including electrolyte abnormalities and metabolic conditions. Laboratory testing and imaging studies are critical to help differentiate among these conditions.

CLINICAL MANAGEMENT AND FOLLOW-UP

A general surgery consultation is indicated when any type of bowel obstruction is suspected in a pregnant woman. The initial treatment is likely to include aggressive fluid resuscitation as well as decompression of the distended bowel. The fluid deficit at presentation can range from 1 to 6 L, depending upon the stage of the process (Vandeven et al., 2010). In the pregnant woman, this is especially worrisome, since hypovolemia results in decreased blood flow to the uterus and can lead to fetal distress or demise. If the fetus is viable, continuous monitoring should be in progress throughout resuscitation. Decompression is with a nasogastric tube for SBO, and with a rectal tube for sigmoid volvulus. Surgery is required for decompression of cecal volvulus.

Initial improvement, and even resolution, is possible with the nonsurgical measures described previously for both SBO and sigmoid volvulus. However, high rates of bowel ischemia, necrosis, and perforation are also seen with conservative management alone (Markogiannakis et al., 2007). Therefore, in practice, surgical intervention for all types of bowel obstruction is seen sooner

and more frequently in pregnant women than in the general population. In fact, "aggressive surgical treatment has been credited with reducing maternal and fetal mortality rates from 20% and 50%, respectively, in the 1930's, to 6% and 26% today" (Vandeven et al., 2010).

CLINICAL PEARLS

- The anatomic and physiologic changes of pregnancy may alter the presentation of a given disease or surgical condition, or make a certain diagnosis more or less likely.
- Urgently indicated surgery is acceptable in a pregnant woman regardless of trimester, while nonurgent surgery is ideally performed during the second trimester. Elective surgeries are not recommended until after delivery.
- Ultrasound and MRI are the preferred imaging techniques in pregnant patients due to lack of appreciable fetal radiation exposure; however, most x-rays, CT scans, and other nuclear medicine imaging studies expose the fetus to a much lower dose of radiation than that associated with fetal harm, and should not be avoided if indicated.

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Management of Biohazardous Exposure in Pregnancy

22

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At any point in time in the United States, 3 million women are pregnant. A biohazard exposure, deliberate or accidental, poses a unique challenge and requires careful assessment and prompt treatment to prevent harm to the woman or infant. Physiologic changes during pregnancy can change the safety and efficacy of medications and vaccines for pregnant women. In addition, the potential effect of many of these measures on the fetus is unknown (Cono, Cragan, Jamieson, & Rasmussen, 2006). This chapter discusses the five such biohazards in pregnancy—smallpox, Lassa fever, Ebola, plague, and anthrax—outlining symptomology and treatment options that may become necessary in the obstetric triage or emergency setting.

The working group on civilian biodefense has identified several biologic agents, including smallpox virus and some of the hemorrhagic fever viruses, which are more severe during pregnancy. These agents must be considered if exposure to bioterrorism is known or suspected.

SMALLPOX

Smallpox, a formerly eradicated disease, has become a bioterrorism threat. One confirmed case of smallpox is a public health emergency. An intense worldwide public health initiative resulted in no documented naturally occurring case of this highly infectious disease occurring since October 26, 1977. The World Health Organization (WHO) officially declared smallpox eradicated in 1980 (Hogan, Harchelroad, & McGovern, 2010). Only two laboratories in the world are known to house smallpox virus: the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, and the State Research Center of Virology and Biotechnology in Koltsovo, Russia. If these stores are weaponized, mass vaccination would be needed; for example, if a terrorism threat becomes real in the United States, more people, especially the military, will need to be vaccinated.

It is essential to plan for the needs of pregnant, postpartum, and lactating women during a biohazard event because of their unique immunology and physiology and the complexities of balancing maternal and fetal risks

(Meaney-Delman et al., 2014). During pregnancy, the woman's susceptibility to infections is altered. Hormonal, cellular, and humoral changes suppress the immune response (Blackburn, 2014). Circulating white cell count is slightly increased, whereas neutrophil chemotaxis and adherence, cell-mediated immunity, and natural killer cell activity decrease.

PRESENTING SYMPTOMATOLOGY

The virus starts attacking the lungs, then invades the bloodstream and spreads to the skin, intestines, lungs, kidneys, and brain. The virus activity creates a rash that starts as macules (flat, red lesions). The rash progresses to vesicles (raised blisters), then pustules (pus-filled pimples) appear about 12 to 17 days after being infected (Hogan, 2015). Clinical experience with smallpox (variola virus) indicates that pregnant women are more susceptible to variola infection and have more severe disease, resulting in an increased smallpox case-fatality rate. They are also more likely to have hemorrhagic smallpox (purpura variolosa; Jamieson, Theiler, & Rasmussen, 2006).

The CDC, the Department of Defense (DOD), and the Food and Drug Administration (FDA) monitor the outcomes of pregnancy in women exposed to smallpox vaccines in the National Smallpox Vaccine in Pregnancy Registry (Ryan & Seward, 2008). In this group, most (77%) were vaccinated near the time of conception, before pregnancy was confirmed. Outcome evaluations have not revealed higher-than-expected rates of pregnancy loss (11.9%), preterm birth (10.7%), or birth defects (2.8%). No cases of fetal vaccinia have been identified (Ryan & Seward, 2008).

Pregnant women are more susceptible to hemorrhagic smallpox or purpura variolosa. Symptoms include fever, backache, diffuse coppery-red rash, and a rapid decline in the health status of mother and infant. Information on the presentation and progression of smallpox is summarized in Exhibit 22.1.

EXHIBIT 22.1

Smallpox: Presentation and Progression

Clinical Presentation

- Fever, chills
- Body aches, headache
- Backache
- Rash appears 48–72 hours after initial symptoms
- Turns into virus-filled sores, later scabs over, process can take 2 weeks

Progression

- Virus enters respiratory tract
- Multiplies, spreads to regional lymph nodes
- Incubation period (12 days)
- Skin eruptions (lesions occur in the mouth, spread to the face, to the forearms and hands, and finally to lower limbs and trunk)

Source: Adapted from CDC (2009a, 2009b)

Within 24 hours of the onset of symptoms, a woman will likely develop spontaneous ecchymosis, epistaxis, bleeding gums, an intense erythematous rash, and subconjunctival hemorrhages. Laboratory analysis during this period may demonstrate thrombocytopenia, increased capillary fragility, and depletion of coagulation factors and fibrinogen (CDC, 2009). Death would generally result from sepsis.

Variola virus can cross the placenta and infect the fetus. It is suggested that during pregnancy, there is an increased susceptibility of the fetus to the variola infection with greater severity of illness. Maternal mortality approaches 50%, compared with 30% for men and nonpregnant women (CDC, 2003a, 2007b, 2009).

HISTORY AND DATA COLLECTION

If infection occurs during the first trimester, it can result in high rates of fetal loss. Nishiura (2006) highlights three points about smallpox in pregnancy: Miscarriage and prematurity do not vary by trimester but case fatality is highest during the last trimester; mild cases were at high risk of causing miscarriage or premature birth; and vaccination or previous miscarriage were not associated with miscarriage and premature birth in the current pregnancy. During the latter half of pregnancy, infection is associated with increased rates of prematurity. For initial screening, the CDC has developed an interactive algorithm that can be quickly completed by the provider online. This algorithm indicates the risk of the current clinical condition being smallpox (CDC, 2007a).

FETAL VACCINIA

Smallpox vaccine comes from a live virus related to smallpox called vaccinia, not smallpox virus (variola). The question remains whether to immunize pregnant women if a release of a biologic agent is confirmed or suspected (Jamieson et al., 2006). During a smallpox outbreak, recommendations for vaccination will change. Anyone exposed to smallpox should get vaccinated, because the risk from the disease is greater than the risk from the vaccine (CDC, 2007b). There is a rare, serious infection of the fetus, called fetal vaccinia, that can occur following vaccination for smallpox. Congenital variola ranges from 9% to 60% during epidemics of the disease. It is characterized by giant dermal pox and diffuse necrotic lesions of viscera and placenta. Fetal vaccinia typically results in stillbirth or death of the infant. There may be maternal immunity that protects the fetus. Smallpox vaccine is not known to cause congenital malformations but, if vaccinated, the woman ought to avoid pregnancy for a month, waiting until the vaccination site has completely healed and the scab has fallen off before trying to become pregnant.

Unvaccinated pregnant women are three times more likely to die from the disease. It is recommended that pregnant women receive the smallpox vaccine only when exposed to a diagnosed case of smallpox because there is a greater risk from the disease than from the vaccine. It is advised that pregnant women not come into contact with anyone who has been recently vaccinated.

If a breastfeeding mother (who has close contact with someone recently vaccinated) develops a rash, it is recommended that the health care provider be contacted to determine if the rash is related to the smallpox vaccine. If a vaccine-related rash occurs, the CDC recommends against breastfeeding until all scabs from the rash have healed. A woman who desires to maintain an adequate milk supply may continue to pump breast milk, but the milk must be discarded until scabs fully separate (CDC, 2009).

Vaccinia immune globulin (VIG) is an alternate treatment for people who have serious reactions to smallpox vaccine. It is an immune globulin from the blood of people who have gotten the smallpox vaccine more than once (usually many times). Antibodies are removed, purified, and stored with the resulting product being VIG. It is administered intravenously and the licensed product is called "VIG-intravenous" (VIG-IV). VIG-IV is available from the CDC under the Investigational New Drug (IND) protocol that will have guidelines for dosage and administration.

It is recommended that women contact their health care provider regarding use of VIG. Currently, CDC's Advisory Committee on Immunization Practices does not recommend preventive use of VIG for pregnant women. If a woman has another complication from smallpox vaccine that could be treated with VIG, it would be appropriate that it be given while the woman is pregnant. The few cases of reported fetal vaccinia infection have occurred after an accidental primary vaccination in early pregnancy, or the woman becoming pregnant within 28 days of vaccination. Smallpox vaccine is not known to cause congenital malformations (CDC, 2003).

LASSA FEVER

Lassa fever is an arenavirus infection that occurs mostly in Africa and can be fatal. It may involve multiple organ systems but spares the central nervous system (CNS). The first reported case of Lassa fever was described in a pregnant woman. The mortality rate is higher for pregnant women and women who have given birth within a month. The mortality rate is 50% to 92% when women are pregnant or among those who have recently given birth (Mays, 2009). Recovery occurs within 7 to 31 days after becoming symptomatic or death may ensue. Evidence suggests that the placenta may be a preferred site for viral replication, which may explain why illness and death increase during the third trimester (Jamieson et al., 2006). Uterine evacuation may reduce maternal mortality. Most pregnant women will experience a pregnancy loss. Human cases of Lassa fever probably result from contamination of food with rodent urine, but human-to-human transmission can occur via urine, feces, saliva, vomitus, or blood.

PRESENTING SYMPTOMATOLOGY AND DATA COLLECTION

Lassa fever begins with a viral prodrome, followed by unexplained disease in any organ system except the CNS. Following laboratory test results, the provider may notice massive proteinuria and elevated liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and lactate dehydrogenase (LDH) levels, which may be 10 times the normal level. Cell cultures are not routine and must be handled in a biosafety level IV laboratory. Lassa IgM antibodies or a four-fold rise in the IgG antibody titer may be detected using an indirect fluorescent antibody technique. Polymerase chain reaction (PCR) is the most rapid test. Chest x-rays may show basilar pneumonitis and pleural effusions (Mays, 2009).

CLINICAL MANAGEMENT

Diagnosis and treatment within the first 6 days may reduce the mortality by up to 10-fold. Supportive treatment includes correction of fluid and electrolyte imbalances. Anti-Lassa fever plasma is helpful as an adjunctive therapy in very ill patients. Antibiotic treatment recommendations can be found in Exhibit 22.2 (Mays, 2009).

EXHIBIT 22.2

Lassa Fever: Treatment

- Ribavirin (Virazole)
  - 30 mg/kg IV (maximum, 2 g) loading dose
  - 16 mg/kg IV (maximum, 1 g/dose) every 6 hours for 4 days
  - 8 mg/kg IV (maximum, 500 mg/dose) every 8 hours for 6 days

IV, intravenous.

Source: Adapted from Mays (2009).

EBOLA HEMORRHAGIC FEVER

Many of the survivors of the 2014 to 2015 epidemic of Ebola virus disease (EVD) in West Africa were women of childbearing age. This epidemic of EVD, centered in West Africa, is the largest EVD epidemic in history. Vertical transmission of Ebola virus (EBOV) from mother to fetus occurs during acute Ebola infection, and can lead to intrauterine fetal death, stillbirth, or neonatal death. Little is known about the risk for transmission of the virus from women to infants outside of the acute infectious period. EBOV has been found in breast milk during acute disease (Kamali et al., 2016).

High amounts of Ebola viral nucleic acid persist in the amniotic fluid of acutely infected pregnant women following clearance of viremia. The question remains whether this amniotic fluid is infectious. Some theoretical concerns remain that interventions during labor and delivery or obstetric anesthetic procedures (e.g., spinal anesthesia) pose an infectious risk to care providers. Similar concerns exist when handling the products of conception or cerebrospinal fluid from EVD survivors. Initial studies following the recent epidemic suggest that women who become pregnant after recovery from EVD pose little risk for transmission of EBOV to the baby or others (Kamali et al., 2016).

PRESENTING SYMPTOMATOLOGY AND DATA COLLECTION

The Ebola virus (EBOV; Filoviridae group) is transmitted by direct contact with blood, secretions, or contaminated objects and is associated with high fatality rates. The EBOV begins to multiply within the body with symptoms beginning 4 to 6 days after infection. The incubation period can be as short as 2 days or as long as 21 days. Of health care workers contracting Ebola following caring for Ebola patients, all had inadequate personal protective equipment (PPE) or used it incorrectly (Beam, 2015; Bebell & Riley, 2015; Dunn et al., 2014).

Presenting symptoms include the sudden onset of flu-like symptoms, such as sore throat; dry, hacking cough; fever; weakness; severe headache; and joint and muscle aches. Diarrhea, dehydration, stomach pain, or vomiting may also occur, accompanied by a rash, hiccups, red eyes, and internal and external bleeding. In dark-skinned women, the rash may not be recognized until it begins to peel. Laboratory findings show low counts of white blood cells and platelets, and elevated liver enzymes (WHO, 2008).

CLINICAL MANAGEMENT

When Ebola exposure has been documented, any woman presenting with fever, together with acute clinical symptoms, signs of hemorrhage such as bleeding of the gums or nose, conjunctival injection, red spots on the body, bloody stools and/or melena, or vomiting blood must be evaluated for possible Ebola. Pregnant women infected with Ebola more often have serious complications, such as hemorrhagic and neurologic sequelae. Pregnant women may not develop hemorrhagic symptoms, particularly in the earlier disease stage or with milder disease. In addition, as in this case, fever may be absent, underscoring the importance of obtaining a comprehensive clinical history and maintaining heightened vigilance for all signs and symptoms of EBOV infection in pregnant women (Oduyebo et al., 2015). Caring for pregnant women at high risk for EBOV disease or those with a diagnosis of EBOV disease based on laboratory confirmation is complex. The Society for Maternal-Fetal Medicine (SMFM) developed an EBOV disease pregnancy web page that links to several general guidance documents for clinicians (www.smfm.org/links/ebola; Riley & Ecker, 2015). Early, aggressive supportive care is the mainstay of management, and massive fluid resuscitation is the key management principle. Patients often may require 5 to 10 L or more per day of intravenous or oral fluid to maintain circulating blood volume. Fluid shifts warrant aggressive monitoring and correction of potassium levels and acid–base disturbances to prevent life-threatening arrhythmias and metabolic complications (Bebell & Riley, 2015; Jamieson et al. 2014).

The risk of death from Ebola is similar among all trimesters of pregnancy, 50% to 90% (Jamieson et al., 2006). Death usually occurs during the second week of symptoms from massive blood loss. The possibility of Ebola must be considered in the differential as a possible primary cause of bleeding (WHO, 2008).

Diagnosis is based on the enzyme-linked immunoassay (ELISA), or specific IgG and IgM antibodies or Ebola-specific antigen detection. These tests are not commercially available and must be sent to specially equipped regional laboratories or WHO collaborating centers. There is no recommended treatment or prophylaxis, and management is supportive therapies with antibiotics used for secondary infections (WHO, 2008).

PLAGUE

Human plague in the United States occurs in scattered cases in rural areas (an average of 10–15 persons each year). Most human cases in the United States occur in two regions: (a) northern New Mexico, northern Arizona, and southern Colorado; and (b) California, southern Oregon, and far western Nevada (CDC, 2015b). During pregnancy, infection with *Yersinia pestis*, the bacteria causing plague, can result in spontaneous abortion. More favorable outcomes have been reported due to the increased availability of treatment.

PRESENTING SYMPTOMATOLOGY AND DATA COLLECTION

Plague bacillus enters the skin from the site of a flea bite and travels through the lymphatic system to the nearest lymph node, resulting in the most prominent sign of human plague, a swollen and very painful lymph gland. Left untreated, plague bacteria invade the bloodstream. As the bacteria multiply,

they spread rapidly throughout the body, causing a severe and often fatal condition. Infection of the lungs causes the pneumonic form of plague. Pneumonic plague develops from inhaling infectious droplets or from untreated bubonic or septicemic plague after bacteria spreads to the lungs. Pneumonic plague, the most serious form of the disease, is spread from person to person by infectious droplets. Untreated, the disease can progress rapidly to death. About 16% of all antibiotic-treated plague cases in the United States are fatal (CDC, 2015a, 2015b).

Presenting symptoms include the sudden appearance of fever, cough, shortness of breath, hemoptysis, tachypnea, and chest pain. These may be accompanied by nausea, vomiting, abdominal pain, and diarrhea. As the disease continues, the woman will progress to sepsis, shock, organ failure, purpuric skin lesions, and necrotic digits (WHO, 2008).

Diagnostic laboratory studies include sputum, blood, or lymph node aspirate with gram-negative bacilli with bipolar staining on Wright, Giemsa, or Wayson stain. X-rays may reveal pulmonary infiltrates or consolidation. Rapid diagnostic tests are available at select health departments, the CDC, and military laboratories (CDC, 2015b; WHO, 2008).

CLINICAL MANAGEMENT

Treatment recommendations are included in Exhibit 22.3. Duration of treatment is typically 10 to 14 days, or until 2 days after fever subsides. Oral therapy may be substituted once the patient improves (CDC, 2015b, 2015c; WHO, 2008).

EXHIBIT 22.3

Plague: Treatment for Pregnant or Breastfeeding Women[a]

- Doxycycline, 100 mg twice daily or 200 mg once daily IV or PO[b]
- Ciprofloxacin, 500–750 mg orally twice daily or 400 mg every 8–12 hours IV[b]
- Gentamicin 5 mg/kg once daily, or 2 mg/kg loading dose, then 1.7 mg/kg every 8 hours[a]

Postexposure Prophylaxis

- Doxycycline, 100 mg bid PO OR
- Ciprofloxacin, 500 mg bid PO

BID, twice daily; IV, intravenous; PO, per os (orally).

[a]Gentamicin is the recommended treatment for breastfeeding women. Due to poor abscess penetration, consider alternative or dual therapy for patients with bubonic disease.
[b]Doxycycline and ciprofloxacin are pregnancy categories D and C, respectively. All recommended antibiotics for plague have relative contraindications for use in pregnant women; however, use is justified in life-threatening situations.

Sources: Adapted from CDC (2015b, 2015c) and WHO (2008).

When compared to other biologic agents, there is little research available about a pregnancy complicated by an anthrax infection. Anthrax affects the lungs, skin, gastrointestinal system, or oropharynx. Diagnosis is classed as suspected, probable, or confirmed. A woman presenting with an illness suggestive of known anthrax clinical forms without definitive, presumptive, or suggestive laboratory evidence of *Bacillus anthracis*, or epidemiologic evidence related to anthrax, would be grouped as *suspected* anthrax (CDC, 2010).

PRESENTING SYMPTOMATOLOGY AND DATA COLLECTION

A woman would be classified as *probable* anthrax when the presentation consists of a clinically compatible illness that does not meet the confirmed case definition, but includes one of four clinical signs. The clinical signs are a documented anthrax environmental exposure; evidence of *B. anthracis* DNA in a clinical specimen collected from a normally sterile site (i.e., blood, cerebral spinal fluid); a lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal); or a positive result in serum specimens using Quick ELISA Anthrax-PA kit (CDC, 2010). A diagnosis is *confirmed* with any one of the criteria summarized in Exhibit 22.4.

CLINICAL MANAGEMENT

Recommended treatment for any type of anthrax involves supportive care and antibiotics. Because of the severity of the disease, pregnant women must receive the same postexposure prophylaxis and treatment regimes as nonpregnant adults (Meaney-Delman et al., 2014). Tetracyclines or ciprofloxacin are not recommended during pregnancy, but they may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose related and may

EXHIBIT 22.4

Criteria for Confirmed Diagnosis of Anthrax

- Identification of *B. anthracis* by Laboratory Response Network (LRN)
- Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining using both *B. anthracis* cell wall and capsule monoclonal antibodies
- Evidence of a 4× rise in antibodies to protective antigen between acute and convalescent sera or a 4× change in antibodies to protective antigen in paired convalescent sera using Centers for Disease Control and Prevention (CDC) quantitative anti-protective antigen antibody (anti-PA) immunoglobulin G (IgG) enzyme-linked immunosorbent assay (ELISA) testing
- Documented anthrax environmental exposure and evidence of *B. anthracis* DNA in clinical specimens collected from a normally sterile site or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal)

Source: Adapted from CDC (2010).

be used for a short time (7–14 days) before 6 months gestation (WHO, 2008). Additional symptomology and treatment recommendations are included in Table 22.1.

Pregnant and postpartum women are at greater risk for fluid shifts than are nonpregnant adults because of lower intravascular oncotic pressure. The normal pregnancy changes, increased blood volume and heart rate, and decreased systemic vascular resistance can exacerbate anthrax-related volume shifts and result in more profound hypotension than in nonpregnant adults.

TABLE 22.1 Diagnostic Symptoms and Treatment Recommendations: Anthrax (*Bacillus anthracis*)

TYPE	DESCRIPTION	TREATMENT
Cutaneous:[a] Most common[b]	• Painless skin lesion developing over 2 to 6 days from papular to vesicular stage to depressed black eschar with surrounding edema • Fever, malaise, lymphadenopathy	• Ciprofloxacin 500 mg bid or doxycycline 100 mg bid × 60 days
Inhalation:[a] Rare[b]	• Viral respiratory prodrome • Hypoxia, dyspnea, or acute RDS with cyanosis/shock • Mediastinal widening or pleural effusion (x-ray)	• Ciprofloxacin 400 mg every 12 hours or doxycycline or doxycycline 100 mg every 12 hours and 1 to 2 additional antimicrobials, that is rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin • Supportive care including controlling pleural effusions
GI:[a] Rare[b]	• Severe abdominal pain and tenderness, nausea, vomiting, hematemesis • Bloody diarrhea, anorexia, fever, abdominal swelling, septicemia	• Same as inhalation anthrax • IV initially. Switch to oral when clinically appropriate
Oropharyngeal: Least common[b]	• Painless mucosal lesion in mouth or oropharynx • Cervical adenopathy, edema, pharyngitis, fever, septicemia	• Same as inhalation anthrax • IV initially. Switch to oral when clinically appropriate

[a]Do **NOT** use extended-spectrum cephalosporins or trimethoprim/sulfamethoxazole because anthrax may be resistant to these drugs.

[b]Breastfeeding women should be offered prophylaxis with the same medications. All of these medications are excreted in breast milk. The babies should be treated with an antibiotic that is safe for the prophylactic treatment of the infant.

bid, twice/day; IV, intravenous; RDS, respiratory distress syndrome.

Source: Adapted from CSTE Position Statement Number: 09-ID-10; CDC (2010).

These cardiovascular changes can decrease placental blood flow and cause fetal compromise. Preterm labor, nonreassuring fetal status, and fetal loss can be seen with anthrax and are seen as clinical indicators of maternal infection or worsening maternal status. A nonreassuring fetal heart rate status may be a very early indicator of cardiovascular compromise; inadequate uteroplacental blood flow may be seen in the fetal heart rate pattern before overt maternal cardiovascular changes are exhibited. Because of these complications, obstetric monitoring is critical in the clinical management of infected pregnant patients with anthrax, as dictated by gestational age. Early, aggressive drainage of pleural effusions and ascites by chest-tube drainage, thoracentesis, and paracentesis is recommended as an adjunct to combination antimicrobial drug treatment. Mother–infant separation is not required for women who deliver while receiving prophylaxis or treatment for anthrax. There is no evidence of anthrax transmission through breast milk, so exposure is not a contraindication to breastfeeding or using expressed human milk. If there are active cutaneous anthrax lesions on the breast, infant contact should be avoided with the affected breast until after 48 hours of appropriate antimicrobial drug therapy (Meaney-Delman et al., 2014).

Whether to vaccinate to protect pregnant women has generated much discussion. There is limited data to guide the use of BioThrax Anthrax Vaccine Adsorbed (AVA; Emergent BioSolutions, Rockville, Maryland) in pregnant, postpartum and lactating (P/PP/L) women. The amount of maternal–fetal transfer of anthrax antibodies to the fetus is not known, but experience with other vaccines suggests that vaccination of pregnant women may provide some protection to newborn infants. The Advisory Committee on Immunization Practices reviewed all safety data available as of March 2008 and concluded that AVA is safe to administer to anthrax-exposed women during pregnancy. In a pre–anthrax event during which there is low risk for anthrax exposure, vaccination of pregnant women is not recommended. If the risk for exposure to aerosolized *B. anthracis* spores is high, pregnancy is neither a precaution nor a contraindication to vaccination. Pregnant women at risk for inhalation anthrax should receive AVA and antimicrobial drug therapy regardless of pregnancy trimester (Meaney-Delman et al., 2014; Wright, Quinn, Shadomy, & Messonnier, 2010).

BIOTERRORISM

CLINICAL MANAGEMENT AND FOLLOW-UP DURING OR FOLLOWING A BIOTERRORISM EVENT

The Federal Emergency Management Agency (FEMA) suggests minimizing negative effects from any biologic agent by quickly moving away from unusual or suspicious substances in the environment, contacting the authorities and listening to the media for official instructions, washing with soap and water, and ensuring that others do the same. In addition, following a known exposure to a biologic agent, individuals must remove and bag clothing and personal items, follow official instructions for disposal of contaminated items, wash with soap and water and put on clean clothes, seek medical assistance, and follow directions to stay away from others or remain in quarantine (FEMA, 2007).

High-efficiency particulate air (HEPA) filters are useful in biologic attacks. If there is a central heating and cooling system with a HEPA filter, leaving it running or turning on the fan will cause movement of the air in the house through the filter and will help to remove the agents from the air. If there is a portable HEPA filter, the recommendation is to turn it on and place it in an

interior room. Apartments or office buildings with a modern central heating and cooling system often have a filtration system capable of providing a relatively safe level of protection from outside biologic contaminants (FEMA, 2013).

It is essential that health care providers are knowledgeable about the diagnosis and treatment of possible biohazard threats during pregnancy. They must remain vigilant, take safety precautions and actions, and avail themselves of resources to protect women and themselves.

CLINICAL PEARLS

- It is essential to plan for the needs of pregnant, postpartum, and lactating women during a biohazard event because of their unique immunology and physiology and the complexities of balancing maternal and fetal risks.
- The normal pregnancy changes, increased blood volume and heart rate, and decreased systemic vascular resistance can exacerbate anthrax-related volume shifts and result in more profound hypotension than in nonpregnant adults.
- A nonreassuring fetal heart rate status may be a very early indicator of cardiovascular compromise; inadequate uteroplacental blood flow may be seen in the fetal heart rate pattern before overt maternal cardiovascular changes are exhibited.

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Sepsis in Pregnancy

23

Catherine M. Albright

Maternal sepsis, especially puerperal sepsis, is a common pregnancy-related condition; in the United States, it is a leading cause of maternal mortality, accounting for up to 28% of maternal deaths and up to 15% of maternal admissions to the intensive care unit (ICU; Bauer, Lorenz, Bauer, Rao, & Anderson, 2015; Chang et al., 2003; Oud, 2015a, 2015b; Pollock, Rose, & Dennis, 2010). More concerning is that sepsis has been increasingly reported as the cause of maternal death, rising by up to 10% per year between 2000 and 2010 (Bauer, Bateman, Bauer, Shanks, & Mhyre, 2013; Oud, 2015a). This is due, in part, to a greater than 200% increase in the incidence of pregnancy-associated severe sepsis over that same period (Oud & Watkins, 2015). One contributing and modifiable factor to these deaths is failure to recognize sepsis, leading to delays in treatment (Bauer et al., 2015; Cantwell et al., 2011). Therefore, rapid and accurate diagnosis and initial management of sepsis in pregnancy in the emergency department (ED) is paramount.

PRESENTING SYMPTOMATOLOGY

Women may present to the obstetric triage unit or ED at any stage of illness. In a review of maternal deaths due to sepsis, almost a third of the women died at home without seeking medical care, demonstrating that many women do not present to the hospital and implying that many others may present late in the course of the disease (Bauer et al., 2015). Additionally, because there are many possible underlying infectious causes of sepsis, each clinical presentation will be different. However, given that the underlying inflammatory and immune processes are similar in many infections, vital signs and laboratory derangements are often present regardless of the specific underlying process. In the study mentioned previously that reviewed maternal deaths due to sepsis, among patients who presented to the hospital with sepsis, 9 out of 12 demonstrated one or more of the following vital sign abnormalities: heart rate greater than 120 beats per minute, respiratory rate higher than 30 breaths per minute, systolic blood pressure below 90 mmHg, peripheral oxygen saturation of less than 95% on room air, or temperature greater than 38°C or lower than 36°C (Bauer et al., 2015).

In pregnancy, the most common causes of sepsis include endometritis and chorioamnionitis, urinary tract infections, and pneumonia; up to 60% of maternal sepsis may be classified as obstetric, meaning it originates from the

genital tract (Kramer et al., 2009; Paruk, 2008). In contrast to sepsis that occurs outside of pregnancy, in which gram-positive bacteria account for approximately 50% of cases, and polymicrobial infections account for only 5%, infections that result in sepsis in pregnancy tend to be polymicrobial, reflecting the anatomic continuity with the vaginal flora (Martin, Mannino, Eaton, & Moss, 2003). However, there has been an increase in severe beta-hemolytic streptococci group A (GAS) infections in pregnancy, leading to increased morbidity and mortality (Kramer et al., 2009; Schuitemaker et al., 1998). Despite its rarity, and because management of sepsis caused by GAS must be aggressive and requires a specific management algorithm, identification or exclusion of this organism is a priority (Rimawi, Soper, & Eschenbach, 2012).

HISTORY AND DATA COLLECTION

A standard history needs to be taken for any woman presenting with signs or symptoms of an infection, with a focus on attempting to elucidate the source of infection. This must include the (a) timing of onset and severity of symptoms and (b) medications taken before presentation to the hospital. Exposures before the onset of symptoms may be contributory, including exposures to sick adults or children, exposures to mosquitos or insects, and food-borne illnesses. A recent travel history may also be instructive. In addition, a thorough medical and surgical history is critical in order to evaluate for risk factors, including prior infections, current treatment for infection, and immunosuppression (e.g., medication, malignancy).

Additional modifiable and nonmodifiable risk factors for sepsis and septic shock include non-White race, public insurance or no insurance, delivery at a low-volume hospital (<1,000 births per year), medical comorbidities such as diabetes and hypertension, and pregnancy-related complications such as preeclampsia and postpartum hemorrhage (Acosta et al., 2013; Mohamed-Ahmed, Nair, Acosta, Kurinczuk, & Knight, 2015). Although many of these conditions cannot be changed, increased vigilance in the setting of these risk factors is warranted.

PHYSICAL EXAMINATION

The initial component of the physical examination is a complete set of vital signs because these are the main diagnostic criteria for sepsis. A comprehensive physical examination can then be performed expeditiously in the pregnant woman with suspected sepsis, focusing on the most common causes of sepsis in pregnancy. A thorough heart and lung examination assesses for cardiopulmonary infections such as pneumonia. An abdominal and back examination assesses for intra-abdominal infections such as cholecystitis, appendicitis, and pyelonephritis. A pelvic examination evaluates for chorioamnionitis or endometritis. Finally, a thorough skin inspection looks for insect or animal bites, cellulitis, and wound infection.

LABORATORY AND IMAGING STUDIES

Initial laboratory studies include a complete blood count with differential, a comprehensive metabolic panel including a blood lactate level, two sets of blood cultures, and a urinalysis and urine culture. Additional cultures of amniotic fluid, wound, or abscess can be collected if the clinical situation warrants. Imaging

studies should focus on the likely source of infection and may include a chest x-ray to evaluate for pneumonia, a computed tomography (CT) scan to evaluate for appendicitis, or an ultrasound to evaluate for cholecystitis. In general, a renal ultrasound is not necessary in the initial management of pyelonephritis but may be considered in cases where the symptoms are refractory to standard medical management.

DIAGNOSIS OF SEPSIS

In 1992, the American College of Chest Physicians and the Society of Critical Care Medicine introduced definitions for the systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, and septic shock, and in 2001, an international group of critical care specialists met to solidify these definitions (Bone et al., 2009; Levy et al., 2003). The goal of the SIRS criteria was to describe a clinical response to a nonspecific insult of either infectious or noninfectious origin (Muckart & Bhagwanjee, 1997).

In 2016, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) were released (Singer et al., 2016). The objective of this consensus was to evaluate and update the definitions for sepsis and septic shock. The consensus notes that the original conceptualization of sepsis as an infection with at least two of the four SIRS criteria focused solely on inflammatory excess. A new definition of sepsis was proposed as life-threatening organ dysfunction caused by a dysregulated host response to infection and proposed the use of the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score to quantify organ dysfunction. The SOFA score is composed of scores from six organ systems (central nervous, cardiovascular, respiratory, gastrointestinal, genitourinary, and coagulation), graded from 0 to 4 according to the degree of dysfunction/failure (Vincent et al., 1996). Organ dysfunction from sepsis, therefore, can be identified as an acute change in the total SOFA score of greater than or equal to 2 points consequent to the infection, with a baseline SOFA score that can be assumed to be zero.

Any nonspecific SIRS criteria will continue to aid in the general diagnosis of infection. However, SIRS can simply reflect an appropriate and adaptive host response, whereas sepsis indicates organ dysfunction plus the accompanying inflammatory response. The definition of septic shock remained overall unchanged and was defined as a subset of sepsis in which underlying circulatory and cellular metabolic abnormalities are profound enough to substantially increase mortality. The term *severe sepsis* was thought to be redundant and was removed from the nomenclature because sepsis itself warrants greater levels of monitoring and intervention. Table 23.1 lists the definitions for SIRS, sepsis, severe sepsis, and septic shock as defined in 2001 and 2016.

The diagnosis of sepsis in pregnancy can be difficult because there is considerable overlap between the SIRS criteria and the SOFA score and normal physiologic changes during pregnancy (Abbassi-Ghanavati, Greer, & Cunningham, 2009; Bauer et al., 2014; Clark et al., 1989; Colditz & Josey, 1970; Cunningham et al., 2013; Guinn, Abel, & Tomlinson, 2007). See Table 23.2 for how the pregnant state differs from the nonpregnant state.

DIFFERENTIAL DIAGNOSIS

Although patients with fever, leukocytosis, and hypotension are often considered septic unless another diagnosis is evident, it is necessary to consider a differential diagnosis. Several noninfectious conditions may mimic sepsis and are sometimes

TABLE 23.1 Definition of Sepsis

DIAGNOSIS	2001 DEFINITION	2016 DEFINITION
Bacteremia	Presence of viable bacteria in the blood	Unchanged
SIRS	Systemic inflammatory response defined by two or more of the following: • Temperature >38°C or <36°C • Heart rate >90 bpm • Respiratory rate >20/min or $PaCO_2$ <32 mmHg • White blood cell count >12 or <4/mcL or >10% bandemia	Unchanged • Not used for the diagnosis of sepsis • Will continue to aid in the general diagnosis of infection
Sepsis	SIRS + source of infection	Life-threatening organ dysfunction caused by dysregulated host response to infection • SOFA score ≥2
Severe sepsis	Sepsis + evidence of organ dysfunction, tissue hypoperfusion, or hypotension	No longer in use
Septic shock	Sepsis + hypotension despite adequate fluid resuscitation	Sepsis + persistent hypotension requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate >2 mmol/L despite adequate volume resuscitation

bpm, beats per minute; MAP, mean arterial pressure; PaCO2, partial pressure of arterial carbon dioxide; SIRS, systemic inflammatory response syndrome; SOFA, Sequential [Sepsis-related] Organ Failure Assessment.

Sources: Definitions from Bone et al. (2009) and Singer et al. (2016).

referred to as *pseudosepsis*. These conditions are listed in Table 23.3 along with differentiating features from sepsis. Discriminating sepsis from pseudosepsis can be difficult, as clinically both can present with fever, leukocytosis, and hypotension, and central monitoring may demonstrate increased cardiac output and decreased peripheral resistance. When the diagnosis is unclear, do not delay sepsis therapy in order to rule out causes of pseudosepsis because timely management of sepsis is among the most critical factors preventing mortality.

CLINICAL MANAGEMENT AND FOLLOW-UP

Severity-of-Illness Scoring Systems

In order to enable early detection of cases of sepsis at risk for rapid clinical deterioration, many disease severity scoring systems related to sepsis have been developed and validated for the general population. Among them, the SOFA score consistently performs the best with regard to predictive value in critically ill obstetric patients. However, it has not been evaluated specifically in pregnant women presenting with sepsis (Jain, Guleria, Suneja, Vaid, & Ahuja, 2016; Kallur, Patil Bada, Reddy, Pandya, & Nirmalan, 2014; Oliveira-Neto, Parpinelli, Cecatti, Souza, & Sousa, 2012).

The Sepsis-3 consensus statement recommends use of the quick SOFA (qSOFA) score (range 0–3 points, with 1 point each for systolic hypotension [≤100 mmHg], tachypnea [≥22/min], or altered mentation) rather than

TABLE 23.2 Normal Values of Pregnancy

SYSTEM	CHANGE FROM NONPREGNANT STATE
General	
Temperature	Unchanged
Lactic acid	Unknown
Glasgow Coma Score*,†	Unchanged
Cardiovascular	
Blood pressure*,†	Systolic: Unchanged Diastolic: Decreased by 5–10 mmHg in second trimester, return to normal by third trimester
Heart rate	Increased by 15%–20% (83 ± 10 beats per minute)
Central venous pressure	Nonpregnant: 9.0 cmH_2O (7.8–11.2) First trimester: 7.5 cmH_2O (6.5–8.2) Second trimester: 4.0 cmH_2O (3.6–4.6) Third trimester: 3.8 cmH_2O (2.0–4.4)
Respiratory	
Respiratory rate*	Unchanged
O_2 saturation	Unchanged
PaO_2/FIO_2†	Unchanged
Gastrointestinal	
Bilirubin†	Decreased
Genitourinary	
Creatinine†	Decreased to 0.3–0.8 mg/dL
Urine output†	Increased (GFR increased 50%)
Coagulation/hematologic	
Leukocyte count	5.7–16.9/mcL by third trimester (up to 30/mcL in labor)
% Immature neutrophils	Unchanged
Platelets†	Decreased

PaO_2, arterial oxygen partial pressure; FIO_2, fractional inspired oxygen; GFR, glomerular filtration rate.
*Indicates value used for quick Sequential [Sepsis-Related] Organ Failure Assessment (qSOFA) score.
†Indicates value used for SOFA score.

Source: Reference values from Abbassi-Ghanavati et al. (2009), Bauer et al. (2014), Clark et al. (1989), Colditz and Josey (1970), Cunningham et al. (2013), and Guinn et al. (2007).

the standard SIRS criteria for rapid diagnosis (Seymour et al., 2016; Singer et al., 2016). The studies on which these recommendations were based did not include pregnant women, and the qSOFA score has yet to be studied specifically in the obstetric population. In addition, many pregnant women will have a systolic blood pressure ≤100 mmHg and a respiratory rate ≥22/min upon presentation, but very few will have altered mentation. The score is not likely to be useful in the rapid evaluation of pregnant women given that only two of the three components are likely to be used.

Clearly, because of the considerable overlap between the SIRS or qSOFA criteria and the normal physiologic parameters during pregnancy and the postpartum period, an efficient, accurate, and reliable predictor of sepsis-related morbidity and mortality is a goal not entirely realized. Therefore, identification

TABLE 23.3 Imitators of Sepsis in Pregnancy

MIMIC	DISTINGUISHING CLINICAL FEATURES	DISTINGUISHING LABORATORY INVESTIGATIONS
	Pump Failure	
Acute myocardial infarction	• Risk factors (may not be present in pregnant women) • Typical chest pain on exertion	• EKG • Serum troponin
Acute pulmonary embolus	• Risk factors • Personal or family history • Sudden dramatic onset with little prodrome • Hypoxia should be prominent	• CT angiogram
	Hypovolemia	
Acute pancreatitis	• Upper abdominal and/or back pain • Nausea and vomiting • History of alcohol, cholelithiasis, or hypertriglyceridemia	• Serum amylase • Lipase • Consider CT abdomen
Acute adrenal insufficiency	• History of steroid use in past year, especially if Cushingoid in appearance • Personal or family history of autoimmune disease • Hyperpigmentation, especially in any new scars	• Serum electrolytes (high potassium and low sodium) • ACTH stimulation test • Empiric stress dose steroid administration
Gastrointestinal hemorrhage	• Usually hematemesis or melena but not always present initially • History suspicious for PUD, gastritis, or varices	• CBC (although may not be reflective of acute status) • Rectal examination for blood • NG tube for gastric lavage
Acute intra-abdominal hemorrhage	• Usually sudden-onset abdominal pain with peritoneal signs	• Ultrasound or CT abdomen for free fluid • Lesions can include ruptured splenic aneurysm, abdominal aortic aneurysm
Overzealous diuresis or extensive third spacing	• Clinical context (diuretic administration or surgery associated with massive fluid shifts) • Review of fluid balance	• Trial of fluid replacement

(*continued*)

TABLE 23.3 Imitators of Sepsis in Pregnancy (*continued*)

MIMIC	DISTINGUISHING CLINICAL FEATURES	DISTINGUISHING LABORATORY INVESTIGATIONS
	Anaphylactoid	
Transfusion reactions	• Clinical context • Reactions can include antigen/antibody mismatch but also leukoagglutination in the lungs	• Laboratory investigations by blood bank
Adverse drug reactions	• Clinical context following a potentially precipitating exposure • 60% of time, the precipitant is not identified • Itching/burning/hives on skin present in ~90% of cases	• Treat with IM epinephrine 0.5–1.0 mg (0.5–1.0 mL of a 1:1,000 [1 mg/mL] solution), fluids, diphenhydramine, ranitidine, and steroids • Confirm diagnosis with serial measurements of levels of histamine and tryptase A
Amniotic fluid embolism	• Clinical context: typically intrapartum • Sudden onset • Associated with hypoxia, hypotension, and bleeding	• DIC screen (INR, aPTT, fibrin degradation products, fibrinogen) • Usually proceeds to full resuscitative efforts with intubation
Fat emboli syndrome	• Typically in the setting of trauma, fracture, TPN, or pancreatitis	• DIC screen • Usually proceeds to full resuscitative efforts with intubation • Steroids may be helpful

ACTH, adrenocorticotropic hormone; aPTT, activated partial thromboplastin time; CBC, complete blood count; CT, computed tomography; DIC, disseminated intravascular coagulation; EKG, electrocardiogram; IM, intramuscular; INR, international normalized ratio; NG, nasogastric; PUD, peptic ulcer disease; TED, thromboembolic disease; TPN, total parenteral nutrition.

Source: Used with permission from Dr. Raymond Powrie.

and prompt treatment of sepsis in pregnancy will remain imprecise until either alternative criteria or a pregnancy-specific sepsis scoring system is developed. One such scoring system has been proposed, the Sepsis in Obstetrics score, but has not yet been validated (Albright, Ali, Lopes, Rouse, & Anderson, 2014b). Until there are pregnancy-specific algorithms for the diagnosis of sepsis, it is recommended to use the current general population algorithm as described by the Sepsis-3 consensus statement. This algorithm initially utilizes the quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) score to triage patients with a suspected infection followed by the SOFA score to make a diagnosis of sepsis. Sepsis plus the need for vasopressors to maintain a mean arterial pressure greater or equal to 65 mmHg, or a serum lactate greater than 2 mmol/L, gives a diagnosis of septic shock (Singer et al., 2016).

Early Goal-Directed Therapy

Early goal-directed therapy (EGDT) includes early initiation and continuation of hemodynamic resuscitation with specified treatment endpoints and was first shown to have a mortality benefit when initiated in the ED in the sentinel

study by Rivers et al. in 2001 (2001). Specifically, EGDT is aimed at correcting the physiologic abnormalities that accompany sepsis, including hypotension and hypoxemia, in order to improve tissue oxygen delivery. This includes early initiation of antimicrobial therapy as well as aggressive hemodynamic resuscitation. Study participants allocated to EGDT were significantly less likely to die in the hospital, and 28 and 60 days after enrollment. Early studies following EGDT implementation showed an almost 20% decrease in overall mortality for septic patients (Gu, Wang, Bakker, Tang, & Liu, 2014; Levy et al., 2015; Rivers et al., 2012). Three more recent randomized controlled trials evaluating EGDT versus usual care did not show a mortality benefit with EGDT (Australasian Resuscitation in Sepsis Evaluation [ARISE] Investigators and Australian and New Zealand Intensive Care Society [ANZICS] Clinical Trials Group, 2014; Mouncey et al., 2015; ProCESS Investigators et al., 2014). This is likely due to the fact that usual care now includes aggressive, early fluid resuscitation and rapid administration of appropriate antibiotics, which reflects the impact of the original trial by Rivers and colleagues (Levy, 2014). In addition, mortality rates in both groups were impressively low in all three studies (18.8%–29.2%), indicating effective treatment (ARISE Investigators and ANZICS Clinical Trials Group, 2014; Mouncey et al., 2015; ProCESS Investigators et al., 2014). Therefore, the continued use of EGDT in management of sepsis is recommended (Levy, 2014; Levy et al., 2015; Nguyen et al., 2016; Rusconi et al., 2015).

The recommendations for initial resuscitation following diagnosis of sepsis have been integrated into bundles. A bundle is a selected set of elements that, when implemented as a group, have an effect on outcomes beyond implementing the individual elements alone. The bundles are the core of the sepsis improvement efforts and aim to simplify and streamline the care of patients with sepsis. The current bundles are designed to be completed within a set period following an individual's presentation with sepsis or septic shock (Dellinger et al., 2013; Levy et al., 2015). Within 3 hours, measure lactic acid level, obtain blood cultures before administration of antibiotics, administer broad-spectrum antibiotics, and administer 30 mL/kg of crystalloid for hypotension or for a serum lactic acid level of ≥4 mmol/L. Within 6 hours, give vasopressors for hypotension that does not respond to initial fluid resuscitation to maintain a MAP ≥65 mmHg (e.g., norepinephrine). In the event of persistent hypotension after initial fluid administration (MAP <65 mmHg) or if the initial serum lactic acid level was greater than 4 mmol/L, reassess volume status and tissue perfusion and remeasure the serum lactic acid level.

Antimicrobial Therapy

Along with aggressive resuscitation, early initiation of appropriate antimicrobial therapy is a critical determinant of survival in sepsis and septic shock. Among nonpregnant adults with sepsis, time to initiation of antibiotic therapy is likely the strongest predictor of mortality (Barie, Hydo, Shou, Larone, & Eachempati, 2005; Ferrer et al., 2009; Kumar et al., 2006; Proulx, Fréchette, Toye, Chan, & Kravcik, 2005; Rivers et al., 2001; Vazquez-Guillamet et al., 2014). One early study demonstrated that initiation of antibiotics within 1 hour following the onset of hypotension was associated with a 79.9% survival to hospital discharge. In the first 6 hours, survival declined by 7.6% for every hour delayed (Kumar et al., 2006).

Initial administration of inappropriate antibiotic therapy increases morbidity and mortality up to fivefold (Barie et al., 2005; Ibrahim, Sherman, Ward, Fraser, & Kollef, 2000; Kumar et al., 2009). Therefore, because the infecting organism is likely not known at the time of antibiotic initiation, empiric regimens need to

be broad spectrum and be based on clinical presentation and epidemiologic factors, including local flora, resistance patterns, and previous antibiotic exposure. Accordingly, the choice of antibiotics may differ for a pregnant or postpartum woman, depending on the suspected source of sepsis.

In severe infections, survival may be improved if the organism(s) can be isolated. It is therefore necessary to obtain site-specific cultures to allow for identification and susceptibility testing. Empiric antibiotic therapy can then be adjusted to a narrower regimen within 48 to 72 hours if a plausible pathogen is identified or if the woman stabilizes. If the source of infection is known or suspected, targeted antibiotic coverage is appropriate initially. Common causes of sepsis in pregnant and postpartum women with suggested site-specific antibiotic coverage are listed in Table 23.4 (Dellinger et al., 2013; Liu et al., 2011; Mandell et al., 2007; Solomkin et al., 2010; Stevens et al., 2014).

TABLE 23.4 Common Causes of Sepsis and Suggested Antibiotic Coverage

CAUSE	CAUSATIVE ORGANISM	SUGGESTED ANTIBIOTIC COVERAGE
Endometritis	Polymicrobial: mixture of two to three genital tract aerobes and anaerobes	Broad-spectrum parenteral antibiotics that include coverage for beta-lactamase-producing anaerobes • Clindamycin 900 mg IV q8hr + gentamicin 5 mg/kg q24hr OR 1.5 mg/kg IV q8hr
Intra-amniotic infection	Polymicrobial, primarily due to ascending colonization or infection	Broad-spectrum parenteral antibiotics with coverage for beta-lactamase-producing aerobes and anaerobes • Ampicillin 2 g q6hr + gentamicin 1.5 mg/kg q8hr for patients with normal renal function • Add clindamycin 900 mg or metronidazole 500 mg to the primary antibiotic regimen if the patient is undergoing a cesarean delivery • Penicillin allergy: substitute vancomycin 1 g q12hr for ampicillin
Urinary tract infections	*E. coli*, *Klebsiella* or *Enterobacter*, *Proteus*, and gram-positive organisms, including *Streptococcus agalactiae*	Parenteral beta-lactams • Avoid fluoroquinolones • Ceftriaxone 1–2 g q24hr OR ampicillin 1–2 g q6hr + gentamicin 1.5 mg/kg q8hr
Group A Streptococcus	*Streptococcus pyogenes*	Parenteral beta-lactam + clindamycin • Penicillin G 4 million units IV q4hr + clindamycin 900 mg IV q8hr • Consider IV immune globulin with worsening
Community-acquired pneumonia	Bacterial: *Streptococcus pneumonia*, *Klebsiella pneumonia*, *Haemophilus influenza*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* Viral: Influenza	Parenteral antipneumococcal beta-lactam + advanced macrolide ± antiviral • Avoid fluoroquinolones • Ceftriaxone 1–2 g daily, cefotaxime 1–2 g q8hr, OR ampicillin-sulbactam 1.5–3 g q6hr + azithromycin 500 mg daily • Antiviral: Oseltamivir 75 mg PO q12hr

(*continued*)

TABLE 23.4 Common Causes of Sepsis and Suggested Antibiotic Coverage *(continued)*

CAUSE	CAUSATIVE ORGANISM	SUGGESTED ANTIBIOTIC COVERAGE
Septic abortion	Polymicrobial	Parenteral broad-spectrum antibiotics • Clindamycin 900 mg q8hr + gentamicin 5 mg/kg daily ± ampicillin 2 g q4hr; OR ampicillin + gentamicin + metronidazole 500 mg q8hr; OR levofloxacin 500 mg daily and metronidazole; OR single agents such as ticarcillin-clavulanate 3.1 g q4hr piperacillin-tazobactam 4.5 g q6hr, or imipenem 500 mg q6hr
Necrotizing fasciitis	Polymicrobial	Surgical debridement + broad-spectrum antimicrobial therapy, including activity against gram-positive, gram-negative, and anaerobic organisms, with special consideration for Group A Streptococcus and *Clostridium* species
Necrotizing fasciitis	Polymicrobial	• Carbapenem or beta-lactam/beta-lactamase inhibitor + clindamycin 600–900 mg q8hr, for its antitoxin effects against toxin-elaborating strains of streptococci and staphylococci, as well as an agent with activity against methicillin-resistant *S. aureus* (MRSA, such as vancomycin, daptomycin, or linezolid) • Options for carbapenems: imipenem, meropenem, or ertapenem • Options for beta-lactam/beta-lactamase inhibitors: piperacillin/tazobactam, ampicillin/sulbactam, or ticarcillin/clavulanate • Patients with hypersensitivity to these agents may be treated either with an aminoglycoside or a fluoroquinolone, plus metronidazole
Toxic shock syndrome	*Staphylococcus aureus*	• Clindamycin 600 mg IV q8hr + vancomycin 30 mg/kg per day IV in two divided doses • Unclear whether antibiotics alter the course; however, they are needed to eradicate organisms and prevent recurrence

IV, intravenous; PO, per os (orally).

Source: Recommendations are expert opinion in accordance with the Infectious Disease Society of America Guidelines (Dellinger et al., 2013; Liu et al., 2011; Mandell et al., 2007; Solomkin, 2010; Stevens et al., 2014).

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Source Control

The term *source control* is used to define the spectrum of interventions whose objective is the physical control of infection. As previously discussed, successful management of sepsis not only requires early and appropriate antibiotic therapy and aggressive fluid resuscitation, but also requires source control. Antibiotic therapy is critical to initiate before any attempt at source control (Dellinger et al., 2013). However, drainage, debridement, and removal of foreign bodies must occur as soon as possible in sepsis care (Boyer et al., 2009; Marshall, Maier, Jimenez, & Dellinger, 2004) and therefore may be appropriate to perform in the ED following initiation of antibiotic therapy.

Although there are no randomized trials comparing techniques of abscess drainage, the optimal method is that which accomplishes full drainage with the least degree of anatomic and physical trauma. In the setting of retained products of conception, dilatation/curettage is indicated. The surgical tenet of source control is never more crucial than it is in the case of GAS puerperal sepsis. In this setting of a mortality rate of approximately 50%, hysterectomy can be lifesaving (Rimawi et al., 2012).

Management Beyond the ED

Once sepsis has been identified and the patient stabilized and admitted to the appropriate service, subsequent management will include decisions regarding blood product administration, glycemic control, venous thromboembolism prophylaxis, and stress ulcer prophylaxis. Because there are limited data regarding each of these components in the critically ill pregnant patient with sepsis, multidisciplinary collaboration with maternal–fetal medicine, infectious disease, and critical care is crucial.

Pregnancy-Specific Management of Sepsis

Maternal Management

The overall goal of EGDT, manipulation of cardiac preload, afterload, and contractility to achieve a balance between systemic oxygen delivery and oxygen demand, is a good general tenet of care, and, in pregnancy, is one that likely aids in the restoration of normal maternal and fetal physiologic functioning. Consequently, the general principles of sepsis teaching seem to hold in pregnant women. For example, one study demonstrated that elevated lactic acid in pregnancy was associated with adverse maternal outcomes from sepsis, highlighting the significance of that measurement (Albright, Ali, Lopes, Rouse, & Anderson, 2014a). In addition, although use of acetaminophen for fever in the critically ill with suspected infections has not shown a mortality or morbidity benefit, its use in pregnancy is crucial because maternal fever can result in fetal tachycardia and subsequent fetal compromise (Barton & Sibai, 2012; Young et al., 2015).

Extrapolating EGDT to pregnant women is not straightforward because of the complex physiologic changes that occur in pregnancy and lack of pregnancy-specific data. However, until pregnancy-specific protocols are developed, utilization of the previously noted sepsis bundles in order to optimize maternal health is appropriate and must be prioritized (Brown & Arafeh, 2015).

Fetal Management

In addition to the sepsis bundles for maternal health, any management algorithm for pregnant women also requires fetal assessment. Maternal sepsis is associated with an increased risk of preterm delivery, low birth weight, and perinatal mortality (Jin, Carriere, Marrie, Predy, & Johnson, 2003; Knowles, O'Sullivan, Meenan, Hanniffy, & Robson, 2015). In fact, fetal mortality approaches 33% in the setting of maternal sepsis requiring ICU admission (Timezguid et al., 2012).

When a pregnant woman presents with sepsis, once maternal stability is assured, if the pregnancy is beyond viability (traditionally beyond 24 weeks gestation, but in certain centers this is changing to 23 weeks gestation), a fetal monitor is applied (American College of Obstetricians and Gynecologists and the Society for Maternal–Fetal Medicine et al., 2015; Raju, Mercer, Burchfield, & Joseph, 2014). With maternal stabilization plus either a reactive nonstress test or biophysical profile of greater than or equal to 8 out of 10, fetal monitoring can be performed intermittently. Below the limit of viability, only a fetal heart rate needs to be documented.

In maternal sepsis, fetal heart rate tracings may demonstrate evidence of fetal acidemia with presence of late decelerations. Additional maneuvers may therefore need to be employed, including but not limited to-left uterine displacement in order to aid in fetal resuscitation. Caution is necessary when monitoring a viable fetus in a critically ill woman because maternal stability is always the primary goal. Attempts to deliver an acidemic fetus may worsen a mother's condition and result in prematurely delivering a fetus who may have recovered with adequate resuscitation in utero. In the setting of maternal sepsis, fetal optimization is frequently best accomplished by meeting maternal hemodynamic, oxygenation, and infection treatment goals (Chau & Tsen, 2014). As maternal acidemia and/or hypoxia resolves, fetal status will improve.

Delivery Management

A recent study evaluated indications for delivery in women presenting with sepsis and septic shock (Snyder, Barton, Habli, & Sibai, 2013). It found that one third of women with sepsis and all women presenting with septic shock required delivery during the same hospitalization, most requiring emergent delivery. The most common indication for delivery was worsening respiratory status.

Delivery in the setting of respiratory failure will almost necessarily be via cesarean. In the setting of sepsis that develops during labor, aggressive maternal treatment followed by attempted vaginal delivery will likely benefit both mother and fetus. Finally, delivery within 5 minutes following a maternal cardiac arrest is vital for both maternal and fetal benefits (Rose et al., 2015).

CONCLUSION

Maternal morbidity and mortality appear to be on the rise in the United States. Although the diagnosis and management of sepsis has been well established in the general population, the ability to apply that same level of expertise to pregnant women is hindered by the lack of data surrounding sepsis in obstetrics. Pregnancy poses a unique challenge given the baseline physiologic changes and the need to care for the mother while simultaneously caring for the fetus. Therefore, without clear pregnancy-specific data, recommendations are to follow the current guidelines for nonpregnant adults, yet be cognizant of the ways in

which pregnancy may change maternal physiology and affect fetal well-being. Prompt identification and treatment of maternal sepsis will undoubtedly lead to the best possible maternal and neonatal outcomes.

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CLINICAL PEARLS

- Rapid identification of sepsis followed by early initiation of fluid resuscitation with 30 mL/kg of crystalloid and broad-spectrum antimicrobial therapy within 1 hour of diagnosis will result in the best maternal and fetal outcomes.
- Time to initiation of antibiotic therapy is the strongest predictor of mortality in sepsis.
- Until pregnancy-specific sepsis identification and treatment algorithms are studied, use of the current sepsis diagnostic criteria and treatment bundles for use in the general population is recommended.

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Infections in Pregnant Women

24

Rosemary J. Froehlich and Brenna L. Hughes

Infectious diseases commonly manifest during pregnancy, ranging from benign to life-threatening conditions. Many of these women will present in the acute care setting. Occasionally, symptoms of pregnancy and disease may overlap, making it difficult to accurately diagnose gravid women. In addition, pregnancy is an immune-altering state, which in certain circumstances affects the management of pregnant women as compared with nonpregnant counterparts. It is crucial that in obstetric triage units and emergency room settings providers are able to diagnose and appropriately treat pregnant women.

INTRA-AMNIOTIC INFECTION

Clinical intra-amniotic infection (IAI) or chorioamnionitis complicates 1% to 4% of all births (Gibbs & Duff, 1991). The major risk factor for IAI in the obstetric triage setting will be rupture of the amniotic membranes. Although chorioamnionitis with intact membranes does occur, it is less common and may be due to *Listeria monocytogenes*, Group B Streptococcus (GBS), or recent obstetric procedures such as cerclage or amniocentesis (Creasy et al., 2014; Tita & Andrews, 2010). Although IAI is more commonly seen during labor, these women may primarily present to the obstetric emergency room. Because of the potential for maternal and neonatal sepsis and death, in pregnant women with fever and other supporting symptomatology, IAI must be considered until proven otherwise.

PRESENTING SYMPTOMATOLOGY

The presenting symptoms of chorioamnionitis may overlap with other diagnoses seen more commonly in the emergency setting in nonpregnant women, such as pyelonephritis. Most women with chorioamnionitis will have ruptured membranes; therefore, leakage of fluid and contractions may be frequent complaints. To differentiate from normal labor, fever, constant abdominal pain, foul-smelling discharge, general malaise, and/or body aches are noted. In rare circumstances, IAI can be present in women with intact membranes. To make the diagnoses of IAI in a pregnant woman, a high index of suspicion is necessary when a patient presents with signs of infection and abdominal pain.

HISTORY AND DATA COLLECTION

A thorough history is recommended. A focus on pregnancy-related symptoms such as leakage of fluid and contractions, any recent procedures, or exposure to foodborne pathogens such as *L. monocytogenes* can be elicited. Listeriosis is 18 times more common in the pregnant population versus the nonpregnant population, and transmission is through ingestion of contaminated foods such as unpasteurized milk and soft cheeses, unwashed meat and vegetables, and processed foods such as deli meat and hot dogs (Lamont et al., 2011). Prevention of listeriosis can be achieved by thoroughly washing all raw fruits and vegetables, thoroughly cooking all meat and poultry, and avoidance of high-risk items such as unpasteurized dairy, deli meats or hot dogs (unless steaming hot), and smoked seafood (unless canned) (Centers for Disease Control and Prevention [CDC], 2014b).

PHYSICAL EXAMINATION

The diagnosis of IAI is usually made on the basis of clinical symptoms. Chorioamnionitis is diagnosed by the presence of fever (>100.4°F) and one or more of the following: uterine tenderness, maternal or fetal tachycardia, maternal leukocytosis, and foul-smelling/purulent discharge (Gibbs, Dinsmoor, Newton, & Ramamurthy, 1988; Tita & Andrews, 2010).

LABORATORY AND IMAGING STUDIES

Amniotic fluid testing, using rapid markers (Gram stain, cell count, glucose, and leukocyte esterase), may be used when considering delivery of a preterm or nonviable fetus when the diagnosis of chorioamnionitis is unclear. A positive Gram stain, low glucose (<15 mg/dL), or elevated white blood cell (WBC) count (>30/mm^3) may be indicative of infection (Romero et al., 1993). Amniotic fluid culture would be of low yield because of the time it takes for obtaining results.

DIFFERENTIAL DIAGNOSIS

Chorioamnionitis may present with a wide range of symptoms. It varies from vague symptoms, such as abdominal pain or malaise, to acute pain with signs of peritoneal irritation. The differential diagnoses include pyelonephritis, gastroenteritis, appendicitis, and preterm labor.

CLINICAL MANAGEMENT AND FOLLOW-UP

The mainstay of treatment in the setting of chorioamnionitis is immediate antibiotic therapy and delivery. Chorioamnionitis alone is not an indication for cesarean delivery. Antepartum treatment with antibiotics decreases the risk of neonatal sepsis and mortality, and so it must be initiated without delay (Gibbs et al., 1988). IAI is usually polymicrobial in nature, and a broad-spectrum antibiotic is recommended; however, the optimal regimen is not well established. A Cochrane Review published in 2014 failed to identify the most appropriate antibiotic regimen for patients with IAI (Chapman, Reveiz, Illanes, & Bonfill Cosp, 2014). A commonly used regimen is ampicillin every 6 hours and

TABLE 24.1 Features of Isolated Maternal Fever, Suspected and Confirmed Triple I

Isolated maternal fever ("documented" fever)	Maternal oral temperature 39.0°C (102.2°F) on any one occasion is documented fever. If the oral temperature is between 38.0°C (100.4°F) and 39.0°C (102.2°F), repeat the measurement in 30 minutes; if the repeat value remains at least 38.0°C (100.4°F), it is documented fever.
Suspected Triple I	Fever without a clear source plus any of the following: • Baseline fetal tachycardia (greater than 160 beats per min for 10 min or longer, excluding accelerations, decelerations, and periods of marked variability) • Maternal white blood cell count greater than 15,000 per mm^3 in the absence of corticosteroids • Definite purulent fluid from the cervical os
Confirmed Triple I	All of the previous items plus: • Amniocentesis-proven infection through a positive Gram stain • Low glucose or positive amniotic fluid culture • Placental pathology revealing diagnostic features of infection

Source: Adapted from Higgins et al. (2016).

gentamicin every 8 hours until delivery. Other regimens, such as those using extended-spectrum penicillin (e.g., ampicillin plus a beta-lactamase-inhibitor, such as sulbactam), may be equally as effective, but have not been compared with standard agents (Creasy et al., 2014). The optimal length of antibiotic treatment postpartum is unknown and varies from one dose of antibiotics after delivery to treatment for 24 to 48 postpartum hours (Chapman et al., 2014; French & Smaill, 2004; Hopkins & Smaill, 2002). If a cesarean delivery is performed, clindamycin 900 mg every 8 hours (or metronidazole) may be added for additional anaerobic coverage (Tita & Andrews, 2010). Acetaminophen for fever may also be administered, not to exceed the maximum dose of 4 g/d.

Historically, the threshold for labeling a patient as having chorioamnionitis has been fairly low, for example, in the presence of maternal fever alone. This may not necessarily take into account the resultant neonatal interventions, which in many institutions involve routine neonatal intensive care unit observation and/or the administration of antibiotics. Thus, recently, a change in terminology has been recommended in order to better characterize cases as "isolated maternal fever" or "intrauterine infection, inflammation, or both (Triple I)." The features of isolated maternal fever versus suspected or confirmed Triple I are presented in Table 24.1 (Higgins et al., 2016).

INFLUENZA

During seasonal influenza outbreaks and influenza pandemics, most recently the H1N1 pandemic of 2009 and 2010, pregnant women are at a greater risk of hospitalization and death from complications of influenza (Siston et al., 2010). The influenza virus is an RNA virus, with three main types: A (most common), B, and C. It is easily transmitted through respiratory droplets, with an incubation period of 2 to 4 days (Cox & Subbarao, 1999). Once a woman is infected, she will remain infectious from about 1 day before the start of symptoms until approximately 1 week after becoming ill (CDC, 2016c).

PRESENTING SYMPTOMATOLOGY

Pregnant women presenting with influenza may have a fever (>100.4°F), cough, dyspnea, sore throat, runny nose, body aches, headache, fatigue, vomiting, or diarrhea. All or some of the symptoms may be present, and not all women will have a fever.

HISTORY AND DATA COLLECTION

A complete history includes the length, type, and severity of symptoms. A vaccination history, infectious contacts, and history of comorbidities including asthma, diabetes, and hypertension are also critical to assist in diagnosis. Pregnant women with asthma or chronic hypertension are more likely to require admission to an intensive care unit (ICU) with influenza complications, and so these women must be clearly identified (Siston et al., 2010; Varner et al., 2011).

PHYSICAL EXAMINATION

A complete physical examination must be performed with attention to the presenting symptoms. Findings may include throat erythema, runny nose, wheezing, rales/rhonchi, tachypnea, and tachycardia. Fetal tachycardia may also be present with maternal fever.

LABORATORY AND IMAGING STUDIES

A rapid influenza test (types A and B) has been recommended in pregnant women if influenza is suspected. However, because of low sensitivity of the rapid tests, confirmation of negative tests may be performed with viral culture or reverse transcription polymerase chain reaction (RT-PCR; Harper et al., 2009). In the absence of a positive test, treatment is indicated if clinical suspicion is high. If there is uncertainty in the diagnosis, a complete blood count with a differential may help to determine if a bacterial infection is present versus influenza. A shielded chest radiograph is indicated if there are respiratory symptoms, such as dyspnea and findings consistent with pneumonia.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses include a variety of other respiratory illnesses. Pneumonia, pharyngitis, the common cold, sinusitis, or bronchitis must all be considered.

CLINICAL MANAGEMENT AND FOLLOW-UP

Pregnant women suspected of having influenza in the obstetric triage setting need to be offered treatment with antivirals and acetaminophen if febrile or in the presence of myalgias (Fiore et al., 2011). Rest and hydration (either oral or intravenous) are also suggested. Oseltamivir (Tamiflu) is recommended by the CDC for use in pregnant women at a dose of 75 mg twice daily for 5 days. To

improve maternal outcomes, treatment initiated within 48 hours of symptom onset is ideal. Early initiation of oseltamivir for pregnant women admitted to the hospital with laboratory-confirmed influenza is associated with reduced length of stay, especially in women with severe disease (Oboho, 2016). For women who respond to antipyretics and have no respiratory compromise, outpatient management may be appropriate. A follow-up visit with a care provider is recommended within 24 to 48 hours.

Hospitalization is recommended for pregnant women who are unable to tolerate oral intake, have fever unresponsive to acetaminophen, or have respiratory compromise. If a superimposed bacterial pneumonia is suspected, the most common organisms are *Streptococcus pneumonia*, *Staphylococcus aureus*, *Haemophilus influenza*, and Group A Streptococci. Empiric therapy with ceftriaxone and azithromycin, for example, may be appropriate (Mandell et al., 2007).

SEPSIS

Sepsis is rarely diagnosed in pregnancy; however, its frequency in the United States is increasing, from 1 in 15,385 in 1998 to 1 in 7,246 in 2008 (Bauer, Bateman, Bauer, Shanks, & Mhyre, 2013). In 2001, the International Sepsis Definitions Conference defined sepsis as a systemic inflammatory response syndrome (SIRS) in the presence of infection. There are varying degrees of sepsis, which are defined clinically and described in Table 24.2 (Levy et al., 2003). Of note, there are no well-established criteria for sepsis in pregnancy, though research is ongoing. Lappen, Keene, Lore, Grobman, and Gossett (2010) demonstrated that neither the SIRS nor Modified Early Warning score (MEWS) were able to identify patients at risk of sepsis or death in the setting of IAI. In contrast, Oliveira-Neto et al. (2012) showed that the Sequential Organ Failure Assessment (SOFA) score performed well in its ability to predict the

TABLE 24.2 Definitions of Sepsis

	DEFINITIONS
SIRS	At least two of the following findings: • Temperature <36°C or >38°C • Heart rate >110 bpm* • Respiratory rate >20/min • WBC >14,000/mcL*
Sepsis	SIRS + infection
Severe sepsis	Sepsis + organ dysfunction; may have the following: • Lactic acidosis (≥4 mmol/L) • Oliguria (<0.5 mL/kg/hr) • Altered mental status
Septic shock	Sepsis + hypotension, SBP <90 mmHg, MAP <60, or reduction in SBP by >40 mmHg from baseline despite fluid resuscitation

bpm, beats per minute; MAP, mean arterial pressure; SBP, systolic blood pressure; SIRS, systemic inflammatory response syndrome; WBC, white blood cell.

*Heart rate and WBC modified to reflect physiologic changes of pregnancy.

Source: Adapted from Dellinger et al. (2013) and Levy et al. (2003).

severity and prognosis in cases of severe maternal morbidity admitted to an obstetric ICU. Another tool, the Sepsis in Pregnancy Score (S.O.S.), was developed by modifying validated scoring systems including the Rapid Emergency Medicine Score (REMS) and the Acute Physiology and Chronic Health Evaluation (APACHE II), in accordance with recognized physiologic changes of pregnancy (Albright, Ali, Lopes, Rouse, & Anderson, 2014). The S.O.S. reliably identified patients at high risk for admission to the ICU in a retrospective cohort of 850 women evaluated in the emergency room. Prospective validation is pending.

PRESENTING SYMPTOMATOLOGY

The presenting symptoms will vary on the basis of the underlying cause. The most common cause of sepsis in the obstetric population is genital tract infection (chorioamnionitis, endometritis, and septic abortion); other nonobstetric causes are urosepsis, pneumonia, appendicitis, meningitis, bowel perforation, and cholecystitis (Kramer et al., 2009; Mabie, Barton, & Sibai, 1997). In the setting of obstetric-related infection, symptoms may include fever, abdominal pain, general malaise, bleeding, foul-smelling discharge, and contractions. Other symptoms may include dysuria, hematuria, cough, chest pain, shortness of breath, nausea/vomiting, headache, and neck or back pain.

HISTORY AND DATA COLLECTION

A quick but thorough history is obtained with a focus on possible causes of infection. It must be kept in mind that the presenting symptoms may overlap with other disease processes. The gestational age or days postpartum, presenting complaints, risk factors (preexisting medical conditions or immunosuppression), recent medications, allergies, and recent activities and/or travel history all need to be carefully documented (Belfort, Saade, Foley, Phelan, & Dildy, 2010).

PHYSICAL EXAMINATION

Physical examination findings will depend on the underlying cause of infection. It is critical to recognize that cardiovascular changes in pregnancy result in physiologically normal increases in heart rate and cardiac output and a decrease in blood pressure (Yeomans & Gilstrap, 2005). Significant findings will vary with the etiology. General findings associated with sepsis include fever, tachycardia, tachypnea, hypotension, warm extremities (early septic shock), cool extremities (late septic shock), fetal tachycardia, and fetal heart rate abnormalities such as variable or late decelerations. Pain with neck flexion or headache may be seen with meningitis. Lung findings such as rales, rhonchi, and decreased breath sounds may be present in the setting of pneumonia or acute respiratory distress syndrome (ARDS). Flank pain, costovertebral angle tenderness, and suprapubic pain are associated with urosepsis. Finally, women with sepsis from IAI may have uterine tenderness, contractions, purulent discharge, cervical motion tenderness, and pain with bimanual examination.

LABORATORY AND IMAGING STUDIES

When pregnant women present with symptoms and physical examination findings consistent with sepsis, the initial laboratory evaluation may be broad in an attempt to narrow the diagnosis. These women are usually ill-appearing with abnormal vital signs. To expedite treatment, complete blood count with differential, basic metabolic profile, liver function tests, lactic acid, arterial blood gas, and blood cultures should be obtained during the initial evaluation. As the physical examination progresses, a more tailored approach may be taken. Further testing may include urine, endometrial, or sputum cultures; rapid influenza; or lumbar puncture (LP).

If the pregnant woman has respiratory symptoms, a chest radiograph is recommended. If there are symptoms consistent with an acute abdomen, a pelvic ultrasound, pelvic and abdominal magnetic resonance imaging (MRI), or computerized tomography (CT) is necessary.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for sepsis is extensive. Some potential noninfectious entities include pulmonary embolus, amniotic fluid embolus, adverse drug reactions, and acute adrenal insufficiency.

CLINICAL MANAGEMENT AND FOLLOW-UP

Recognizing sepsis is critical to the initial management of pregnant women presenting for treatment. Early goal-directed therapy has been shown to improve survival in nonobstetric women (Rivers et al., 2001) and consists of fluid resuscitation, vasopressors, packed red cells, and inotropic agents aimed at normalizing clinical parameters (as listed in the following text). The optimal goals for therapy in pregnant women are not known, but the same principles can be applied using these goals or frequent clinical assessment. The initial focus is largely on maternal stabilization because fetal compromise is often due to maternal disease (Fernandez-Perez, Salman, Pendem, & Farmer, 2005).

The following sepsis guidelines are largely derived from the Surviving Sepsis Campaign (Dellinger et al., 2013). Upon presentation, with sepsis, hypotension, and a lactate of 4 mmol/L or greater, early and aggressive fluid resuscitation is recommended. The goal for adequate resuscitation is a central venous pressure (CVP) of 8 to 12 mmHg or urine output of 0.5 mL/kg/hr or greater. A Foley catheter may be placed if necessary. If the mean arterial pressure (MAP) is not maintained above 65 mmHg with fluid, vasopressors are needed. If the hematocrit is less than 30%, packed red cells are recommended. Rapid identification of the infectious source and infection control (e.g., wound debridement) is paramount. Immediately after obtaining cultures, empiric antibiotics with broad-spectrum coverage are administered, ideally within an hour of presentation. Antibiotic coverage is chosen with the possible source, common organisms, community resistance patterns, and fetus in mind. See Table 24.3 for suggested antibiotic regimens with specific suspected sources. A commonly used antibiotic in the setting of sepsis of unknown source is meropenem. Vancomycin may be added depending on clinical risk factors. Fetal monitoring of a viable fetus is recommended. Tocolysis is contraindicated.

TABLE 24.3 Suspected Sources of Sepsis and Recommended Antibiotic Treatment

SOURCE	RECOMMENDED ANTIBIOTIC
Sepsis with unknown source	Meropenem
Endometritis	Gentamicin plus clindamycin
Chorioamnionitis	Ampicillin plus gentamicin
Pyelonephritis	Ceftriaxone
Pneumonia	Ceftriaxone plus azithromycin
Appendicitis	Cefoxitin
Bowel perforation	Cefoxitin (if severe infection, may use meropenem)
Cholecystitis	Ceftriaxone or cefazolin

Note: Antibiotic regimens should be chosen with community resistance patterns in mind.

Source: Chapman et al. (2014); Mackeen, Packard, and Ota (2015); Mandell et al. (2007); Solomkin et al. (2010); Wing, Hendershott, Debuque, and Millar (1998).

Delivery is recommended only for obstetric indications and must be balanced with the maternal status if a cesarean delivery becomes necessary (Fernandez-Perez et al., 2005).

The recognition and prompt treatment of sepsis in the obstetric triage setting is imperative because early treatment may improve survival. Consultation with maternal–fetal medicine and hospital intensivists is recommended for further management. After stabilization, the pregnant woman can be admitted to the appropriate medical unit for ongoing care.

MENINGITIS

Although meningitis is a relatively rare event, with an estimated incidence of 1.38 cases of bacterial meningitis per 100,000 in the United States, it is a life-threatening emergency that must be recognized promptly in the emergency setting (Thigpen et al., 2011). Meningitis is defined as inflammation of the meninges surrounding the brain and spinal cord. The main causes of bacterial meningitis are *Neisseria meningitides, S. pneumoniae, H. influenzae* serotype B, and GBS. The primary causes of viral meningitis are enteroviruses, influenza, mumps, and herpesvirus (CDC, 2016e).

Women may present with sudden onset of fever, headache, and a stiff neck. They may also have photophobia, mental status changes, nausea, and emesis. If there is a suspicion of bacterial meningitis, an LP should be performed. Blood cultures and empiric antibiotic therapy must be initiated promptly. If the woman is immunocompromised or has a history of central nervous system disease, a new onset seizure, papilledema, abnormal level of consciousness, or a focal neurologic deficit, a CT scan of the head should be performed before the LP (Hasbun, Abrahams, Jekel, & Quagliarello, 2001). In this case, if the LP is delayed, blood cultures must be obtained and empiric antibiotic therapy must be administered before imaging. Dexamethasone should also be given at the same time as antibiotic therapy because glucocorticoids may decrease the risk

of death and neurologic complications in certain settings (Tunkel et al., 2004). Fetal monitoring of a viable fetus is recommended; however, one must consider the maternal risk of a cesarean delivery if it is warranted.

The cerebrospinal fluid (CSF) obtained on LP should be sent for Gram stain, culture, glucose, protein, and cell count. In bacterial meningitis, the Gram stain is 60% to 90% sensitive and depends on the bacterial concentration (Tunkel et al., 2004). The WBC count is usually elevated, and the protein level may be high. The diagnosis of bacterial versus viral meningitis, however, depends on the Gram stain and culture.

After the LP, when the pregnant woman is stabilized with empiric antibiotics, admission is appropriate if there is a strong suspicion of bacterial meningitis. Further antibiotic treatment is tailored to the microbiology results.

TRAVEL-ASSOCIATED INFECTIONS

Travel and immigration history is information that is essential to properly diagnose an infectious process in a pregnant woman. The recent Ebola epidemic, as well as growing concerns for continued spread of the Zika virus (linked to microcephaly and severe neurologic abnormalities in the offspring of infected mothers), highlight not only the ease with which individuals (and disease) may travel, but also the particular vulnerabilities of women during pregnancy (Jamieson et al., 2014; Rasmussen et al., 2016). Pregnant women may be more susceptible to and/or more severely affected by travel-associated infectious diseases; they may suffer fetopathy (disease in the fetus) or other pregnancy complications such as preterm labor or stillbirth as a result of infection (Jamieson et al., 2006). Although the exact frequency of travel during pregnancy is unknown, the limited data available suggest that pregnant women are often traveling abroad without consulting an obstetric care provider and with limited knowledge of the potential risks (Kingman & Economides, 2003). Women may also be traveling to or from an endemic area without awareness of their pregnancy status. Alternatively, obstetric providers may encounter travel-associated infections when caring for women emigrating from endemic areas.

Travel-associated infections are commonly transmitted by insect bites (vector-borne) or ingestion of contaminated food or water. Alternatively, diseases such as tuberculosis, in which transmission involves inhalation of infectious particles, may be acquired by close contact with high-risk populations. For some of these diseases, significant overlap in clinical features exists; therefore, knowledge of endemic areas becomes important for accurate diagnosis and treatment.

Providers working in obstetric triage need to routinely obtain a travel history on all patients and become familiar with the most common travel-associated infections, outlined in Table 24.4. In addition, health care facilities ought to prioritize training for all staff with direct patient contact on the appropriate use of personal protective equipment to prevent the spread of disease. It is critical that this training is updated at least yearly, with special training as needed during times of acute need (e.g., the Ebola epidemic). Ebola virus infection is discussed in detail in Chapter 22. Zika virus is also discussed in Chapter 27.

TABLE 24.4 Travel-Associated Infections

DISEASE AND PATHOGEN	ENDEMIC AREA(S)	VECTOR/HOST AND MODE OF INFECTION	CLINICAL FEATURES	TREATMENT
Chikungunya				
Chikungunya virus	West Africa	*Aedes* species mosquitoes Mosquito bites	Fever, arthralgias, myalgias, headache, rash	Supportive
Dengue fever				
Dengue virus	Central and South America, Africa, India, Southeast Asia	*Aedes* species mosquitoes Mosquito bites	Fever, headache, retro-orbital pain, myalgias, arthralgias, spontaneous bleeding	Supportive
Ebola				
Ebola virus	Africa	Unknown Direct contact (blood or bodily fluids)	Fever, myalgias, vomiting, diarrhea, spontaneous bleeding	Supportive
Malaria				
Plasmodium falciparum, *vivax*, *ovale*, and *malariae*	South America, Africa, India, Southeast Asia	*Anopheles* species mosquitoes Humans Mosquito bites	Fever, headache, myalgias, arthralgias, jaundice, anemia, seizures, coma, death	Chloroquine Atovaquone/ proguanil Artemether/ lumefantrine (chloroquine resistance)
Schistosomiasis				
Schistosoma mansoni, *haematobium*, and *japonicum*	Africa, South America, Caribbean, Asia	Fresh water snails Direct contact (contaminated fresh water)	*Acute*: rash, pruritus, fever, chills, cough, myalgias *Chronic*: abdominal pain, hepatomegaly, hematochezia, hematuria	Praziquantel
Tuberculosis				
Mycobacterium tuberculosis	Global (greatest burden in Africa, India, Southeast Asia)	Humans Inhalation of droplet nuclei	*Active*: persistent cough, chest pain, hemoptysis, fatigue, weight loss *Latent*: asymptomatic	Isoniazid Rifampin Ethambutol Pyrazinamide

(*continued*)

TABLE 24.4 Travel-Associated Infections (*continued*)

DISEASE AND PATHOGEN	ENDEMIC AREA(S)	VECTOR/HOST AND MODE OF INFECTION	CLINICAL FEATURES	TREATMENT
Typhoid fever				
Salmonella typhi	Global (rare in industrialized nations)	Humans Ingestion of contaminated food/drink	Fever, abdominal pain, headache, anorexia, "rose spots" on trunk/abdomen	Ceftriaxone Azithromycin
Yellow fever				
Yellow fever virus	Africa, South America (tropical areas)	*Aedes* or *Haemagogus* species mosquitoes Mosquito bites	Fever, chills, headache, myalgias, nausea, vomiting; severe form yields high fever, jaundice, bleeding, shock. and multisystem organ failure	Supportive
Zika				
Zika virus	Central and South America, Mexico, Caribbean	*Aedes* species mosquitoes Mosquito bites, sexual (male to male or female partner) and vertical (mother to fetus)	Fever, rash, joint pain, or conjunctivitis	Supportive Evaluation for fetal risk with serology and/or ultrasound

Source: Centers for Disease Control and Prevention (2012, 2013, 2014a, 2015, 2016a, 2016b, 2016d, 2016f, 2016g).

CLINICAL PEARLS

- The threshold for labeling a patient as having chorioamnionitis has been low, but may not take into account the resultant neonatal interventions, and so a change in terminology has been recommended in order to better characterize cases as "isolated maternal fever" or "intrauterine infection, inflammation," or both (Triple I).
- Treatment with antivirals is recommended in pregnant women suspected of having influenza (even with negative rapid testing results).
- All staff with direct patient contact need to be educated on the appropriate use of personal protective equipment to prevent the spread of disease, with regular trainings in times of acute need (e.g., the Ebola epidemic).

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25 *Intimate Partner Violence and Sexual Assault in Pregnancy*

Donna LaFontaine

Intimate partner violence (IPV) and sexual assault are common violent crimes perpetrated on women. Accurate statistics are difficult to obtain because these crimes are significantly underreported to both law officers and medical personnel. Sadly, pregnant women are not exempt from becoming victims of these crimes. When a woman is in a dysfunctional relationship, pregnancy may function as a stressor leading to increased episodes of violence (Jasinski, 2001). Depending on the patient population, prevalence rate estimates of physical abuse in pregnancy range widely. A recent review concurs with a likely rate of approximately 1 in 5 women (Gazmararian et al., 1996; Mendez-Figueroa, Dahlke, Vrees, & Rouse, 2013). In one trauma center, 31.5% of pregnant trauma patients suffered their injuries as a direct result of IPV (Poole et al., 1996). Obstetric (OB) complications associated with trauma include miscarriage, preterm labor, and placental abruption. IPV is not just physical in nature; it also includes behaviors such as stalking as well as verbal and psychologic aggression. Ongoing mental health issues, including depression and anxiety, are more prevalent in pregnant women subjected to any form of IPV, whether or not direct physical violence is involved. One study showed that pregnant women subjected to verbal threats were twice as likely to deliver low-birth-weight infants (Gentry & Bailey, 2014). All women who present to an OB triage unit or an emergency department (not just those who present with an injury or complication) must be screened for IPV. An organized plan for providing the victim with resources must be readily available when a screen is positive.

PRESENTING SYMPTOMATOLOGY

If a woman has sustained obvious or major trauma, it is likely the patient will first be taken to a general emergency room or a regional trauma center. The emergency room physician will stabilize the woman and likely call for an OB consultation. If a woman identifies herself as a victim of partner violence or sexual assault at the point of entry, the waiting time needs to be minimized. The victim ought to be brought immediately to a private room for evaluation. If a woman does not want to involve law enforcement, the medical provider is not obligated to report to the police unless she is considered a vulnerable person, such as a child or someone who is mentally or physically incapacitated.

EXHIBIT 25.1

Screening Tool for Domestic Violence

Patients are screened for domestic violence with the following questions:

- Is anyone close to you threatening or hurting you?
- Is anyone hitting, kicking, choking, or hurting you physically?
- Is anyone forcing you to do something sexually that you do not want to do?

Source: Courtesy of Women & Infants Hospital, Providence, RI.

Mandated reporting is state specific, and therefore it is critical to know the requirements in the state where the medical provider practices.

Women who have sustained minor trauma may spontaneously present to an OB triage unit. Although complaints of preterm contractions, abdominal pain, or vaginal bleeding may raise awareness to ask specifically about trauma events, often pregnant women who have sustained IPV will not truthfully admit to the cause of trauma; they seek care only for the purpose of ascertaining fetal well-being. A woman may present to an OB triage unit and admit to the cause of trauma, with subsequent complaints of head, neck, back, or neurologic symptoms. If a normal fetal heart is found and there are no obvious signs of labor or vaginal bleeding, strong consideration can be given to transfer the woman for a complete trauma evaluation by an emergency physician. More extensive fetal evaluation can be arranged in the trauma unit or after the mother is stabilized.

When a woman presents late in gestation with little or no prenatal care, the provider must consider that she may be a victim of IPV and the partner might not have allowed her to seek prenatal care earlier. There are several IPV screening tools currently available, and most hospitals have policies for screening. An example of a quick and effective screening tool is presented in Exhibit 25.1. IPV increases the risk of anxiety, depression, and persistent substance abuse in pregnancy. A pregnant woman may be afraid to answer the screening questions honestly; therefore, IPV needs to be considered when one of these conditions is revealed or the patient's account of trauma seems unlikely given the physical findings.

It is crucial to be able to screen the woman alone. Many times a perpetrator will exert significant control over a victim, and even when asked, the partner will not leave the room. A simple diversion may be attempted once, but if the triage staff feels threatened at any time, it is crucial to have security alerted and available. There has been a significant rise in violence perpetrated against health care workers in emergency room settings (Gates, Ross, & Mcqueen, 2006).

PHYSICAL EXAMINATION

A complete physical is performed on all women, especially noting any bruises, lacerations, reddened areas, or evidence of bleeding. If the victim is pursuing charges against the perpetrator, photographic documentation of any findings will be helpful after obtaining consent. Emergency rooms typically have policies regarding photographing injuries, and a similar policy needs to be established in OB triage units. If the police have already photographed the victim, repeating the process will be unnecessary. A written, detailed description of any injuries can be thoroughly documented in the medical record.

In cases of physical trauma, a blood type and potentially a Kleihauer–Betke (KB) test will need to be obtained. This is a measure of fetal blood cells in the maternal circulation. If trauma and/or bleeding have occurred in an Rh-negative woman, there is a risk of fetomaternal hemorrhage with subsequent Rh D sensitization. All women with a history of trauma need to receive Rh D immunoglobulin within 72 hours of the incident, but the KB test is necessary in order to determine the correct dose of Rh D immunoglobulin. If more than 30 mL of fetomaternal hemorrhage is determined to have occurred on the basis of the KB value, then it will be necessary to administer more than the standard 300-mcg dose of Rh D immunoglobulin. A blood bank can determine the appropriate dosing, depending on the test results.

Injuries that cause tenderness and swelling can be x-rayed for evidence of fractures, and the pregnant uterus will need to be shielded. In the case of head injuries or other severe injuries, if CT is indicated, this test must be performed. A complete ultrasound examination is indicated if gestational age is unclear or there is vaginal bleeding. If a fetal nonstress test is indicated and is nonreactive, a biophysical profile is then performed to further evaluate the fetal condition.

CLINICAL MANAGEMENT

The gestational age of the fetus must be carefully obtained. In the previable fetus, no fetal monitoring is necessary other than documentation of the fetal heart rate. It is often reassuring for the pregnant woman to see the fetus on bedside ultrasound, if available. If the woman is reporting painful contractions and is beyond 20 weeks gestation, there may be some utility in monitoring for contractions only. If regular contractions are identified, prolonged observation may be indicated to ensure discharge is not carried out prematurely. Once a viable gestation has been reached, prolonged monitoring may be indicated. Monitoring is used to assess for contractions, which will be present in cases of preterm labor or placental abruptio. A significant placental abruption may be indicated by persistent late decelerations. A nonreassuring fetal status in a viable gestation would indicate the need for emergency delivery.

Anyone who is identified as a victim of interpersonal violence must receive caring, emotional support from the medical providers working in an OB triage unit or emergency care setting. When a victim is identified, social services, behavioral health, or psychiatry are frequently helpful and can thoroughly assess a woman's needs. A safety assessment must be performed for each victim, specifically asking if the perpetrator had a weapon, where the victim will go after release from the hospital, if there is access to a cell phone, and who will be available for support. The pregnant woman may also need assistance in obtaining shelter. Occasionally, a victim will express suicidal or homicidal ideation, which must be evaluated by a behavioral health professional.

Interpersonal violence leading to trauma of a pregnant woman is common and potentially life threatening to both the woman and the fetus. The well-being of both the mother and the fetus must be ascertained when a woman presents with a history of trauma. Often, the medical staff will suspect IPV, but the woman will deny being subjected to violence. Asking the screening questions will allow the pregnant victim to know she can turn

to an OB triage unit if she becomes ready to reveal her secret. A checklist of information and resources needed in the event of a positive IPV screen is included in Exhibit 25.2.

EXHIBIT 25.2

Information and Checklist of Resources Needed When a Violence Screen Is Positive

1. The pregnant woman must first be medically stabilized. If there is a history of significant trauma, especially if the patient has head, neck, back, or neurologic symptoms, or mental status changes, consider consulting or transferring the patient to a trauma center.
2. Once the pregnant woman is stable, ascertain if there is any danger of the perpetrator presenting to the OB triage. Contact security or local police if there is a possibility of this happening.
3. If the patient would like to report to the police, call the police office in the town where the violent episode occurred. Do not call the police without the patient's permission.
4. Know your state's laws on mandated reporting, especially in the case of an adolescent. If there are questions, contact your risk management department.
5. Perform an assessment of the pregnant woman and her fetus. Thoroughly document. Consider:
   - ☐ Photography of bruises, lacerations, marks
   - ☐ X-rays or CT scans, if necessary for a complete evaluation
   - ☐ Fetal evaluation with ultrasound, nonstress test (NST), prolonged fetal heart monitoring, or biophysical profile as determined by fetal age
   - ☐ Administering tetanus vaccine or Rh immune globulin when appropriate
6. Perform a safety assessment:
   - ☐ Does the perpetrator have a weapon?
   - ☐ Does the victim have a cell phone?
   - ☐ Has the victim ever thought of hurting herself or others?

   If the pregnant woman expresses suicidal or homicidal ideation, this is an emergency. Behavioral health or psychiatry and nursing management must be contacted and the patient needs to not be left alone.
   - ☐ Where will the victim go?

   Maintain a list of local domestic violence advocacy centers. The National Domestic Violence Hotline can be reached at 1-800-799-7233 or on the Internet at www.ncadv.org.

   Contact your hospital social worker for assistance in arranging discharge planning and shelters. A list of women's shelters that accept pregnant patients needs to be maintained.
   - ☐ Does the victim have support systems?
7. Make certain the patient has access to follow-up prenatal care.
8. Make posters, cards, or brochures with local IPV resources easily available for patients in your triage unit.

IPV, intimate partner violence; OB, obstetric.

Most victims of sexual assault will not report the crime either to medical professionals or to law enforcement. Women who are already pregnant comprise a small percentage of victims who present for a sexual assault evaluation. Unless it is the local protocol to care for victims in an OB triage unit, it is likely the victim will be directed to an emergency department or a rape crisis center. Immediate medical needs must be assessed and treated before evidence collection. Most sexual assault victims are not severely injured (Linden, 2011), but there are occasions where substantial trauma has occurred. In these cases, it is likely the OB care provider will be called to an emergency trauma room; if fetal monitoring is deemed appropriate, it could be performed on site. Calls to an OB triage unit from a rape crisis center or a general emergency room will likely question the need for fetal monitoring, the safety of radiographic imaging, or the safety of the prophylactic medications. Hospitals need policies regarding under what conditions fetal monitoring is indicated.

CLINICAL MANAGEMENT

In the instances where physical trauma to the victim has been minimal and the woman has no complaints of vaginal bleeding or pelvic pain, it may be appropriate to have the emergency department document a normal fetal heart rate (110–160 beats per minute), perform any necessary evidence collection, and then transfer the victim to OB triage for prolonged fetal monitoring.

If the victim wants an evidence collection kit performed, usually time limits are in effect. These time limits differ by state, but they typically range between 72 and 96 hours. The numerous steps that need to be performed to complete the forensic exam are beyond the scope of this book. Best practices in evidence collection and prophylaxis are seen when the examiner has received specific training, such as a sexual assault nurse examiner (SANE) or a sexual assault forensic examiner (SAFE; Campbell, 2005; Sievers, Murphy, & Miller, 2003). These examiners have extensive training in obtaining the history, performing and documenting the physical exam, collecting forensic evidence, providing appropriate prophylaxis against sexually transmitted infections (STIs), and arranging for counseling and follow-up care that may be needed. The steps that must be completed for complete and comprehensive care of a pregnant woman presenting for evaluation of sexual assault are outlined in Exhibit 25.3.

If a woman describes a loss of memory or motor skills, or suspects she was given something that affected her mental capabilities, drug-facilitated sexual assault (DFSA) must be suspected. Special consent needs to be obtained before blood and urine can be collected to examine for those drugs associated with DFSA. A special drug screen needs to be performed and the chain of evidence needs to be maintained. If there is concern for DFSA, a forensic examiner will need to be contacted to collect the samples.

Prophylaxis for STIs

Once the maternal physical exam, a forensic exam (if requested), and a fetal evaluation have been completed, there needs to be a thorough discussion with regard to the risk of contracting STIs. Transmission risks are difficult to ascertain and depend on the prevalence of the STI in the locale and the exact

EXHIBIT 25.3

Steps in the Complete Assessment of a Pregnant Sexual Assault Victim

1. Prompt assessment/treatment of the maternal and fetal medical conditions. Location and order to be determined on the basis of the stability of patient and fetal condition, as well as local protocols. The initially contacted provider needs to coordinate care promptly.
2. Sexual assault evidence collection, if desired by the victim. As soon as indicated, on the basis of the medical condition, contact a SANE, SAFE, or an emergency room physician. Findings need to be clearly documented and chain of evidence must be maintained.
3. Contact police in the town where the assault occurred, if desired by the victim. Know local and state mandatory reporting requirements, typically when the assault has been perpetrated on a minor or a member of another vulnerable population.
4. Offer to call an advocate who can assist the patient with the exam and during the postdischarge period. Contact local sexual assault advocacy services if desired.
5. Arrange for social service referral, behavioral health evaluation, or psychiatry evaluation, if needed, on the basis of the victim's situation and social condition.
6. Assess the need for STI and HIV prophylaxis and administer those medications that are safe for pregnancy (see Exhibit 25.4).
7. Postdischarge follow-up can be quite lengthy to arrange. As needed, the victim may seek assistance with:
   - Safe shelter
   - Prenatal follow-up appointments (With the victim's permission, contact her obstetrician if she has one.)
   - Medical follow-up (recommended for 2 weeks, 6 weeks, 3 months, and 6 months post assault)
   - Follow-up with maternal–fetal medicine or an infectious disease specialist (if taking HIV prophylactic medications)
   - Ongoing counseling
   - Legal advocacy

SAFE, sexual assault forensic examiner; SANE, sexual assault nurse examiner; STI, sexually transmitted infection.

history of the sexual assault. In a nonpregnant population, the estimated risks of STI transmission are below 20% for gonorrhea, chlamydia, and syphilis (Reynolds & Peipert, 2000). Appropriate STI prophylaxis is safe and effective in pregnancy. The Centers for Disease Control and Prevention (CDC) publishes updated guidelines recommending which medications are appropriate for STI prophylaxis following a sexual assault. Exhibit 25.4 lists the currently recommended medications, all of which are considered safe for use in pregnancy.

The discussion for potential HIV transmission following a sexual assault is complicated. The incidence of HIV transmission to a woman after a single

EXHIBIT 25.4

Recommendations for Chlamydia, Gonorrhea, and Trichomonas Prophylaxis

Ceftriaxone 250 mg IM in a single dose
PLUS
Metronidazole 2 g orally in a single dose
PLUS
Azithromycin 1 g orally in a single dose

If patient is penicillin allergic with a history of a serious adverse reaction, the small but significant cross-reaction with cephalosporins can be addressed in an infectious disease consultation.
When cephalosporin allergy or other considerations preclude treatment with this regimen and spectinomycin is not available, consultation with an infectious-disease specialist is recommended.

Other recommendations to be considered safe in pregnancy under special circumstances

- Tetanus toxoid, if patient has lacerations and has not received a vaccination within 10 years
- Hepatitis B vaccination: The first in the series of three to be given, if patient not immune
- If perpetrator is known to be hepatitis B positive, and patient is not immune, consider hepatitis B immune globulin

IM, intramuscular.

Source: Adapted from Centers for Disease Control and Prevention (2015).

incidence of unprotected penile–vaginal sex (without injury) is estimated at 1 in 1,000, even if the man is known to be HIV positive (Varghese, Maher, & Peterman, 2002). Since no randomized trials are available, this estimate was extrapolated from studies involving health care workers exposed to blood and maternal–fetal transfer studies (Cardo, Culver, & Ciesielski, 1997; Connor, Sperling, & Gerber, 1994). There are several factors that may relatively increase or decrease the incidence of HIV transmission, and these are listed in Table 25.1.

For HIV prophylaxis to be effective, it must be administered within 72 hours of exposure. Other issues complicating HIV prophylaxis include the high cost of medications and the common incidence of side effects, which often lead to discontinuance of the medication. In one study of nonpregnant patients, even when provided with a complete course of medication, only 33.6% of patients who requested HIV prophylaxis completed the recommended 28 days of prophylaxis (Dumont et al., 2008). An incomplete course of HIV prophylaxis may lead to viral resistance to the medication used. Another important consideration is the ongoing laboratory testing, which needs to be followed in women taking HIV prophylaxis. Tests to be monitored include a complete blood count, chemistries, and liver functions. Recommendations

TABLE 25.1 Factors That May Decrease or Increase the Risk of Acquiring Human Immunodeficiency Virus After a Sexual Assault

DECREASE RISK	INCREASE RISK
No ejaculation	Blood exchange through traumatic injury
Condom use	Anal assault
Perpetrator known to victim	Multiple assailants
Oral assault without blood exchange	Assailant known to be from a high-risk group such as an intravenous drug user

Source: Adapted from Draughon (2012).

regarding HIV prophylaxis must be made on an individual basis, particularly when the HIV status of the perpetrator is unknown.

The nonoccupational postexposure HIV prophylaxis (nPEP) regimens are continually evolving, and those used in pregnancy may be different from those used in a nonpregnant patient (CDC, 2016). Specifically, Efavirenz is linked with teratogenicity, and avoidance is recommended in pregnancy. Didanosine (ddI), Stavudine (dT4), Nevirapine, and Indinavir are not recommended owing to concerns for potential maternal toxicity. The CDC maintains nPEP-recommended regimens on its website and phone app. Owing to the many complexities involving nPEP in the pregnant woman, if HIV prophylaxis started, consultation with a maternal–fetal medicine or an infectious disease specialist needs to be considered.

Follow-up examinations after a sexual assault are rarely pursued by nonpregnant female victims. One study that listed follow-up rates quotes figures below 50% (Ackerman, Sugar, Fine, & Eckert, 2006). There are no studies specifically identifying follow-up rates in pregnant women, but the fact that the patient may be receiving regular prenatal care at least provides the opportunity for closer follow-up. If the woman has declined prophylaxis for STIs, the initial postassault examination is scheduled for 2 weeks later. Chlamydia and gonorrhea need to be retested. Ideally, the woman is evaluated at 6 weeks, 3 months, and 6 months to retest for HIV, hepatitis C, hepatitis B, and syphilis. If the series of hepatitis B vaccinations was started at the time of the assault, the remaining doses are to be given at the sixth-week and the sixth-month visits. Currently, there are no recommendations for prophylaxis of herpes infections following a sexual assault. The patient must be educated regarding the symptoms of herpes and instructed to present for an examination if any lesions develop.

Rape is a heinous violent crime and has significant potential to cause the victim to experience acute as well as prolonged emotional and behavioral symptoms. Before discharge, a thorough assessment of the woman's emotional state and safety needs to be completed. A social services or psychiatric evaluation is indicated if there are expressions of suicidal or homicidal thoughts or if the woman has a limited support system, displays mental status or behavioral changes, is unwilling to communicate, or is inconsolable. The hospital social worker or the local sexual assault advocacy group can assist in arranging follow-up counseling. There is a 30% risk that a victim of sexual assault will experience symptoms of posttraumatic stress disorder, known as rape trauma disorder (Linden, 2011). Symptoms may include anxiety, depression disorders, or substance abuse. These issues, in addition to the stressors of having a new infant, require that the pregnant sexual assault victim have substantial support in place.

CLINICAL PEARLS

- IPV, including sexual assault, regularly occurs in the pregnant population. In some circumstances, the pregnancy may serve as a stressor that triggers violent behavior, and all pregnant women who present to an obstetric triage unit need to be screened for IPV.
- When physical violence is involved, maternal injuries must first be assessed and, if severe, may be treated in a trauma center. Once a fetus has reached a viable gestation, fetal monitoring is indicated to rule out preterm labor or abruption.
- Following a sexual assault, pregnant patients need competent counseling with regard to evidence collection and sexually transmitted disease prophylaxis, including HIV, if indicated.

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Substance Use and Other Psychiatric Disorders in Pregnancy

26

Catherine R. Friedman

Pregnancy is a unique time of change in an individual's family, social, medical, and interpersonal support systems as well as the pregnant woman's physiology. This convergence of internal and external motivators and mediators can result in both stress and positive impetus for change with effects on psychiatric conditions including substance use. The issues of substance use disorders (and any substance use) in pregnancy as well as other psychiatric disorders seen during pregnancy are the focus of this review. Substance use in pregnancy, including alcohol, benzodiazepines, and opioids, is presented in the first part of this review. Other preexisting or new psychiatric disorders that are often evaluated in an obstetric triage or emergency setting include depression, anxiety, panic attacks, and insomnia. These topics encompass the remaining portion of the chapter.

SUBSTANCE USE

Substance use in pregnancy prevails when a woman with a preexisting drug or alcohol use problem becomes pregnant and continues using. Pregnant women are aware that these substances are not healthy for fetuses, and almost no woman initiates drug or alcohol use in pregnancy. Yet, even infrequent or light substance use (that may not meet the criteria for a substance use disorder) may represent a danger to the pregnancy.

Often before problematic substance use is identified by a medical care provider, women may use a range of strategies to decrease or change substance intake to reduce potential harm to the fetus. Such changes include decreasing or stopping usage, switching the drugs used, and entering prenatal care or a substance treatment program. Substance use in pregnancy decreases for all substances, both spontaneously and with treatment, as pregnancy progresses. Muhuri and Gfroerer (2009) used epidemiologic data to show that this is true for multiple substances. This change reverses during the postpartum period, but does not return to preparenting levels. For example, in this sample, daily cigarette use was 20.1% in nonparenting and nonpregnant women. The percentage subsequently decreased to 12.4% in the first trimester and to 9.3% by the third trimester of pregnancy. Binge alcohol use decreased from 25.8% to 7.6% in the first trimester and 1% in the third trimester of pregnancy.

The etiology of substance misuse is both genetic and environmental. Associations with substance use in pregnancy include missed or inadequate prenatal care; recurrent somatic complaints (chronic pain, nausea, sleep, etc.), which may in turn result in multiple visits to obstetric triage; history of substance misuse and/or treatment; active psychiatric diagnosis; and a psychiatric history and/or history of trauma (including intimate partner violence), prior unexplained fetal death, and a previous child with alcohol-exposure related disorders.

Smoking nicotine cigarettes and alcohol use during pregnancy have well-defined risks. Smoking increases the risk of low birth weight and prematurity. No amount of alcohol is considered safe in any stage of pregnancy, and there appear to be differences in individual fetal vulnerability to the toxic effects. Alcohol exposure in the first trimester is associated with low birth weight, decreased birth length and head circumference, minor physical abnormalities, and neurodevelopmental disorders. Second- and third-trimester exposure can lead to developmental abnormalities such as intellectual deficits and behavioral abnormalities. The full constellation of effects is called fetal alcohol syndrome (FAS). However, fetal alcohol spectrum disorders (FASD) not meeting the full criteria for FAS are common.

HISTORY AND DATA COLLECTION

Screening Questions

Universal screening for pregnant women is recommended by many professional organizations (Wright et al., 2016). However, the substance use screening questions developed for the general population are not as accurate among reproductive-aged and pregnant women. The screening tool for drug use, The 4 Ps Plus© (Chasnoff, Wells, McGourty, & Bailey, 2007), consisting of Parents, Partner, Past, and Pregnancy, has been validated for drug use (alcohol, cannabis, heroin, cocaine, and methamphetamines) in pregnant women. T-ACE© (Sokol, Martier, & Ager, 1989) and TWEAK© screening tools (Russell et al., 1994) have been validated for alcohol use in pregnant women. See Exhibit 26.1 for these screening tools.

Some experts encourage the use of the National Institute on Drug Addictions (NIDA) Quick Screen, three open-ended questions regarding use of tobacco, alcohol, and other drugs:

1. In the past year, how many times have you drunk more than 4 alcoholic drinks per day?
2. In the past year, how many times have you used tobacco?
3. In the past year, how many times have you taken illegal drugs or prescription drugs for nonmedical reasons?

This approach is useful because women are more likely to report lifetime use or use of substances before pregnancy than use during pregnancy, given the stigma and risks of such use (Wright et al., 2016). Women who screen positive on any of these screens require further assessment for current use and possibly intervention and treatment, as indicated.

Screening, Brief Intervention, and Referral to Treatment (SBIRT) is a public health-based approach to identify those with substance use disorders, provide early intervention, and, when appropriate, offer referral to treatment services. It is used in emergency settings and obstetric and primary care settings for alcohol and tobacco use and has been endorsed by the United States Preventive Services Task Force as well as the American College of Obstetricians

EXHIBIT 26.1

Screening Tools for Tobacco, Alcohol, and Drugs in Pregnancy

4 Ps Plus© Verified for any substance in pregnancy

Parents: Did either of your parents have a problem with alcohol or drugs?
Partner: Does your partner have a problem with alcohol or drugs?
Past: Have you ever drunk beer, wine, or liquor?
Pregnancy: In the month before you knew you were pregnant, how many *cigarettes* did you smoke?
In the month before you knew you were pregnant, *how many beers/how much wine/how much liquor* did you drink?

Scoring: Women who acknowledge any use of tobacco or alcohol in the month before pregnancy have a positive screen and need further assessment for current substance use.

T-ACE© Verified for alcohol in pregnancy

- **T** **Tolerance:** How many drinks does it take to make you feel high?
- **A** Have people **annoyed** you by criticizing your drinking or drug use?
- **C** Have you ever felt you ought to **cut down** on your drinking or drug use?
- **E** **Eye-opener:** Have you ever had a drink or drug first thing in the morning to steady your nerves or get rid of a hangover?

Scoring: A score of 2 or more is considered positive, and these patients need further assessment for current substance use.

A, C, E = Affirmative answers are 1 point each.
T = Reporting tolerance to more than 2 drinks = 2 points.

TWEAK© Verified for alcohol in pregnancy

- **T** **Tolerance:** How many drinks can you hold (positive if ≥6 drinks)? *or* How many drinks does it take before you begin to feel the first effects of alcohol (positive if ≥3 drinks)?
- **W** Have close friends or relatives **worried** or complained about your drinking in the past year?
- **E** **Eye-opener:** Do you sometimes take a drink in the morning when you first get up?
- **A** **Amnesia:** Has a friend or a family member ever told you about things you said or did while drinking that you could not remember?
- **K** Do you sometimes feel the need to **cut down** on your drinking?

Scoring: A score of more than 2 is positive; these women need further assessment for current substance use.

E, A, K = Affirmative answers are 1 point each.
T, W = Affirmative answers are 2 points each.

Sources: Adapted from Chasnoff et al. (2007); Reis et al. (2014); Russell et al.(1994); Sokol et al. (1989).

and Gynecologists (ACOG). No past or current use or low use that stopped immediately before pregnancy or immediately following knowledge of pregnancy is considered low risk. Brief advice, and possibly a written pamphlet on the risks of substance use, is given to low-risk patients. Moderate risk is defined as having used heavily in the past, recent treatment for substance use disorder, stopping use later in pregnancy, and/or continued low use. These women should have a brief intervention such as motivational interviewing in the obstetrical triage setting. When permission is given, this moderate level of risk is also communicated to the obstetrical care provider and more frequent prenatal and postpartum visits are recommended. High-risk patients currently meet substance use disorder criteria and are to be referred to specialized treatment programs when available. More frequent prenatal and postpartum visits are also recommended (Wright et al., 2016). In order to facilitate care, obstetric triage units should maintain a list of regional treatment programs able to accommodate pregnant women.

Assessing Current Drug Use and Drug History

All questions must be asked in a private and nonjudgmental manner, including questions about drug usage in pregnancy. Each common and suspected substance needs to be questioned specifically, beginning with those perceived as the most common and least harmful and progressing to more stigmatized substances. For example, one can begin with caffeine or cigarettes and proceed through alcohol and marijuana, then nonprescribed pills and other drugs (cocaine, heroin, methamphetamine, etc.). Many people do not think of beer and wine as alcohol, so it is important to ask about these specifically. Likewise, many people do not think about marijuana and nonprescribed pills when asked about drugs, so these need to be specifically noted as well. The language women use to describe drug names and quantities can be unfamiliar and can change rapidly. Either asking the woman to describe what she means, or doing a fast online search for "street drug names" or "street drug amounts," can provide more detailed information. Sites kept updated include drugabuse.com (drugabuse.com/library/list-of-street-names-for-drugs) and addictionresource.com (addictionresource.com/drugs/street-names).

PHYSICAL EXAMINATION

Physical and behavioral indicators of possible substance misuse include a woman who smells of alcohol or chemicals and inappropriate behavior such as quick or unfocused anger. Changes in mental status such as extreme mood lability and mood extremes, disorientation, somnolence, and loose associations can be due to intoxication and/or withdrawal.

Physical signs of substance abuse or withdrawal vary by substance. They can include increased pulse and blood pressure, increased body temperature, low body weight (failure to gain weight in pregnancy), dilated or constricted pupils, rapid eye movements, nystagmus, inflamed or eroded nasal mucosa, nose bleeds, gum or periodontal disease (meth mouth), hair loss, track marks, injection sites, abscesses, and skin sores.

Maternal–fetal abnormalities associated with substance use in pregnancy include intrauterine growth restriction, failure to gain adequate weight, placenta abruptio, preterm labor, and nonreassuring fetal status. Both maternal and infant withdrawal symptoms can occur in the peripartum period.

EXHIBIT 26.2

Urine Toxicology Screen: Time Limits for Positive

Heroin	1–3 days
Methadone	2–4 days
Cocaine	1–3 days
Benzodiazepines	Up to 30 days
Marijuana	1–3 days (occasional use)
	Up to 30 days (chronic use)

Source: Adapted from Reis, Fiellin, Miller, and Saitz (2014).

LABORATORY AND IMAGING STUDIES

Urine drug screening is the standard test for drug use in pregnancy. However, it has a number of limitations and negative consequences. Regulations on urine drug screening, and reimbursement for this test, vary from hospital to hospital and state to state. There are restrictions on ordering this test, and it is never performed without the woman's consent. Urine drug screens are immunoassays that inherently have many limitations with regard to both specificity and sensitivity. For example, urine drug testing will often not detect synthetic opioids including methadone, dilaudid, fentanyl, and buprenorphine unless testing is ordered specifically. Many common cold preparations (e.g., pseudoephedrine) can cause false positives for amphetamines. Urine drug screens can also miss some common benzodiazepines like low-dose clonazepam. When in doubt of a result, a more specific confirmatory screen can be ordered and performed via gas chromatography/mass spectrometry. Furthermore, there are variable time limits to the detection of each substance tested, as noted in Exhibit 26.2. Only current alcohol use can be reliably detected with a breathalyzer or by blood alcohol level. There are no other reliable means to determine recent or chronic use. In addition, opiates and benzodiazepines are often administered for medical reasons in an obstetric triage setting before urine is obtained for drug screening.

CLINICAL MANAGEMENT

Generally, drug intoxication and withdrawal are managed symptomatically in pregnant women. Overall safety for mother and fetus represent paramount concerns. Alcohol, benzodiazepines, and opioids represent notable exceptions.

Alcohol and Benzodiazepines

Although greater than 95% of alcohol-withdrawal cases are uncomplicated and self-limited, intoxication and withdrawal occasionally can prove fatal. Alcohol, benzodiazepine, and phenobarbital withdrawal are managed similarly. Management options include a standing protocol or a symptom-triggered protocol that is linked to a standardized assessment such as the Alcohol Withdrawal Scale (AWS) or Clinical Institute Withdrawal Assessment (CIWA). For a symptom-triggered protocol, signs and symptoms of withdrawal are monitored regularly

(q 10–60 min). Lorazepam is initiated (2–4 mg PO or IV) at the earliest sign of withdrawal. Benzodiazepine is given until sedated or signs and symptoms of withdrawal cease.

All women presenting with alcohol withdrawal, intoxication, or suspicion of heavy alcohol use and related malnutrition should receive 50 or 100 mg thiamine intramuscularly or intravenously. This is followed by daily oral thiamine supplementation to prevent development of Wernicke's encephalopathy and other complications.

Opioids

Opioid withdrawal can be objectively and subjectively measured with a withdrawal scale such as the Clinical Opioid Withdrawal Scale (COWS; Wesson & Ling, 2003). This tool quantifies signs and symptoms of opioid withdrawal including resting pulse rate, sweating, restlessness, pupil size, joint and bone aches, running nose or eyes, gastrointestinal upset, tremor, yawning, gooseflesh skin, and anxiety/irritability.

Methadone maintenance treatment (MMT) is the recommended treatment for opioid dependence in pregnancy, with over 40 years of evidence for safety and efficacy. The primary goal of treatment with methadone is to prevent relapse to illicit substance use. Even medically supervised withdrawal is not the standard of care due to poor outcomes and the potential catastrophic consequences of relapse (Jones et al., 2010). Buprenorphine—a partial opioid agonist—is associated with a reduced incidence and severity of neonatal abstinence syndrome, but is not appropriate treatment for many pregnant women (Jones et al., 2010; Substance Abuse and Mental Health Services Administration [SAMHSA], 2016). Specifically, buprenorphine is not appropriate for women on high doses of opioids because they may experience withdrawal symptoms when treated with it. Women with a severe substance use disorder require the structured daily treatment setting of a methadone maintenance clinic for safe treatment (American Society of Addiction Medicine [ASAM], 2015).

Initiation of opioid replacement therapy (ORT) in opioid-dependent pregnant women varies from hospital to hospital. It is performed on an inpatient basis in some settings and outpatient in others. Sometimes, emergency rooms and obstetric triage settings are involved in initiation. Before hospital initiation of ORT, it is imperative to address the logistical issues of where the ORT will be continued after hospital discharge. For methadone, one must have the ability to seamlessly transition the woman from inpatient to outpatient MMT—for example, to go from inpatient methadone maintenance to entry into an outpatient methadone maintenance treatment program (MMTP) the day of or after discharge. Yet many MMTPs do not admit on a daily basis and others require an intake appointment a few days before the opioid users actually get admitted and dosed. One cannot write a prescription for methadone for opioid dependence; *this is illegal in the United States*. Methadone must be provided through a licensed facility when prescribed for opioid maintenance. Furthermore, outpatient pharmacies will not fill a methadone prescription unless it is written on the script that the indication is for pain. Buprenorphine must be prescribed by a practitioner with a specific Drug Enforcement Agency (DEA) waiver, and acceptance for follow-up with an outpatient provider must be ensured before discharge from the hospital. Usually, only a few days to a week of this prescription is appropriate when making the transition from the inpatient to an outpatient setting.

Note that if a pregnant woman presents with opioid overdose, emergency naloxone is not contraindicated in pregnancy. Risks of use are theoretical and are far outweighed by the very real risk of maternal and fetal death from untreated opioid intoxication (ACOG Opinion No. 524, 2012).

Involvement of Child Services

Reporting requirements vary by law from state to state, and they often vary in practice from institution to institution within a state. In some states, drug use in pregnancy is not reported. In other states, requirements for reporting vary by trimester. Each institution's social services and legal advisors can determine specific reporting requirements and processing. The Substance Abuse and Mental Health Services Administration (samhsa.gov) and National Advocates for Pregnant Women (advocatesforpregnantwomen.org) also provide resources on this topic.

FOLLOW-UP

Women using cigarettes, drugs, and alcohol need to be referred for appropriate treatment. Social services can assist with available local resources.

OTHER PSYCHIATRIC DISORDERS IN PREGNANCY

When necessary while awaiting psychiatric consultation, acute treatment of many common psychiatric symptoms may be initiated in the obstetric triage setting. These treatments are listed in Table 26.1.

Contrary to popular belief, the incidence of many common psychiatric disorders actually decreases during pregnancy, as seen in Table 26.2. A list of online resources for the identification and treatment of psychiatric disorders in pregnancy is noted in Exhibit 26.3.

DEPRESSION

Depression can present with a depressed or sad mood, lack of enjoyment, and/or irritability. Other somatic complaints such as changes in appetite and sleep, concentration, energy, libido, and fatigue are common. Many of these changes are common in pregnancy and the postpartum period. Care must be taken to distinguish physical changes that are within normal limits for this period and those that are unusual and associated with other symptoms of depression. Depression may also be related to a medical disorder, substance use (including prescribed medications), or unipolar or bipolar depression. Medical causes and substance use must be assessed before assigning a depression diagnosis.

Pregnant women who present with depression require further assessment for suicidal ideation, thoughts and plans to harm others, and the ability to care for themselves and dependents. If there is any question, psychiatric consultation is sought. This may involve referral to an outside psychiatric emergency room once obstetric stability is ensured. If a pregnant woman is considered at risk to herself or others, she must be kept in obstetric triage or an emergency setting under constant observation. In less severe cases, outpatient referral can be made for further psychiatric evaluation and therapy and/or psychotropic medications.

TABLE 26.1 Psychiatric Disorders: Symptoms and Triage Interventions

	ENVIRONMENTAL, BEHAVIORAL	PRN MEDICATIONS
Anxiety	Support and empathy Reassurance about signs and symptoms Education about the etiology and treatment of this disorder	Diphenhydramine (12.5–50 mg PO q 4 hr) *or* hydroxyzine (10–50 mg PO q 4 hr) *or* lorazepam (0.25–1 mg PO q 8 hr) *or* clonazepam (0.25–1 mg PO q 8 hr)
Panic	Calm, quiet environment Support and empathy Reassurance about signs and symptoms Education about the etiology and treatment of this disorder	Lorazepam (0.25–1 mg PO or 0.25–1 mg IM) *or* clonazepam (0.25–1 mg PO)
Agitation	Calm, quiet environment When necessary, remove objects that could be used to hurt oneself or others	Lorazepam (0.25–1 mg PO or 0.25–1 mg IM) For psychotic agitation, or agitation refractory to lorazepam or haloperidol 0.5–1 mg PO or IM
Severe suicidality, with danger of attempt	Remove all objects that could be used to harm oneself from the immediate environment Constant observation to ensure safety. STAT psychiatric consult or transfer to psychiatric emergency room for evaluation once medically stable	To calm thoughts, consider lorazepam (0.25–1 mg PO or 0.25–1 mg IM) *or* clonazepam (0.25–1 mg PO) For associated psychotic features, haloperidol 0.5–1 mg PO or IM
Psychosis	Calm, quiet environment Dimmer lighting When indicated, remove objects that could be used to hurt oneself or others Constant observation to ensure safety	Haloperidol (0.5–1 mg PO or IM) Atypical antipsychotics (such as risperidone, olanzapine, and ziprasidone) can be used in pregnancy. At this time little is known about the fetal safety profile; if they are known to work for an individual, and there are safety concerns, they should be used in preference to no treatment even in the triage setting

IM, intramuscular; PO, per os (orally); PRN, as needed; STAT, immediately.

Source: Adapted from Riba and Ravindranath (2010).

Initiation of antidepressants in the obstetric triage setting or emergency setting needs to be performed with care. Only pregnant women who are already established in prenatal and/or psychiatric care and who will have access to outpatient follow-up within a week ought to be started on medication. Furthermore, before initiating an antidepressant, screening is required for a history of mania, hypomania, and bipolar disorder. Initiating antidepressants in women with a history of mania can precipitate a manic episode. Recommendations as to the safest antidepressant in pregnancy change frequently because this is an area of active research. Online databases such as Reprotox (available at many institutions through Micromedex) provide the most recent information as to known drug safety in pregnancy. If an antidepressant has worked in the past, and it is not a contraindicated medication in pregnancy, this is considered a first-line treatment.

TABLE 26.2 Psychiatric Disorders by Pregnancy Status

	PAST-YEAR NONPREGNANT WOMEN % (SE; *N* = 13,025)	PAST-YEAR PREGNANT WOMEN % (SE; *N* = 1,524)	ADJUSTED ODDS RATIO (95% CI)	POSTPARTUM WOMEN % (SE; *N* = 994)	ADJUSTED ODDS RATIO (95% CI)
Any psychiatric disorder	30.1 (0.8)	25.3 (1.3)	**0.75 (0.62–0.90)**	25.7 (1.8)	0.81 (0.65–1.02)
Any substance use disorder	19.9 (0.7)	14.6 (1.2)	**0.68 (0.57–0.82)**	12.0 (1.3)	**0.44 (0.33–0.59)**
Any mood disorder	13.7 (0.5)	13.3 (1.1)	1.04 (0.83–1.32)	15.2 (1.5)	1.28 (0.97–1.69)
Major depressive disorder	8.1 (0.9)	8.4 (0.4)	1.24 (0.94–1.64)	9.3 (1.1)	**1.52 (1.07–2.15)**

CI, confidence interval; SE, standard error. Statistically significant results indicated in bold.

Source: Adapted from Vesga-Lopez et al. (2008).

EXHIBIT 26.3

Online Resources*

- The Marce Society for Perinatal Mental Health (**www.marcesociety.com**)
- Massachusetts General Hospital Center for Women's Mental Health Reproductive Psychiatry Resource and Information Center (**womens-mentalhealth.org**)
- Motherisk (**www.motherisk.org/prof/index.jsp**)
- MotherToBaby, a service of the Organization of Teratology Information Specialists (OTIS) (**www.mothertobaby.org**)
- National Advocates for Pregnant Women (**advocatesforpregnant-women.org**)
- Reprotox (**www.reprotox.org**) Subscription, but currently free for trainees. This may also be available through institutional subscription websites such as Micromedex
- Toxnet (**www.toxnet.nlm.nih.gov**) Medications in pregnancy and lactation. Select "Lactmed" for safety in lactation

*http://www.who.int/substance_abuse/publications/pregnancy_guidelines/en/

ANXIETY AND PANIC ATTACKS

Anxiety is characterized by combined physiologic and psychologic manifestations. Physiologic signs frequently include those of autonomic hyperactivity: flushing and pallor, tachycardia, palpitations, sweating, dry mouth, cold hands, diarrhea, and urinary frequency. Other signs are dizziness, increased startle response, muscular tension, physical pain such as headaches and body aches, shortness of breath, hyperventilation, trembling, and restlessness. Psychologic manifestations include feelings of worry, feelings of doom, hopelessness, inability to concentrate, and hypervigilance. Physical symptoms often precipitate

presentation to medical care, and many visits to obstetric triage with vague somatic complaints and unclear physical findings may ultimately be attributed to previously undiagnosed anxiety and/or depressive disorders. However, underlying and precipitating medical disorders must be ruled out before diagnosing a pure anxiety disorder.

Panic attacks occur or recur when the signs and symptoms of anxiety develop abruptly, peak within 10 minutes, and then decrease significantly. Women who experience a panic attack for the first time will often present to an emergency room because they are afraid they are having a heart attack or dying. Pregnant women are no exception and may present with these concerns. Other conditions must be ruled out before a panic attack can be diagnosed, including cardiac, endocrine, and pulmonary etiologies, and substance use/toxins. The specific medical evaluation is guided by the presenting physical and psychologic signs and symptoms.

Panic attacks can occur without a clear acute precipitating stressor. Other times, attacks are associated with agoraphobia—the fear of and avoidance of situations from which one might not be able to escape such as crowds, public transportation, and being alone in open spaces. Panic attacks often occur/recur in places or situations that can cause panic to become a learned reaction. Agoraphobia can develop when a person with prior panic attacks begins to fear similar places and situations. A panic disorder is diagnosed when a person has had at least one panic attack and then develops at least 1 month of persistent worries about having another attack or associated changes in behavior. Panic disorder usually begins in the mid-20s and is more common in women than in men.

Treatment for anxiety and panic involves support and empathy, including reassurance about their symptoms and education about the disorder. Benzodiazepines, particularly lorazepam (0.25–1 mg PO every 8 hr as needed for anxiety), are often the treatment of choice in the obstetric triage or emergency setting. These can both alleviate acute symptoms and facilitate the remainder of the evaluation (Stewart, 2011). Lorazepam can also be administered sublingually for faster onset of action. Low-dose diphenhydramine (12.5–50 mg PO q 4 hr) and hydroxyzine (10–50 mg PO q 4 hr) can also be used in women hesitant to take a prescription medication such as a benzodiazepine in pregnancy and for women with past or current substance abuse or dependency. Discharge prescriptions for benzodiazepines should only be written for a few days' worth of medication. Subsequent follow-up through the obstetric or psychiatric provider must be assured.

INSOMNIA

Disturbed sleep is often another symptom of psychiatric disorders. In all pregnant women presenting with psychiatric symptoms, sleep must be evaluated (initiation, quality, disturbance, etc.) as part of the assessment. Difficulty falling asleep can be treated symptomatically in the short term with diphenhydramine (12.5–50 mg nightly), trazodone (25–100 mg nightly), or zolpidem (2.5–10 mg nightly).

CONCLUSION

Psychiatric and substance abuse issues are common in the pregnant population. These can present in acute and dramatic ways in a triage setting. Obstetric providers may not be immediately familiar with how to approach the multiple

associated acute medical and psychosocial issues. This can range from doses of the acute medications used to referral for further appropriate treatment. Therefore, obstetric triage units must maintain protocols for dealing with acute intoxication and withdrawal. Lists of consultants and both outpatient and inpatient treatment centers need to be available and maintained.

CLINICAL PEARLS

- Ten percent of women drink alcohol in pregnancy, 15% smoke cigarettes, and 5% use an illicit substance.
- The primary goal of treatment with ORT in pregnancy (methadone or buprenorphine) is to prevent relapse to illicit substance use.
- Contrary to popular belief, the incidence of many common psychiatric disorders actually decreases during pregnancy.

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Sexually Transmitted Infections

27

Donna LaFontaine

Sexual intercourse is a risk factor for both pregnancy and the acquisition of a sexually transmitted infection (STI). Therefore, STIs represent a fairly common diagnosis in pregnant women. The Centers for Disease Control and Prevention (CDC) estimate that approximately 20 million cases of STIs are diagnosed annually in the United States (CDC, 2015a). The 15- to 24-year age group has the highest reported rates of chlamydia and gonorrhea infections, and these years overlap age groups with high-pregnancy rates. Since symptoms may be absent, vague, or generalized, a thorough history including a sexual history must be obtained on all pregnant women presenting for evaluation to an obstetric triage unit. Many STIs can cause fetal infections, which are contracted either in utero or during delivery as the infant passes through an infected birth canal. Pregnancy complications such as preterm labor are also associated with some STIs. Effective prenatal screening, diagnosis, and treatment of these infections will reduce most of the pregnancy complications that are attributable to STIs. The general clinical features of STIs in pregnancy are presented first, followed by more specific, detailed information regarding the most prevalent and clinically significant STIs.

The risk of acquiring an STI in pregnancy is related to the prevalence of STIs in the community. Information on the prevalence rates of STIs at the state level may be available at the state's Department of Health (DOH) website or at the CDC website (www.cdc.gov). All treatment recommendations in this chapter are consistent with the CDC's "Sexually Transmitted Diseases Treatment Guidelines, 2015" and are considered safe in pregnancy (CDC, 2015b).

PRESENTING SYMPTOMATOLOGY

Several of the STIs, including chlamydia and gonorrhea, frequently go unrecognized by women. The most effective key to diagnosis and treatment in the pregnant woman is to perform screening tests at the initial prenatal visit. STIs commonly screened for at the first prenatal visit include chlamydia, gonorrhea, hepatitis B, hepatitis C, HIV, and syphilis. At this time, there are no recommendations for routine prenatal screening for bacterial vaginosis (BV), trichomonas, and herpes simplex virus (HSV; CDC, 2015b). Given recent global infectious disease concerns, particularly with Zika virus, which can be sexually transmitted, immigration and travel histories of both the patient and any partners must be included in initial screening tests (Oster et al., 2016). Recommendations for Zika screening and testing are evolving. When a travel history raises concern for either the

TABLE 27.1 Sexually Transmitted Infections Implicated in Increasing Risk of Pregnancy Loss

INCREASES RISK OF SPONTANEOUS ABORTION	INCREASES RISK OF PRETERM LABOR	INCREASES RISK OF PERINATAL DEATH
Primary herpes	BV	Primary herpes
	Gonorrhea	Syphilis
	Chlamydia	
	Syphilis	
	Trichomonas	
	Primary herpes	

BV, bacterial vaginosis.

Sources: Adapted from CDC (2011) and Klein and Gibbs (2004).

pregnant woman or partner, state departments of health or the CDC website can be consulted for updated testing recommendations.

If a woman presents with symptoms, complaints typically will be dependent upon the specific infection. Symptoms of chlamydia and gonorrhea include vaginal discharge, irritation, vaginal spotting, cramping, discomfort, or pain. Herpetic lesions may present as itchy or painful ulcerations of the genital tract. Generalized symptoms of fever, fatigue, and nausea can be seen with a HSV primary outbreak, hepatitis B, hepatitis C, HIV, and Zika infection. Skin lesions or rashes on the body can appear in syphilis, disseminated gonorrhea, HIV, Zika, and scabies. Warty vulvar or vaginal lesions can appear with human papillomavirus (HPV).

If a pregnant woman presents complaining of vaginal spotting, cramping, or preterm contractions, STI testing must be considered since many STIs have been shown to increase the risk of miscarriage or preterm labor (Klein & Gibbs, 2004). Table 27.1 lists STIs that have been associated with increased risks for a pregnancy loss; causal relationships have not been proven. Note that treatment of these STIs in pregnancy has not been proven to lower risks of preterm delivery, as is discussed in the following text.

HISTORY AND PHYSICAL EXAMINATION

A complete sexual history includes any history of prior STIs and if there is an exposure to a new partner. The social history may reveal information about other risk factors, such as intravenous (IV) drug use or a partner with IV drug use. Women at high risk need screening for hepatitis C. A recent immigration or travel history may be helpful because infections in addition to Zika, such as lymphogranuloma venereum (LGV) and chancroid, are much more common in warmer, tropical countries.

At any obstetric triage visit, available prenatal records must be reviewed to verify what STI screening evaluations have already been performed. If the pregnant woman is late to prenatal care and has not been recently screened, screening for HIV, hepatitis B, syphilis, chlamydia, and gonorrhea are recommended. Ideally, STI screening is performed in the setting of continuous prenatal care, but if a woman is noncompliant, an obstetric triage or emergency setting visit might be the only contact point for screening.

A general physical examination is to be performed. Many of the STIs are manifested in the form of skin lesions, so a thorough examination of the skin is indicated. Table 27.2 describes common skin findings associated with STIs.

TABLE 27.2 Cutaneous Manifestations of Sexually Transmitted Infections

STI	POSSIBLE FINDINGS ON SKIN EXAMINATION
BV	Mild vulvar irritation secondary to excessive moisture exposure
Chancroid	Start as small red bumps around the genitalia that fill with pus, ulcerate, and become painful; takes weeks to heal. Frequently associated with enlarged firm inguinal lymph nodes that become tender (buboes)
Chlamydia	No associated skin changes
Granuloma inguinale	Small beefy red nodules found in the genitalia, painless but persist; as the skin wears away, granulation tissue appears
Gonorrhea	Disseminated gonorrhea, which is rare, may be associated with septic emboli that start as reddened papules then turn into hemorrhagic lesions
Hepatitis B and C	With infections severe enough to raise liver function tests, one may see jaundice of sclera and skin
HIV	Initial infection may be associated with a rash typical of viral syndrome, meaning a diffuse macular reddened rash, which may or may not be pruritic and associated with fever, malaise, and fatigue; usually starts in head and neck Kaposi's sarcoma—seen in late stages, full blown AIDS, purple to red or brown, flat or raised skin growths
Human papillomavirus	White- or flesh-colored growths, typically cauliflower-like, usually seen around vaginal opening, anus, cervix, or within the vagina
HSV	Small, reddened areas that at first may itch. They will blister, then ulcerate, then crust over and heal over the course of 5 to 7 days. Typically painful and usually seen near the vaginal opening or anus. May be associated with enlarged inguinal lymph nodes
LGV	Genital papules that ulcerate; lymphatics may be infected, and there may be significant vulvar swelling
Pubic lice	Reddened areas of the skin, which are pruritic and may have small spots of blood where the lice fed and/or can be visualized in pubic hair, armpits
Scabies	Mites burrow under the skin, leaving a red brown wavy line visible on the skin. These burrows are more commonly seen between fingers, the elbow crease, or the buttocks; itching is intense, especially at night. Scattered itching reddened papules are allergic reaction to the mites and their feces
Syphilis	Primary—painless chancre typically in the genitals at the site of infection inoculation, classically described as punched out with rolled-up borders Secondary—rash-disseminated small macules, reddened or brown, may be seen in palms, soles, and oral mucosa; these represent the disseminated organisms Condyloma lata—painless gray white lesions in moist, warm sites
Trichomonas	Vulvar and vaginal redness and irritation
Zika	Pruritic and diffuse, maculopapular rash +/– conjunctivitis

BV, bacterial vaginosis; HSV, herpes simplex virus; LGV, lymphogranuloma venereum; STI, sexually transmitted infection.

Source: Adapted from CDC (2015b).

In cases of hepatitis, jaundice or right upper quadrant tenderness may be recognized. A vulvar examination and a vaginal speculum examination are essential. Herpetic blisters and lymphogranuloma venereum (LGV) classically present with painful vulvar lesions, while secondary syphilis can present as a nonpainful vulvar lesion. Occasionally herpetic lesions can also be identified on the cervix. Abnormal discharge is a hallmark feature of gonorrhea, BV, and trichomonas. Of note, BV is not considered a STI. It is typically identified as a creamy off-white, gray discharge that is adherent to the vaginal walls. Discharge from BV typically releases an amine or "fishy" odor when exposed to potassium hydroxide (KOH), consistent with a positive "whiff" test. Trichomonas is classically described as a frothy, gray to green discharge that may be malodorous. With trichomonas, the cervix may be irritated and covered with punctuate hemorrhages, a condition commonly referred to as a "strawberry cervix." Gonorrheal vaginal discharge is frequently yellow and mucopurulent.

LABORATORY STUDIES

A saline wet mount microscopic examination of any vaginal discharge can be used to diagnose trichomonas and BV. Trichomonas will appear as a flagellated motile protozoan. However, microscopy is only 60% or less sensitive for trichomonas (van der Schee et al., 1999). The rapid antigen testing or direct hybridization techniques that are more sensitive and specific are becoming more widespread in their usage. BV is diagnosed when three out of four of Amstel's criteria are identified. These criteria include an off-white vaginal discharge adherent to the vaginal walls, an amine odor or positive "whiff test," a pH greater than 4.5, and greater than 20% clue cells per high-powered field. A clue cell is an epithelial cell whose borders are completely obscured by bacteria.

Nucleic acid amplification tests (NAATs) identify specific DNA sequences. NAATs have replaced cultures as the preferred test for chlamydia and gonorrhea in many institutions, as they are the most sensitive tests available. The Food and Drug Administration (FDA) has approved NAATs for use with urine, cervical, and urethral specimens. Herpetic lesions can be diagnosed with a viral culture or by polymerase chain reaction (PCR) testing. Herpes viral cultures have a very high false negative rate, especially with recurrent lesions, but more institutions are still using cultures over the more sensitive PCR tests (Geretti & Brown, 2005). Serologic testing for HSV is also available. Often HSV-1 and -2 serotypes will be positive from unrecognized prior infections. IgM is present only in the first several weeks of an infection, so a finding of IgM antibodies in the absence of IgG antibodies is indicative of a new infection. Blood work is necessary to test for HIV, hepatitis B and C, and syphilis antibodies. Both urine and serum testing are presently used to test for Zika virus.

CLINICAL MANAGEMENT AND FOLLOW-UP

Treatment recommendations are disease specific. Table 27.3 includes the 2015 CDC's "Sexually Transmitted Diseases Treatment Guidelines" (CDC, 2015b), but it is specifically modified to include only those treatments that are safe in pregnancy. These treatment guidelines are also available, both online and as a phone app that can be downloaded for free under the title, "CDC 2015 STD Tx Guide."

TABLE 27.3 Sexually Transmitted Infections and Recommended Treatments in Pregnancy

INFECTION	COMMON SYMPTOMS OR FINDINGS	DIAGNOSIS	RECOMMENDED TREATMENT	SPECIAL CONSIDERATIONS
BV	Asymptomatic Vaginal discharge with an odor	Vaginal swab for DNA probe identification of *Gardnerella vaginalis* Amstel's criteria (3 of 4): pH 4.5; creamy, off-white discharge adheres to vaginal walls; 20% clue cells; fishy odor	Asymptomatic infections—the only efficacy in treatment decreasing PTL is in patients with previous preterm delivery Treat all symptomatic patients with choice of: Metronidazole 500 mg PO bid × 7 d, *OR* Metronidazole 250 mg PO tid × 7 d, *OR* Clindamycin 300 mg PO bid × 7 d	Strictly not considered a STI, but more prevalent in women with multiple partners
Chancroid (*H. ducreyi*)	Painful genital ulcer and enlarged inguinal lymph nodes	Special culture or PCR testing	Azithromycin 1 g PO once, *OR* Ceftriaxone 250 mg PO once, *OR* Erythromycin base 500 mg PO tid × 7 d	Typically seen in the Caribbean, Africa No adverse effects on pregnancy have been reported
Chlamydia	Asymptomatic Spotting, cramping	NAAT: vaginal swab or urine Test of cure should be obtained 4–6 weeks posttreatment	Azithromycin 1 g PO once Amoxicillin 500 mg PO tid × 7 d Erythromycin base 500 mg PO qid × 7 d	Can cause conjunctivitis or pneumonia in infant
Genital HSV	Asymptomatic Vulvar itching, irritation, painful lesions or blisters Primary outbreaks may also be associated with generalized flu-like symptoms	PCR Viral cultures (poor sensitivity; only 50% positive) Tzanck prep	First lesion: Acyclovir 200 mg PO 5 × for 7–10 d *OR* Acyclovir 400 mg PO tid for 7–10 d Recurrence: Acyclovir 400 mg PO tid for 5 d Prophylaxis: Acyclovir 400 mg PO bid	Cesarean indicated for active lesion at the time of delivery If lesion has completely crusted *OR* if lesion is nongenital, cover with barrier dressing and cesarean not necessarily recommended

(*continued*)

TABLE 27.3 Sexually Transmitted Infections and Recommended Treatments in Pregnancy *(continued)*

INFECTION	COMMON SYMPTOMS OR FINDINGS	DIAGNOSIS	RECOMMENDED TREATMENT	SPECIAL CONSIDERATIONS
Granuloma inguinale	Large painless ulcers or buboes	Donovan bodies seen on dark field prep	Azithromycin 1 g PO q wk for 3 wk or until healed, *OR* Erythromycin base 500 mg PO qid for 3 wk or until healed	Seen in the Caribbean, Africa, Australia, India
Gonorrhea	Asymptomatic Yellow discharge, spotting Disseminated infection arthralgia, rash, meningitis	NAAT–vaginal swab or urine culture	Ceftriaxone 250 mg IM, *OR* Cefixime 400 mg PO, *OR* Azithromycin 1 g PO once Disseminated ceftriaxone 250 mg IM q day, *OR* IV q day until better, then Cefixime 400 mg PO bid for 1 wk	Can cause conjunctivitis in neonate Can cause rectal/pharyngeal infection Check with local DOH regarding resistance
Hepatitis B	Nausea, jaundice, pain	Hepatitis B surface Antigen	Supportive	Cesarean not absolutely recommended at this time, but since theoretically can be transmitted during delivery, consider cesarean
Hepatitis C	Nausea, jaundice, pain		Supportive	Cesarean not absolutely recommended at this time, but since theoretically can be transmitted during delivery, consider cesarean
HPV	Asymptomatic, warty lesion vulvar irritation	Clinical exam or biopsy	Delay treatment postdelivery or surgical removal	Cesarean may be considered if massive infection; can cause laryngeal papillomas in infant
LGV			Erythromycin base 500 mg PO qid for 21 d	

Pediculosis pubis (pubic lice)	Itching	Lice visualized	Permethrin 1% cream rinse applied to affected areas and washed off after 10 min	
Scabies	Itching, rashes	Scrape lesion and identify under microscope	Permethrin cream (5%) applied to all areas of the body from the neck down and washed off after 8–14 hr	Wash bedding with hot water
Syphilis	Chancres Rashes Neurologic symptoms Early latent (<1 yr)	RPR VDRL Treponemal testing	Benzathine penicillin G 2.4 million units IM for primary and secondary or early latent phase Benzathine penicillin G 2.4 million units IM once a week for 3 weeks for late latent phase or unknown duration or tertiary Aqueous crystalline penicillin G 4 million units IV q 4 hr for 10 d Pregnant women with a penicillin allergy should be desensitized	Treatment with penicillin may initiate a Jarisch Herxheimer reaction—fever, which can lead to fetal distress
Trichomonas	Asymptomatic Yellow green foul-smelling discharge, spotting or cramping	Rapid diagnostic kits using DNA probes Microscopy only identifies 60% of cases	Asymptomatic infections—treatment shows does not prevent PTL; may increase PTL Symptomatic infections treat with: Metronidazole 2 g PO once, *OR* Metronidazole 500 mg PO bid for 7 d	Neonates who travel through an infected birth canal can obtain fever, nasal, or vaginal discharge

BID, twice a day; BV, bacterial vaginosis; DOH, Department of Health; HPV, human papillomavirus; HSV, herpes simplex virus; IM, intramuscular; IV, intravenous; LGV, lymphogranuloma venereum; NAAT, nucleic acid amplification test; PCR, polymerase chain reaction; PO, per os (orally); PTL, preterm labor; QID, four times a day; RPR, rapid plasma reagin; STI, sexually transmitted infection; TID, three times a day; VDRL, Venereal Disease Research Laboratory.

Source: CDC STD Treatment Guidelines (2015b).

Reporting requirements for specific diseases will vary depending on a specific state's DOH; this information is typically available on their websites. Treatment of the sexual partner is critical to prevent reinfection. More than half of all state health departments have developed expedited partner therapy (EPT) protocols. EPT allows for treatment of the sex partners of patients with an STI, without a complete medical evaluation of the partner. Providers must contact the pertinent DOH website in order to clarify the particular EPT laws in effect for that state. A test of cure needs to be considered in the case of some STIs to minimize risks to the fetus. If NAAT is used, wait at least 4 weeks to retest, so there is opportunity to clear the DNA of the organism.

Chlamydia

Chlamydia is the most commonly transmitted bacterial STI in the United States. If an infant travels through a birth canal of a woman infected with chlamydia, the infant can also become infected. Neonatal chlamydial infections are manifested in the form of pneumonias or conjunctivitis. Nearly half of all patients diagnosed with gonorrhea are concomitantly infected with chlamydia (Datta et al., 2007).

Gonorrhea

Continually evolving antibiotic resistance to *Neisseria gonorrhoeae* is a growing U.S. public health concern. The CDC recommends that adults receive dual therapy with ceftriaxone and azithromycin. The dual therapy is recommended to account for strains of the bacteria that have been found to be less susceptible to either of the two antibiotics alone (CDC, 2015b). The CDC continues to have surveillance systems in place to continue to monitor for gonorrheal strains resistant to antibiotics and up-to-date information is available on their website.

Bacterial Vaginosis

There is no consensus as to the exact significance of BV in the pregnant woman. When women with BV are exposed to gonorrhea, chlamydia, or HSV, they are more likely to become infected with STIs than women who do not have BV (Schwebke, 2003; Weisenfeld, Hillier, & Krohn, 2003). An observational study showed that pregnant women with BV are at higher risk of spontaneous abortion, preterm delivery, and chorioamnionitis (Klein & Gibbs, 2004). There are, however, no interventional trials demonstrating that treatment of BV decreases these complications (Leitich et al., 2003; MacDonald, Brocklehurst, & Gordon, 2007; U.S. Preventive Services Task Force, 2008). There are no recommendations that necessitate treatment in asymptomatic pregnant women, and only symptomatic pregnant women are treated for BV.

Genital HSV

Genital HSV can cause devastating neonatal complications or mortality if the patient has an active infection at the time of the delivery, especially a primary outbreak. The clinical manifestations of a primary outbreak are highly variable.

Classically a primary outbreak includes fever, flu-like symptoms, inguinal lymphadenopathy, and multiple, painful genital ulcers. Up to one-third of primary infections, however, will be asymptomatic, or cause only mild symptoms. Between 1% and 2% of pregnant women will serologically convert to HSV positive during pregnancy, but only 36% of those gravidas recognized a clinical lesion (Brown & Selke, 1997). When patients have previously received the diagnosis of HSV, recurrent lesions are typically experienced as pruritic or an area of minor pain and irritation. The differentiation between serotype 1 (HSV-1) and type 2 (HSV-2) is not clinically important at the time of delivery, as both serotypes cause neonatal sequella. Disseminated HSV in the neonate can cause lesions as well as encephalitis, which can lead to neonatal death or long-term diminished mental capacity.

If a pregnant woman presents to an obstetric triage or emergency setting complaining of symptoms of vulvar irritation, dysuria, or pain in the setting of a vulvar lesion, the woman must be tested for herpes virus. If available, PCR is obtained, as viral cultures have a low sensitivity. Serologic testing is typically unhelpful in a triage setting, as the results may be negative in an early primary infection. If serologies are obtained and are negative, follow-up will be necessary at a future prenatal visit approximately 6 weeks from the obstetric triage visit. A genital herpes outbreak diagnosed during pregnancy can be treated with acyclovir during any trimester. A study based on over 1,000 pregnant women followed in a registry found no increased risk in birth defects above the baseline risk of the general population (Stone, Reiff-Eldridge, & White, 2004). The data regarding safe use of famciclovir and valacyclovir are limited, but have not been associated with any identifiable risks to the pregnancy.

When a woman with a history of HSV presents with contractions, a thorough examination of the vulva, vagina, and cervix must be performed. When an active lesion is present in the genital tract at the time of delivery, a cesarean delivery is currently indicated. Cesarean deliveries will not eliminate the risk of neonatal transmission completely. In diagnosed cases of neonatal herpes, approximately 25% were delivered by cesarean (Brown et al., 2003). Although primary outbreaks at the time of delivery carry the highest risk of infection for the neonate, recurrent outbreaks at the time of delivery also have significant risk. If the woman has a history of herpes but no active lesions, a cesarean delivery is not recommended. A completely crusted over lesion is not considered to be active. When a recurrent herpetic lesion appears on the thigh or buttocks, it can be covered, and a vaginal delivery pursued without neonatal complications.

If a pregnant woman presents with premature rupture of membranes at term and an identifiable herpetic lesion, a cesarean section is indicated. In the case of premature preterm rupture of membranes without labor, a maternal fetal medicine consultation may be helpful in planning the optimal delivery time. In this circumstance, the risk of neonatal herpes must be balanced against the risks of prematurity, and these risks may be difficult to quantify and may institutionally depend upon the resources immediately available. There is no expert consensus as to the point in the gestation when the risk of prematurity outweighs the risk of HSV. At least one study suggested that in patients less than 28 weeks gestation with an active lesion, the risk of sequelae due to prematurity typically outweighs the risk of neonatal infection (Major, Towers, Lewis, & Garite, 2003). In cases where expectant management is chosen, glucocorticoids may be given to assist in lung development and IV

acyclovir 8 mg/kg every 8 hours is recommended. The American College of Obstetricians and Gynecologists (ACOG) supports daily prophylaxis for women with a history of HSV with acyclovir starting at 36 weeks, as there are research studies available showing a lower incidence of herpetic lesions at the time of delivery when compared with women without prophylaxis (Scott, Hollier, & McIntire, 2002; Sheffield, Hollier, & Hill, 2003; Watts, Brown, & Money, 2003).

HIV

Optimal treatment of HIV infection in the pregnant woman can be complicated and research is still rapidly evolving. Ideally, an HIV screen will be obtained at the first prenatal visit. The ACOG supports universal HIV testing of all pregnant women using an "opt-out" approach. Most states have laws in place regulating HIV testing and these are available at the individual state's DOH website. The HIV screen may be repeated at the 36-week appointment, especially if the patient is in a high-risk category. Women at high risk include IV drug users, sexual partners of male IV drug users, sexual partners of men diagnosed with HIV, and sex workers.

Pregnant women diagnosed with HIV need treatment with antiviral agents for improvement or maintenance of maternal health, as well as to reduce the risk of perinatal transmission. The HIV transmission rate from mothers to neonates is highest for mothers with high viral loads (>30,000 copies/mL)—23% compared with only 1% for women with a nondetectable viral load (<400 copies/mL; Cooper et al., 2002). In high-resource areas, combination antiretroviral (cART) therapy is the gold standard for viral suppression and immune recovery (National Institutes of Health [NIH], 2016). Certain antiviral agents have been identified as safe in pregnancy, while others may be toxic either to the mother or to the developing fetus. A maternal fetal medicine or infectious disease consultation is advised to create a prenatal care plan that will treat the mother, as well as lower the perinatal transmission risk to the child. It is vital to start cART as soon as the diagnosis of HIV is made in a pregnant woman, and if drug resistance is subsequently identified as an issue, the cART can be modified. Since cART recommendations are continually changing, the National Institutes of Health (NIH) provides frequent updates via its website (http://aidsinfo.nih.gov/guidelines). The NIH also maintains the National Perinatal HIV Hotline (1-888-448-8765), which provides free clinical consultation on all aspects of perinatal HIV, including infant care.

Even if HIV was not screened prenatally, there is tremendous value in obtaining a rapid HIV screening test at the time of a late gestation obstetric triage visit, especially if it appears that the woman will be delivering. Antiretroviral prophylaxis is indicated in all HIV positive women at the time of labor and delivery, regardless of whether the maternal viral load is known. Currently, IV zidovudine (AZT) is recommended in labor, but recommendations are still evolving. In addition, elective cesarean deliveries have been shown to lower risks of maternal-to-child transmission, especially in instances where the viral load is greater than 1,000 copies/mL or is unknown (European Collaborative Study, 2005). Finally, the infant can receive antiviral prophylaxis, which has been proven to lower infection risks for the infant. For the woman with HIV infection identified at the time of labor, maternal prophylaxis with antivirals together with 6 weeks of prophylaxis of the infant reduces the risk of maternal-child transmission by 60% (Wade et al., 1998).

Syphilis

The incidence of syphilis in the United States has been slowly rising since 2001, but most of the increase is attributable to infections in men having sex with men. There were 377 cases of congenital syphilis in the United States in 2010 (CDC, 2010). Untreated syphilis infections in pregnant women can result in stillbirth, neonatal death, or can result in infants living with congenital syphilis.

The primary stage of syphilis is marked by a small, round painless genital lesion referred to as a chancre. The chancre typically lasts up to 6 weeks and, if untreated, progresses into secondary syphilis, which is marked by a rough, brown-red rash on the palms and feet. Symptoms of the rash may be mild. Constitutional symptoms of fever and fatigue may be present. If still untreated, syphilis will next proceed into a latent phase. If the syphilitic treponema enters the neurologic system, neurosyphilis with seizures and headaches can result.

Penicillin is used for the treatment of syphilis, but the forms and the dosage change depending on the stage at the time of diagnosis. The CDC's *"Sexually Transmitted Diseases Treatment Guidelines, 2015"* recommend desensitization in penicillin-allergic pregnant women, followed by treatment with penicillin.

Zika Virus

As of 2016, there is limited research into perinatal transmission, infection, and outcomes associated with the Zika virus. Zika was originally described in Africa, but the virus has rapidly spread throughout the world, especially in warmer climates where the *Aedes* species of mosquito can be found. The major concern at this time is for fetal microcephaly, intracranial, or placental calcifications and growth restriction. Microcephaly is estimated to occur in up to 13% of infants born to infected mothers (CDC, 2016). Cases of sexual transmission of Zika from men to their sexual partners have been confirmed in the United States (Oster et al., 2016). Only one in five nonpregnant people infected with the virus will become ill. If a patient does display symptoms, these include fever, maculopapular rash, conjunctivitis, headache, arthralgias, and myalgias. Symptoms typically last between 2 and 7 days. When associated with a mosquito bite, if symptoms are noted they will occur between 3 and 12 days after the bite. The duration of Zika virus within the male genitourinary tract and the length of viral shedding is unknown at this time. If a woman presents with any of the previous symptoms, consider testing for the presence of Zika virus. As knowledge of Zika is rapidly evolving, the CDC website contains up-to-date recommendations for testing. As of yet, there is no treatment available.

Pelvic Inflammatory Disease

The diagnosis of pelvic inflammatory disease (PID) in pregnancy is controversial. The hormonal changes in pregnancy cause thickening of cervical mucus, theoretically making it difficult for STIs to ascend to the uterus and adnexa. If chronic PID exists prior to pregnancy, successful implantation of the embryo should be very rare, due to the inflammatory changes affecting the endometrium. However, the literature does contain case reports of tubo-ovarian abscesses diagnosed in pregnancy (Navada & Bhat, 2011; Yalcin, Tanir, & Eakalen, 2002). More common infectious processes like appendicitis and inflammatory bowel syndrome must first be ruled out before a diagnosis of PID in pregnancy is considered.

CLINICAL PEARLS

- Immigration and travel history are important tools needed to identify STIs that are more prevalent in other countries.
- There is huge value in obtaining a rapid HIV test for women not screened antenatally. IV zidovudine given in labor followed by neonatal prophylaxis administration has been shown to decrease risk of maternal-child transmission by 60%.
- Since there is such a wide variety of infections that can be transmitted sexually and since testing and treatment recommendations may change rapidly, an online up-to-date resource is particularly valuable, such as resources maintained by the CDC and the NIH.

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28 *Postpartum Preeclampsia Complications*

Mollie A. McDonnold

Hypertensive disorders are one of the most common causes of presentation for emergency care in the postpartum period, ranking second to infections (Clapp, Little, Zheng, & Robinson, 2016). Although many women experience hypertensive disorders during pregnancy, either due to chronic disease or to the spectrum of gestational hypertension and preeclampsia, de novo development of hypertension is seen in 42% to 77% of women with postpartum hypertension (Al-Safi et al., 2011; Goel, 2015). Eclampsia is one of the most concerning complications of hypertensive disorders of pregnancy and contributes significantly to maternal mortality. In Canada, a case fatality rate of 3.4 per 1,000 deliveries was noted from 2003 to 2009, making the risk of death from eclampsia 26.8 times greater than those who do not experience eclampsia (Liu et al., 2011). In addition, eclampsia is associated with increased risk of morbidity including the need for assisted ventilation, adult respiratory distress syndrome, acute renal failure, and cardiac arrest (Liu et al., 2011).

Significant research and resources have been devoted to the problem, leading to a marked reduction of eclampsia in the antenatal period. However, women with hypertensive disorders in the postpartum period have been excluded from this research (Sibai, 2011). As women will frequently manifest problems due to postpartum hypertension following discharge from the hospital, they are often initially managed in an obstetric triage or emergency room setting. Of women who presented with seizure in the postpartum period, more than 90% presented within 7 days of the original hospital discharge (Al-Safi et al., 2011). While women with mild preeclampsia are 25 times more likely to experience hypertension during the postpartum period, hypertensive disorders, including eclampsia, do initially present in the postpartum period (Cruz, Gao, & Hibbard, 2011).

It is difficult to define the incidence of hypertensive disorders of pregnancy presenting in the postpartum period. Overall, the incidence of new-onset hypertensive disorders in the postpartum period ranges from 0.3% to 27.5% (Sibai, 2011). In a 10-year review of 3,899 cases of preeclampsia, 5.7% of cases were initially diagnosed in the postpartum period, of which 66% occurred after the original discharge date (Matthys, Coppage, Lambers, Barton, & Sibai, 2004). Chames, Livingston, Ivester, Barton, and Sibai (2002) noted that 79.3% of women with eclampsia in the postpartum period presented late (>48 hours after delivery), and of these, only 22% had a history of preeclampsia in the

index pregnancy. Al-Safi found 63% of women with postpartum preeclampsia and 77.3% of those with eclampsia had no antecedent history of hypertensive disorder of pregnancy (Al-Safi et al., 2011). Similarly, a review of 988 deliveries found 184 women presented for evaluation of postpartum hypertension, and of these, 77 cases were new onset in the postpartum period (Goel et al., 2015).

Traditionally, the postpartum period has been considered to extend into the fourth postpartum week (Yancey, Withers, Bakes, & Abbot, 2011). After discharge, many women are not seen in follow-up until 6 weeks and may not present earlier unless they experience symptoms. Women with the antenatal diagnosis of pregnancy-induced hypertensive disorders do not normalize blood pressure immediately following delivery. In one study of 62 patients, 81% had normalized by 3 months postpartum and required a mean of 5.4 weeks to reach normal blood pressures (Podymow & August, 2010). However, there may be a brief 48-hour window following delivery of normal blood pressures followed by an increase in blood pressure between postpartum days 3 to 6, likely due to physiologic volume expansion and fluid mobilization (American Congress of Obstetricians and Gynecologists [ACOG], 2013; Ghuman, Rheiner, Tendler, & White, 2009; Podymow & August, 2010). As most women are discharged home prior to the fifth postpartum day in which blood pressure has been shown to reach peak values, the need for possible postpartum blood pressure treatment may not be identified (Podymow & August, 2010). Given this, blood pressure evaluation at 72 hours postpartum, and then again 7 to 10 days postpartum, is recommended for women with known hypertensive disorders of pregnancy (ACOG, 2013).

Rates of eclampsia have been declining. In Canada, the rate of eclampsia was noted to fall from 12.4 per 10,000 deliveries in 2003 to 5.9 in 2009 (Liu et al., 2011). While there has been reduction in the incidence of antenatal eclampsia due to improved prenatal care, screening, and prophylactic treatment with magnesium sulfate, in the past 60 years there has been no decrease in the incidence of postpartum eclampsia, with 14% to 26% of eclamptic seizures noted to occur greater than 48 hours after delivery (Chames et al., 2002; Liu et al., 2011; Yancey et al., 2011).

It is critical to quickly evaluate and treat those who present with elevated blood pressure, especially if associated with prodromal symptoms such as headache. Headache was the most common presenting symptom in women with delayed postpartum preeclampsia in Al-Safi's series, present in 69.1% (Al-Safi et al., 2011). In Chames's series, 91% of women with postpartum eclampsia were noted to have prodromal symptoms. Only seven sought care prior to the onset of seizure activity, but six of these women were deemed to have had a preventable seizure due to failure to consider a diagnosis of preeclampsia in the postpartum setting (Chames et al., 2002). Since the differential diagnosis of postpartum hypertension is broad, a careful history and physical examination must elucidate the etiology and appropriate management.

PRESENTING SYMPTOMATOLOGY

Although it is unclear how many women with elevated blood pressure are not evaluated postpartum due to lack of symptoms, it is clear that those with postpartum eclampsia will likely experience symptoms. Women with 91% to 100% of postpartum eclampsia are noted to have prodromal symptoms (Al-Safi et al., 2011; Chames et al., 2002). In multiple studies, headache has been shown to be the most common symptom (Al-Safi et al., 2011; Chames et al., 2002; Matthys et al., 2004; Yancey et al., 2011). Other common symptoms are displayed in Table 28.1.

TABLE 28.1 Common Symptoms Associated With Postpartum Preeclampsia

SYMPTOM	PERCENTAGE OF POSTPARTUM WOMEN WITH PREECLAMPSIA (%)
Headache	62–82
Visual changes	19–31
Shortness of breath/chest pain	13–30
Nausea	12.5–18
Vomiting	11.2–14
Abdominal pain	7–14
Edema	9–10.5
Neurologic deficits	5.3

Sources: Al-Safi et al. (2011); Matthys et al. (2004); and Yancey et al. (2011).

It is essential to note that while headache is the most common presenting symptom, and headache with associated elevated blood pressure prompts evaluation for preeclampsia, headache itself is nonspecific and is associated with a broad differential. Hypertensive disorders of pregnancy represent 24% of postpartum headaches, second most common behind tension-type headaches (Stella, Jodicke, How, Harkness, & Sibai, 2007).

HISTORY AND DATA COLLECTION

Given the broad differential associated with postpartum hypertension, a thorough history is critical. In addition to talking with the patient, prenatal and hospital admission records are obtained and reviewed to obtain the following: determination of the interval between delivery and clinical presentation, a thorough medical and pregnancy history, determination of associated symptoms, family history with particular attention to cerebrovascular accidents, and confirmation of medication usage.

The time course of postpartum hypertensive disorders has classically been defined to extend into the fourth postpartum week, but postpartum hypertensive disorders primarily present within the first week (Yancey et al., 2011). In Goel's study, 62% of women presented between 48 and 72 hours postpartum, 27.2% presented on day 4, 5.4% on day 5, and the remaining after the first week (Goel et al., 2015). It is the most common reason for readmission on day 3 postpartum (Clapp et al., 2016). After 6 weeks postpartum, an alternative diagnosis, especially essential hypertension, is considered. While it is critical to know about the antenatal history, many cases of hypertension postpartum, especially eclampsia, have not been previously diagnosed. In a series of 152 cases readmitted for delayed postpartum preeclampsia or eclampsia, 96 cases (63.2%) had no antecedent diagnosis, and in a separate study of 184 women seen for hypertensive disorders in the postpartum period, 77 (42%) were de novo cases (Al-Safi et al., 2011; Goel et al., 2015).

Some studies have noted that African American women are at higher risk for the development of eclampsia, but specific risk factors have not been well established for the development of postpartum preeclampsia or eclampsia, as they have been for the antepartum period (Al-Safi et al., 2011; Matthys et al., 2004). One series evaluated 1,964 women and found independent risk

factors for development of postpartum hypertension which included: assisted reproductive technology, obesity, chronic nephritis, hypothyroidism, high normal blood pressure before or at delivery, and cesarean section (Takaoka et al., 2016). Chronic hypertension itself does not appear to be a risk factor for postpartum eclampsia. Of 543 women with chronic hypertension with superimposed preeclampsia, only 5.2% were readmitted postpartum and none developed eclampsia (Al-Safi et al., 2011). In the same study that found women with mild preeclampsia had 25 times the risk of having elevated pressures postpartum, women with chronic hypertension were only seven times more likely than women without hypertensive disorders to have elevated blood pressure postpartum (Cruz et al., 2011). However, while women with chronic hypertension were six times more likely to have a seizure as compared with normal controls, those with preeclampsia had only four times the risk (Cruz et al., 2011). Ultimately, knowledge of any underlying history may help to distinguish worsening essential hypertension from developing preeclampsia.

Other associated symptoms may be clues that an alternative diagnosis or diagnoses must be considered. Hyperthyroidism, either Graves' disease or the hyperthyroid phase of postpartum thyroiditis, may present with palpitations and heat intolerance. Shortness of breath and chest pain are associated with peripartum cardiomyopathy, of which 23% to 46% of cases have associated hypertension (Sibai, 2011). Symptoms of other cerebrovascular complications often overlap with those of preeclampsia and include refractory or thunderclap headache (a sudden onset pain often described as the worst headache a woman has ever experienced), visual disturbances, or neurologic deficits (Stella et al., 2007). Pheochromocytoma, although a rare entity, is associated with high morbidity and symptoms such as palpitations, excessive sweating, chest pain, and dizziness (Sibai, 2011).

Medication usage is an essential part of the history. The use of nonsteroidal anti-inflammatory medications like ibuprofen is common practice. These medications have been shown to lead to hypertension by reducing compensatory renal prostaglandin synthesis in hypertensive patients while concomitantly increasing renal synthesis of vasoconstricting agents (Makris, Thronton, & Hennessy, 2004). They may also inhibit salt and water loss postpartum as well as decrease the effectiveness of many antihypertensive drugs including beta blockers, angiotensin-converting enzyme inhibitors, and thiazide diuretics (Ghuman et al., 2009). Anticongestants such as ephedrine and phenylpropanolamine are other commonly used medications associated with exacerbation of hypertension. Ergot alkaloids like methylergonovine, administered for uterine atony in the postpartum period, cause vasoconstriction by acting on alpha adrenergic receptors and therefore can contribute to the hypertensive issues (Sibai, 2011).

PHYSICAL EXAMINATION

Potential life-threatening complications of postpartum hypertension include cerebral infarction or hemorrhage, congestive heart failure, pulmonary edema, or renal failure (Sibai, 2011). Signs of these processes may be detected while performing a thorough physical examination. Vital signs alone may provide clues as to the etiology of the hypertension. Acute onset, severe hypertension (defined as systolic pressure greater than or equal to 160 mmHg or diastolic pressure greater than or equal to 110 mmHg) that persists greater than 15 minutes is a hypertensive emergency. The degree of systolic hypertension appears to be the most significant predictor of cerebral injury and infarction. In a series of 28 patients with preeclampsia and stroke, all but one had severely elevated

systolic pressures just prior to experiencing hemorrhagic stroke, while only 13% had severely elevated diastolic pressures (ACOG, 2015). Widened pulse pressure and tachycardia may be seen with hyperthyroidism, postural hypotension with pheochromocytoma, and decreased oxygen saturation with congestive heart failure or pulmonary edema (Sibai, 2011).

A thorough neurologic examination including evaluation of cranial nerves, visual fields, motor strength, sensation, cerebellar function, reflexes, and presence of clonus must be performed. Brisk reflexes, especially if associated with clonus, are classically associated with a preeclamptic state. Forty-seven percent of women presenting with postpartum hypertension or eclampsia were noted to have hyperreflexia (Yancey et al., 2011). It is critical to urgently evaluate any neurologic deficits as they are indicative of possible serious intracranial abnormalities.

Cardiovascular and respiratory examination may reveal possible fluid overload, which is associated with pulmonary edema; this is not an uncommon complication of both preeclampsia and peripartum cardiomyopathy. Abdominal examination may reveal right-upper-quadrant tenderness. In Yancey's study of women presenting with postpartum preeclampsia or eclampsia, 18% were noted to have this finding (Yancey et al., 2011). Although it is a very common finding seen in as high as 84% of women presenting with postpartum hypertension, edema (generalized or peripheral) is a nonspecific finding (Yancey et al., 2011). The presence may be noted but may not help elucidate etiology.

LABORATORY AND IMAGING STUDIES

A complete laboratory panel upon presentation consists of a complete blood count, liver enzymes, serum creatinine, and electrolytes. As proteinuria is only seen in 29% to 79% of postpartum eclampsia, and as the degree of proteinuria does not determine the severity of preeclampsia, assessment of the presence of proteinuria is less critical. While the presence strongly suggests preeclampsia as an etiology, its absence does not rule out preeclampsia and possible impending eclampsia (ACOG, 2013; Yancey et al., 2011). In addition, as normal postpartum lochia may influence the presence of proteinuria, it is necessary to obtain the sample by catheterization.

Hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome, another serious complication of preeclampsia, has also been noted to initially present in 30% of women who develop this syndrome from postpartum days 1 through 7 (Sibai, 2011). In Yancey's study of 22 women with postpartum hypertension or eclampsia, 41% had elevated liver enzymes, 24% had anemia, but none were noted to have thrombocytopenia (Yancey et al., 2011).

As with physical examination findings, other laboratory findings may help to identify alternative etiologies of hypertension. For example, serum potassium levels less than 3 mEq/L with associated metabolic acidosis are indicative of hyperaldosteronism. Confirmation of adrenal tumor may then be made with either computerized tomography (CT) or magnetic resonance imaging (MRI) of the abdomen (Sibai, 2011). Low serum creatinine is suggestive of volume overload (Sibai, 2011).

Presenting symptoms and physical examination findings concerning for pheochromocytoma include: paroxysmal hypertension associated with headache, profuse sweating, palpitation, tachycardia, pallor, and possible fever. Measurement of 24-hour urine epinephrine, norepinephrine, and metabolites (metanephrine and normetanephrine) can lead to the diagnosis, which is then confirmed with either CT or MRI of the abdomen (Sibai, 2011). Symptoms and physical examination findings that point to pulmonary edema necessitate further evaluation with chest x-ray and possible echocardiography (Sibai, 2011).

In the antepartum evaluation of hypertensive disorders of pregnancy, neurodiagnostic imaging is rarely indicated. However, in the postpartum period, the differential diagnosis is wider, especially as distinguishing laboratory findings, such as proteinuria, are not always present. In addition, treatment modalities may be dictated by diagnosis made by imaging. Different studies have examined the utility of neurodiagnostic imaging. In Yancey's series of 22 women with postpartum hypertension or eclampsia, 40.9% underwent head CT, and of these, three had significant findings including diffuse edema, cerebellar hypodensities, and small white matter hypodensities (Yancey et al., 2011). In the evaluation of postpartum headache, Stella found normal imaging in only 32% by employing indications including focal neurologic deficits, new-onset seizures, recurrent seizures despite prophylactic magnesium sulfate, persistent visual changes, or persistent refractory headache (Stella et al., 2007). These abnormal findings included pituitary hemorrhage, posterior reversible encephalopathy syndrome (PRES), cerebral venous thrombosis, inflammatory changes, thalamic lesions, and subarachnoid hemorrhage (Stella et al., 2007). Ultimately, neurodiagnostic imaging studies aimed at evaluating the cerebral vasculature—MRI and arterial and venous angiography—will need to be obtained if these findings are present.

PRES is commonly associated with eclampsia and is clinically characterized by acute onset headache, altered mental status, cortical blindness, and seizures with parietooccipital involvement (Cozzolino et al., 2015; Stella et al., 2007). Primarily occurring in the setting of preeclampsia, one theory of pathophysiology is that severe hypertension exceeds the limits of autoregulation, resulting in brain edema (Lamy, Oppenheim, & Mal, 2014). In addition, in preeclampsia, endothelial cells are damaged and this pressure imbalance leads to vasogenic edema (Bushnell & Chireau, 2011). MRI is the gold standard for diagnosis (Cozzolino et al., 2015). Classic findings of edema in the parietooccipital white matter are seen in Figure 28.1, which shows extensive areas of subcortical increased T2 signal with enhanced diffusivity involving posterior parietal and occipital white matter.

Reversible cerebral vasoconstrictive syndrome is a similar condition, classically presenting with a thunderclap headache, which is more severe and

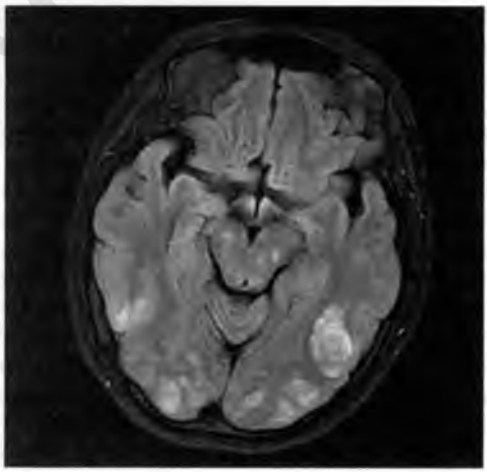

Figure 28.1 MRI findings in PRES

Source: Courtesy of Radiology Department, Women & Infants Hospital, Providence, RI.

TABLE 28.2 Possible Neurologic Etiologies of Postpartum Hypertension

ETIOLOGY	CLINICAL PRESENTATION	RADIOGRAPHIC FINDINGS
PRES	Acute onset headache, altered mental status, cortical blindness, and seizures	MRI shows edema in the white matter of the parietooccipital areas of the cerebral hemisphere
Cerebral vasoconstriction syndrome	Thunderclap headache, visual changes, neurologic deficits, onset postpartum days 3–14	Similar to PRES but with the presence of segmental vasoconstriction on MRI or angiography ("beading"), areas of T2/FLAIR hyperintensity especially in watershed areas
Cerebral venous thrombosis/stroke	Gradual or acute headache, neurologic deficits, seizures, onset postpartum days 3–7	Evidence of thrombus on cerebral venography, possible associated cerebral hemorrhage; MR angiography may show reversible vasospasm of large and medium vessels

FLAIR, fluid attenuated inversion recovery; PRES, posterior reversible encephalopathy syndrome.

Sources: Del Zotto et al. (2011); Sibai (2011); and Stella et al. (2007).

sudden than that associated with PRES. Although the pathophysiology is unclear, it is likely due to a disturbance in the control of cerebral vascular tone (Bushnell & Chireau, 2011). Other possible intracranial etiologies and associated radiographic findings are displayed in Table 28.2.

DIFFERENTIAL DIAGNOSIS

The most common etiology of postpartum hypertension remains the hypertensive disorders of pregnancy, including gestational hypertension and preeclampsia, whether diagnosed originally in the antepartum period or newly onset during postpartum. In a series of 988 women, 77 developed de novo hypertension in the postpartum period. Interestingly, these women were found to have clinical risk factors and antepartum angiogenic factors that were similar to those women who developed preeclampsia in the antepartum period, thus representing a spectrum of disease (Goel et al., 2015). Although the blood pressure may initially appear controlled in the first 48 hours, prompting discharge from the hospital following delivery, it will rise again between postpartum days 3 and 6 (ACOG, 2013; Sibai, 2011). Prior to discharge, women with known hypertensive disorders need to be advised to have blood pressure checked in 2 to 3 days and receive counseling to seek care for severe headaches, which do not respond to pain medications, visual changes, shortness of breath, or chest pain. Women may either present to an emergency facility due to routine blood pressure checks at home or due to associated symptoms and may require antihypertensive therapy in the postpartum period. Possible etiologies of postpartum hypertension are reviewed in Table 28.3.

Other medical causes of hypertension need to be considered and evaluated if the clinical situation is suspicious. These conditions are usually associated with hypertension refractory to treatment, as is the case with renal artery stenosis, and also with associated findings on evaluation. For example, in hyperaldosteronism, the elevated progesterone of pregnancy simulates spironolactone and reverses hypokalemia and hypertension. With the rapid decrease of progesterone

TABLE 28.3 Differential Diagnosis of Postpartum Hypertension

ETIOLOGY	POSSIBLE CONDITIONS
Pregnancy related	Gestational hypertension/preeclampsia (prior antepartum diagnosis or de novo postpartum) Volume overload postdelivery HELLP syndrome Postpartum eclampsia
Medical conditions	Chronic hypertension Preexisting renal disease Hyperthyroidism Cardiomyopathy Lupus nephritis Primary hyperaldosteronism Renal artery stenosis Pheochromocytoma TTP/HUS
Intercranial	Posterior reversible encephalopathy syndrome Cerebral vasoconstriction syndrome Cerebral venous thrombosis/stroke Hypertensive encephalopathy
Medications	Nonsteroidal anti-inflammatories Anticongestants (phenylpropanolamine, ephedrine) Ergotamine, methylergonovine

HELLP, hemolysis, elevated liver enzymes, and low platelets; TTP/HUS, thrombotic thrombocytopenic purpura/hemolytic uremic syndrome.

Sources: Ghuman et al. (2009); Graeber, Vanderwal, Stiller, and Werdmann (2005); and Sibai (2011).

postpartum, exacerbations of hypertension and severe hypokalemia may occur (Sibai, 2011). Graves' disease or postpartum thyroiditis may present with palpitations, tachycardia, sweating, dry skin, and associated heart failure.

When seizures are present, the differential is wide and includes eclampsia, cerebral venous thrombosis, intracerebral hemorrhage, cerebral vasoconstriction syndrome, PRES, hypertensive encephalopathy, space occupying lesions of the brain, and metabolic disorders such as hypoglycemia or hyponatremia (Graeber et al., 2005). A stroke, either due to cerebral hemorrhage or cerebral venous thrombus, may initially present with hypertension due to increased intracranial pressure with increased peripheral vascular tone (Sibai, 2011). In addition, stroke shares many other presenting symptoms with postpartum preeclampsia. A series of 27 women with hemorrhagic or ischemic stroke found that 96% experienced headache, 63% had nausea and vomiting, 71% had focal neurologic changes, and 37.5% had visual changes (Bushnell & Chireau, 2011).

Although it remains rare, stroke incidence in pregnancy, either hemorrhagic or ischemic, has increased. Analysis of the Nationwide Inpatient Sample, the largest nationwide hospital inpatient care database in the United States, showed a rise in all stroke types by 47% in antenatal hospitalizations (0.15–0.22 per 1,000 deliveries) and 83% in postpartum hospitalizations (0.12–0.22 per 1,000 deliveries) from 1994 to 2006 (Kuklina,Tong, Bansil, George, & Callaghan, 2011). A similar rise in pregnant women with heart disease and hypertensive disorders, strong risk factors for stroke, were also seen during this time period, a likely contributor to increased stroke events (Kuklina et al., 2011). However, it can also be noted that, compared to nonpregnant women, women with

stroke in pregnancy or the postpartum period are less likely to have a history of hypertension (Leffert et al., 2016).

Pregnancy itself is a hypercoagulable state associated with venous stasis. These procoagulant changes are highest in the immediate postpartum period and do not return to normal until 3 weeks after delivery (Del Zotto et al., 2011). Data consistently show that the highest risk time for stroke is in the postpartum period (Bushnell & Chireau, 2011; Leffert et al., 2016). One study found a 0.7 relative risk of cerebral infarction during pregnancy, which increased to 5.4 in the first 6 postpartum weeks (Del Zotto et al., 2011). While 28% to 46% of stroke cases in pregnancy have no determined etiology, preeclampsia and cardioembolic events are frequently responsible (Del Zotto et al., 2011). Stroke and preeclampsia share many common risk factors including endothelial dysfunction, dyslipidemia, hypertension, hypercoagulability, and abnormal cerebral vasomotor reactivity. Preeclampsia is seen with 6% to 47% of stroke events, placing women at four times the risk of stroke as compared to women without preeclampsia (Bushnell & Chireau, 2011; Del Zotto et al., 2011). Prompt diagnosis with neuroimaging, especially in women with neurologic changes, is necessary to initiate proper treatment.

CLINICAL MANAGEMENT AND FOLLOW-UP

As the presentation of postpartum hypertension has been largely excluded from studies examining the management of pregnancy-associated hypertension, there are no clear guidelines for management. Appropriate blood pressure control and prevention of seizures are the key management steps. In cases of isolated hypertension, it is appropriate to initiate antihypertensive medications if the systolic blood pressure is persistently above 150 mmHg or the diastolic blood pressure is persistently above 100 mmHg (ACOG, 2013; Podymow & August, 2010). Women with severely elevated blood pressures upon presentation (>160 mmHg systolic or >105 mmHg diastolic) may receive initial treatment with intravenous injections of labetalol or hydralazine, or oral nifedipine (ACOG, 2015; Sibai, 2011). Possible hypertensive regimens are displayed in Table 28.4.

It is necessary to continue treatment until the blood pressure remains below 150/100 mmHg for at least 48 hours, and possibly for several weeks thereafter. Postnatal use of furosemide is associated with a reduced use of antihypertensive therapy in the hospital, but ultimately, the data are too limited, and the likelihood of a large placebo-controlled trial in the future is low (Magee & von Dadelszen, 2013). A Cochrane Review concluded that any antihypertensive agent can be used to maintain blood pressures based on the clinician's familiarity with the drug (Magee & von Dadelszen, 2013). In those women requiring antihypertensives prior to pregnancy or with comorbid conditions such as diabetes or heart disease, it is reasonable to restart the pregestational medication regimen (Sibai, 2011). Nearly all antihypertensive medications are secreted into breast milk. However, overall, antihypertensive medications are safe during lactation and require a dialogue between the woman and physician regarding risks and benefits (Ghuman et al., 2009). Of note, while thiazide diuretics are rated as compatible with breastfeeding by the American Academy of Pediatrics, the drug class has been shown to decrease milk production and can be used in large doses to suppress lactation (Ghanem & Movahed, 2008; Ghuman et al., 2009). However, although randomized controlled trials are not available to fully guide therapy, given the risks of cerebral edema postpartum, this choice of medication in the postpartum period, at lower doses to avoid lactation suppression, is often ideal.

TABLE 28.4 Postpartum Antihypertensive Regimens

MEDICATION	DOSAGE	BENEFITS	METHOD OF ACTION	SIDE EFFECTS	BREASTFEEDING CLASS
ACUTE INTRAVENOUS TREATMENT					
Labetalol	10–20 mg followed by 20 mg incremental increased doses up to 80 mg every 10 min, total cumulative dose 300 mg	Response within 5–10 min, lasts 3–6 hr	Combined alpha-beta blocker, vasodilatory effects	Nausea, vomiting, bronchoconstriction, dizziness, heart block, orthostatic hypotension, avoid in heart failure	Secretion into breast milk, concentration varies, compatible with breastfeeding
Hydralazine	5 mg followed by additional 5–10 mg in 20 min, maximum bolus 20 mg, total cumulative dose 30 mg	Response within 10–30 min, lasts 2–4 hr	Direct acting arteriolar vasodilator	Reflex tachycardia, hypotension, flushing, headache, aggravation of angina, lupus-like syndrome	Relatively low concentration in breast milk, compatible with breastfeeding
MAINTENANCE ORAL TREATMENT					
Labetalol	200–400 mg every 8–12 hr, maximum 2.4 g/d	Lack of associated flushing, tachycardia noted with nifedipine	Combined alpha-beta blocker, vasodilatory effects	Nausea, vomiting, bronchoconstriction, dizziness, heart block, orthostatic hypotension, avoid in heart failure	Secreted into breast milk, concentration varies, compatible with breastfeeding
Nifedipine	10–20 mg every 4–6 hr, maximum 180 mg/d	Improved renal blood flow with resultant diuresis as compared with labetalol	Calcium channel blocker, dihydropyridine type, decreases vascular smooth muscle contractility	Tachycardia, headache, flushing	Secreted into breast milk, relatively high concentration, compatible with breastfeeding
Nifedipine XL	30–90 mg every 24 hr, maximum 120 mg/d	Once daily dosing	Extended release calcium channel blocker, decreases vascular smooth muscle contractility	Tachycardia, headache, flushing, symptoms may be less than with rapid release	Secreted into breast milk, compatible with breastfeeding

Note: All ratings are compatible with breastfeeding as per the American Academy of Pediatrics.

Sources: Ghanem & Movahed (2008), Ghuman et al. (2009), and Sibai (2011).

The treatment of women diagnosed with severe preeclampsia postpartum based on severe pressures and possible associated symptoms includes magnesium sulfate for seizure prophylaxis. This is the preferred management in the antepartum period and its use has been continued in postpartum patients. In Al-Safi's study, 84.9% of patients received magnesium sulfate during their postpartum admission (Al-Safi et al., 2011). A 4 to 6 g loading dose over 20 minutes followed by a maintenance dose of 2 g/hr for at least 24 hours is the recommended regimen (ACOG, 2013; Sibai, 2011). When other etiologies are suspected, a multidisciplinary approach based on the most likely diagnosis is recommended.

CLINICAL PEARLS

- It is critical to quickly evaluate and treat postpartum women who present with elevated blood pressure, especially if associated with prodromal symptoms such as headache.
- Hypertensive disorders commonly present within the first week postpartum.
- Severe complications include eclampsia and stroke. Markedly elevated blood pressures must be treated promptly with antihypertensive medications. Intravenous magnesium sulfate for seizure prophylaxis may be considered if not previously administered antenatally.

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Postpartum Breast Complications

29

Chelsy Caren and David Edmonson

Women commonly present to the obstetric triage/emergency department during the postpartum period with breastfeeding concerns and complications. Breastfeeding has become increasingly popular secondary to worldwide research that has consistently demonstrated significant benefits to both infant and mother. Whereas only 24.7% of women in the United States initiated breastfeeding in 1971, 79% did so in 2011, 49% continued for at least 6 months, and 27% were still breastfeeding 1 year postpartum (American Congress of Obstetricians and Gynecologists Committee on Obstetric Practice, 2016).

The most common difficulties encountered by breastfeeding women are generalized engorgement of the breasts, plugged ducts, and nipple trauma. These conditions generally respond well to supportive care and continued attempts at feeding, and will be discussed briefly at the beginning of this chapter. Postpartum inflammatory breast disease, including puerperal, or lactational, mastitis and breast abscess are less common. It has been estimated that up to 33% of breastfeeding women experience mastitis (Jahanfar, Ng, & Teng, 2013), while only 0.1% (Kvist & Rydhstroem, 2005) to 0.4% (Amir, Forster, McLachlan, & Lumley, 2004) develop abscesses. These latter disorders are infectious in nature and require more intensive treatment, including antibiotics and possible surgery. They will be the topic of the remainder of the chapter.

COMMON BREASTFEEDING DIFFICULTIES

Engorgement and Plugged Ducts

Breast engorgement is the swelling of the breasts resulting from incomplete emptying of milk. Early engorgement occurs with the onset of increased milk production that characterizes the first few days postpartum, when the breasts swell secondary to edema and inflammation in addition to milk accumulation. The lactating mother will commonly report distinct tenderness, firmness, and warmth of the breasts. These findings are usually bilateral and generalized, and erythema tends to be absent. Late engorgement is generally due to milk stasis alone and can be either localized or generalized, though swelling is often not as pronounced. It is uncommon for women with either type of engorgement to report systemic symptoms such as fever or malaise. Both types are generally attributable to incorrect or inconsistent breastfeeding technique, prohibiting efficient drainage of milk from the breasts.

Plugged ducts are also commonly seen in women who report suboptimal breastfeeding technique, or who have increased milk supply relative to demand

due to a change in feeding frequency or intensity. Localized distension of breast tissue occurs as a result of inadequate drainage in a single duct, and can be palpable by the breastfeeding woman as a distinct, tender mass. As with engorgement, systemic symptoms are absent. If unrelieved, a galactocele, or milk retention cyst, may form. Though these are full of milk initially, the contents can become thicker over time. Tenderness usually resolves as well. A soft cystic mass, with no evidence of infection, is often the sole finding on clinical examination. Ultrasound imaging of a galactocele may show a well-defined mass with internal complexity, as shown in Figure 29.1.

The key to the management of generalized engorgement without infection as well as plugged ducts is prevention. This is best accomplished by frequent emptying of the breast, and is most efficiently achieved by breastfeeding the infant directly. A satisfactory latch-on is essential, which proves difficult for many nursing women to establish. Proper positioning of the infant, consistency in feeding techniques, and an environment that is conducive to breastfeeding are all instrumental in allowing the infant to latch-on successfully. Lactation consultants can be called upon when needed to advise and demonstrate to women how best to optimize these factors.

If the latch-on is not sufficient for relief of engorgement or a plugged duct, the use of a breast pump to drain the breasts is recommended. Manual expression and massage can also be helpful. While cold compresses are preferred to address the swelling that accompanies early engorgement, heat is more useful in cases of late engorgement and plugged ducts, both for symptom relief and to encourage milk flow. Galactoceles may resolve spontaneously or may be treated with aspiration or surgical removal.

Of note, a very recent randomized double-blind placebo-controlled trial suggests that efforts to prevent infectious mastitis may begin during pregnancy as well. Significantly lower rates were found in women who received an oral

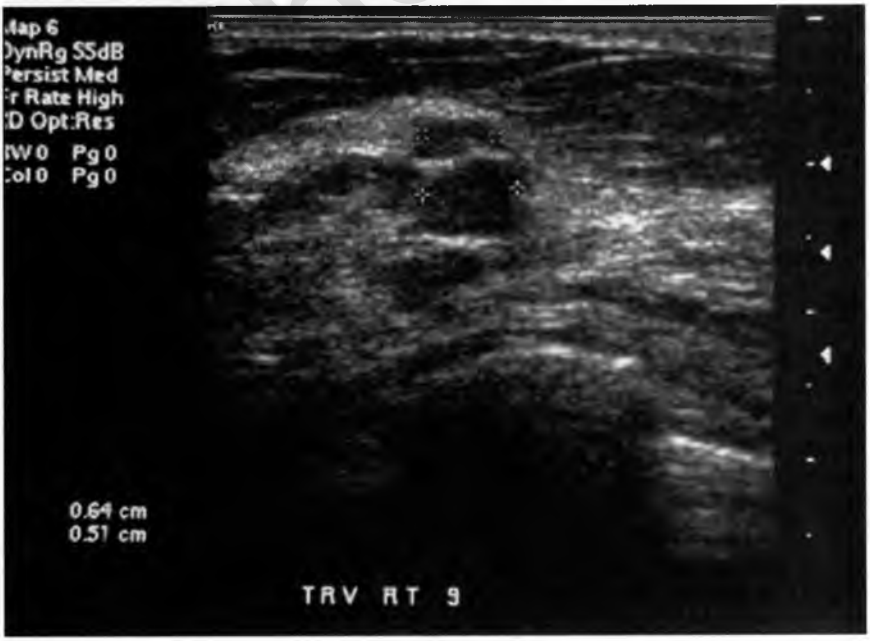

Figure 29.1 Ultrasound appearance of a galactocele

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

TABLE 29.1 Lactation Resources

RESOURCE	WEBSITE
The Academy of Breastfeeding Medicine	www.bfmed.org
Baby Friendly USA	www.babyfriendlyusa.org
La Leche League	www.llli.org
National Association of Professional and Peer Lactation Supporters	www.napplsc.org
Medications and Mother's Milk	www.medsmilk.com/menu.html
US Breastfeeding	www.usbreastfeeding.org
US Lactation Consultant Association	www.uslca.org

Source: Briggs et al. (2011).

probiotic during the third trimester of pregnancy, 25% versus 57% with mastitis in the placebo group (Fernandez et al., 2016). In addition, the bacterial counts in the milk of women who had been given the probiotic but still developed mastitis were significantly lower than the counts for the women with mastitis in the placebo group.

Nipple Trauma

Nipple trauma, including abrasions, cracking, blistering, or bruising, can be the cause or result of a poor latch-on, thereby discouraging ongoing efforts to breastfeed. The best preventative measure is proper positioning of the infant to ensure optimal latch-on. When this is complicated by an anatomic abnormality of the woman's nipples or the infant's mouth, a lactation consultation is recommended.

Once present, various treatments are available that can be used to decrease soreness and heal traumatized nipples. These include purified lanolin ointments, hydrogel dressings, or the combination of antibiotic, antifungal, and mild steroid therapy known as "all-purpose nipple ointment." In addition, breast shields may be utilized to prevent friction to nipples between feedings as needed. Since infections of the skin and breast, most commonly with *Candida albicans* or *Staphylococcus aureus* (see the following text), occur more frequently in women with injured nipples (Lawrence & Lawrence, 2015), it is crucial to address nipple trauma early in its course.

Resources

Women presenting with the previous general breastfeeding difficulties may be experiencing a great deal of distress and anxiety. The ability to provide information and guidance to these nursing mothers can help to reassure them that such challenges are not uncommon, and encourage them to continue breastfeeding. Some popular resources are listed in Table 29.1, and can assist in providing lactation support or verifying the compatibility of a certain recommended treatment with breastfeeding.

POSTPARTUM INFLAMMATORY BREAST DISEASE

The term "postpartum inflammatory breast disease" includes both lactational mastitis and breast abscesses. Mastitis is caused when bacteria, commonly skin flora and/or oral flora from the infant, have access to stagnant milk in the

breast, generally via the nipple. If left untreated, the infection may progress to abscess formation, which is estimated to occur approximately 3% to 11% of the time (Amir et al., 2004).

The most common etiologic organism in postpartum inflammatory breast disease is *S. aureus* and *Staphylococcus albus* (Jahanfar et al., 2013). *Streptococcus pyogenes*, *E. coli*, *Bacteroides* species, Coagulase negative staphylococci, *Proteus*, and *Corynebacterium* species are also found in some milk cultures. *Candidal* breast infections will be discussed separately in the Differential Diagnosis section. Methicillin-resistant *Staphylococcus aureus* (MRSA) is gaining increasing importance as a causative organism of mastitis as well as skin infections in general (Schoenfeld & McKay, 2010). Risk factors for the presence of MRSA include recent hospitalization, positive culture results confirming colonization by MRSA in the past (personal or close family member), chronic illness or non-healing wounds, or failure of treatment directed toward methicillin-sensitive *S. aureus*. In one study of milk cultures from women who required hospitalization for treatment of mastitis, MRSA was the most common organism isolated; 44% (24 of 54) for women with mastitis alone, and 67% (18 of 27) in women with abscess formation (Reddy, Qi, Zembower, Noskin, & Bolon, 2007).

PRESENTING SYMPTOMATOLOGY

The most common complaints reported by a breastfeeding woman with mastitis include pain and tenderness in the affected breast. Warmth and/or redness of the breast and nipple discomfort, cracking, or excoriation are often noted as well. Fever and flu-like symptoms including malaise and myalgias are common. Axillary pain due to reactive swelling of the lymph nodes on the affected side may also occur. Finally, when a breast abscess is present, the breastfeeding woman may report the presence of a painful mass in the affected breast. Septic shock is rare.

HISTORY AND DATA COLLECTION

The postpartum woman with the previous symptoms will typically describe a history of difficulty with breastfeeding. Reports of poor milk production or a sensation of incomplete emptying of the affected breast are common, as is a history of prolonged engorgement, a blocked duct, or nipple trauma. Weaning may be in progress. Any factor that increases the likelihood that stagnant milk is present increases the risk of postpartum inflammatory breast disease. A prior episode of mastitis and/or breast abscess while breastfeeding either the current or a previous infant increases this risk as well.

A woman who presents with worsening symptoms despite standard treatment for mastitis is at increased risk for having either less common or resistant organisms such as MRSA present in the breast milk. A breast abscess is more likely under these circumstances as well. Breast abscesses are more frequently seen in primigravidas, women over the age of 30, and women who delivered at 41 or more weeks gestation (Kvist & Rydhstroem, 2005). Smokers, obese women, and African Americans are at higher risk of both lactational as well as nonlactational abscesses (Bharat, Gao, Aft, Gillanders, Eberlein, & Margenthaler, 2009).

PHYSICAL EXAMINATION

Examination of the affected breast of a woman with postpartum inflammatory breast disease usually reveals erythema and swelling. Early in the course of

the infection, subtle streaks of light pink in a single region of the breast may be the only visible abnormality. In later stages, a firm, red, swollen area of the breast, exquisitely tender to palpation or to ongoing attempts to breastfeed, may develop. Classically, these findings are limited to one region of the breast, extending from the nipple outward in a wedge-shaped pattern. However, either localized or generalized engorgement may be found as well. A fluctuant mass is often palpable when an abscess is present. Fever may be documented, and, if so, tachycardia may present as well. Hypotension is uncommon except in rare cases of systemic inflammatory response syndrome (SIRS) or sepsis related to an ongoing or inadequately treated infection.

LABORATORY AND IMAGING STUDIES

Lactational mastitis can be diagnosed by clinical examination alone, and empiric antibiotic therapy may be initiated without laboratory testing or culture results. If a complete blood count (CBC) is drawn, however, the white blood cell count may be elevated. Breast milk can and often should be cultured, especially with a severe or recurrent infection, or with one that is persistent despite prior antibiotic treatment. The results can then be used to tailor the ultimate antibiotic selection, since mixed flora, anaerobes, and *Proteus* are found more commonly in these cases (Bharat et al., 2009). Blood cultures are recommended only if the breastfeeding mother appears septic.

Imaging studies are not required for the diagnosis of lactational mastitis, nor are they necessary to make a diagnosis of a lactational abscess if a fluctuant mass is found on clinical breast exam. However, as will be discussed later in the chapter, ultrasound is often used to confirm an uncertain diagnosis, as well as to direct aspiration of a fluid collection. Figure 29.2 shows the typical appearance of a breast abscess on ultrasound.

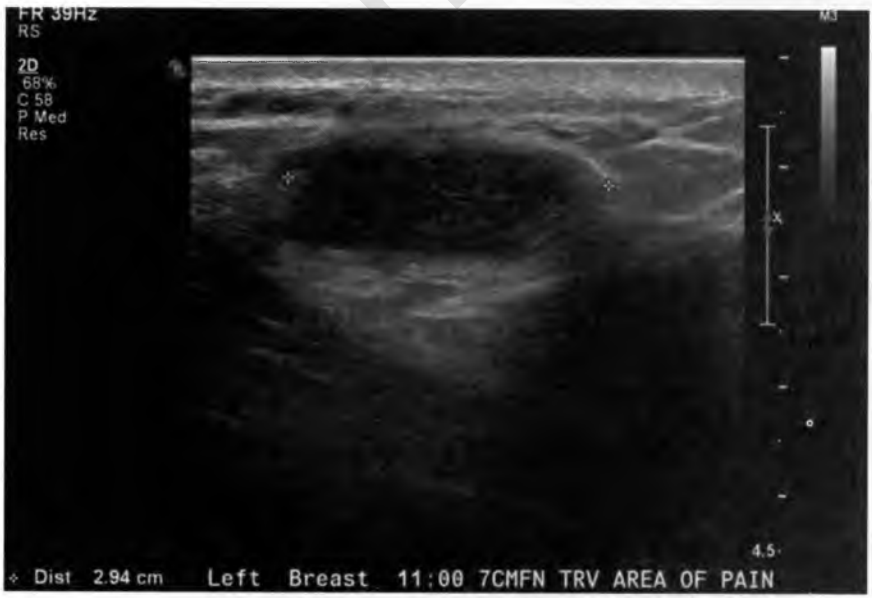

Figure 29.2 Ultrasound appearance of breast abscess

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

DIFFERENTIAL DIAGNOSIS

Lactational mastitis is the most common, benign, inflammatory breast disorder (Pearlman & Griffin, 2010). The differential diagnoses for postpartum inflammatory breast disease include conditions similarly unique to breastfeeding women, such as generalized engorgement and plugged ducts (discussed previously), and infections with *C. albicans*. Several additional nonpuerperal inflammatory skin conditions and breast disorders are included as well, the most common of which are discussed here.

Candidal Breast Infections

The lactating woman with a candidal infection of the breast will often present complaining of "shooting pains" in the breast along with redness and nipple discomfort. A history of a recent diagnosis of or treatment for oral thrush in the infant may also be reported. The inflammation seen with candida of the breast, as elsewhere, is typically a localized erythema with satellite lesions, consistent with but not essential for the diagnosis. Systemic findings are generally absent. Candidal infections are treated with the topical or oral antifungal agents listed in Table 29.2 (Pearlman & Griffin, 2010). Of note, unlike the ointments used for the treatment of nipple trauma mentioned previously, topical preparations of nystatin should be washed off prior to breastfeeding.

Superficial Skin Conditions

Additional skin conditions such as eczema and contact dermatitis may be part of the differential diagnosis in some breastfeeding mothers as well. A thorough medical history including any possible exposures to substances that may cause such skin conditions will assist in making an accurate diagnosis. These conditions often respond to conventional therapies. Of note, recurrent scaling/crusting of the nipple is seen in Paget's disease. If this diagnosis is entertained, evaluation with a breast specialist for a biopsy should be arranged, in order to investigate the possibility of an underlying inflammatory breast cancer, as noted in the following text.

Periductal Mastitis

Squamous metaplasia of the breast duct lining along with keratin plugging of the ducts is thought to lead to a condition known as periductal mastitis, or "mammary duct-associated inflammatory disease syndrome" (MDAIDS). This is a focal, often recurrent, benign inflammation specifically of the periareolar area of the affected breast. It can be accompanied by abscess formation or mammary duct fistula, can occur at any age, and is particularly common in smokers (70% of affected women are active smokers [Degnim, 2011]). Empiric antibiotic therapy is broad-spectrum, to include for anaerobes as well as for *Staphylococcus* species. In addition to cultures, prompt imaging evaluation and biopsies are advocated to exclude inflammatory breast cancer, especially when worrisome skin findings (see the following text) or nipple retraction are present. With the rate of recurrence and/or chronic fistula formation estimated to be as high as 80% to 90%, definitive surgical treatment is often warranted (Degnim, 2011).

TABLE 29.2 Presentation and Treatment of Common Postpartum Breast Complications

COMPLICATION	BREAST ENGORGEMENT	PLUGGED DUCTS	CANDIDA
Symptoms/ Signs	• Pain, fullness/firmness, warmth and tenderness of breasts • Bilateral and generalized • Absence of erythema • Absence of systemic symptoms	• Distinct, painful breast mass • Absence of erythema • Absence of systemic symptoms	• "Shooting pains" in the breast • Erythema often localized with satellite lesions • Nipple discomfort
Management	• Frequent emptying of the affected breast • Cold compresses with early presentation • Warm compresses with late presentation • Treatment of nipple trauma • Pain management (Ibuprofen, other NSAIDs)	• Frequent emptying of affected breast • Warm compresses • Pain management (Ibuprofen, other NSAIDs)	**First line:** Topical nystatin 100,000 units/g; apply bid-tid after breastfeeding and wash off prior to next feeding **Second line:** Oral fluconazole 100 mg PO daily × 10–14 d

COMPLICATION	LACTATIONAL MASTITIS	LACTATIONAL ABSCESS	INFLAMMATORY BREAST CANCER
Symptoms/ Signs	• Pain and tenderness of the affected breast • Erythema and warmth of one region of the affected breast • Usually unilateral • Fever and flu-like symptoms are common	• Same as for mastitis **Plus:** • Distinct, painful breast mass • Systemic symptoms are common	• Same as for mastitis and abscess **Possible:** • Skin thickening and/or edema • "Peau d'orange" • Persistence of symptoms and signs despite appropriate treatment for mastitis and/or abscess
Management	• Dicloxacillin 500 mg PO qid OR Cephalexin 500 mg PO qid **If beta-lactam hypersensitive:** Clindamycin 300 mg PO qid **If MRSA suspected:** Trimethoprim-sulfamethoxazole 1–2 tabs PO bid OR Clindamycin 300 mg PO qid (All of the above for 10–14 d) **If severe:** Vancomycin 30 mg/kg IV in two divided doses daily	• Antibiotics as for mastitis • General surgery consultation • Needle aspiration OR • I&D	• Imaging • Breast surgery consultation

bid, twice daily; I&D, incision and drainage; IV, intravenous; MRSA, Methicillin-resistant *Staphylococcus aureus*; *NSAIDs, Nonsteroidal antiinflammatory drugs;* PO, per os (orally); qid, four times daily; tid, three times daily.

Sources: American Congress of Obstetricians and Gynecologists (2016); Jahanafar et al. (2013); Lawrence and Lawrence (2015); Pearlman and Griffin (2010).

As previously mentioned, inflammatory breast cancer has many characteristics in common with postpartum breast disease. It is crucial to consider this diagnosis in cases where a presumed mastitis does not respond to the usual treatments. It is also more likely when skin thickening, edema, or "peau d'orange" appearance (shown in Figure 29.3) or nipple retraction are present. Imaging and referral to a breast surgeon for definitive diagnosis is recommended in such cases. Of note, while ultrasound and/or mammogram are usually performed initially, magnetic resonance imaging (MRI) of the affected breast can be helpful in distinguishing between mastitis and inflammatory breast cancer (Renz et al., 2008). However, it is generally reserved for cases in which the latter is suspected, as in Figure 29.4.

Postoperative and Postirradiation Mastitis

In established breast cancer patients, surgical site infections as well as radiation changes can mimic puerperal disease, but the clinical history and treatment will differ accordingly. Postoperative or postirradiation mastitis is a delayed cellulitis found in women who have undergone prior surgery or radiation for breast cancer, commonly 3 months to several years post-treatment. It is recommended that these women be referred to their oncologists for evaluation, as this may be a sign of altered lymphatic or venous circulation.

CLINICAL MANAGEMENT AND FOLLOW-UP

The management of a breastfeeding woman with mastitis includes empiric antibiotic therapy as well as supportive care intended not only to provide relief

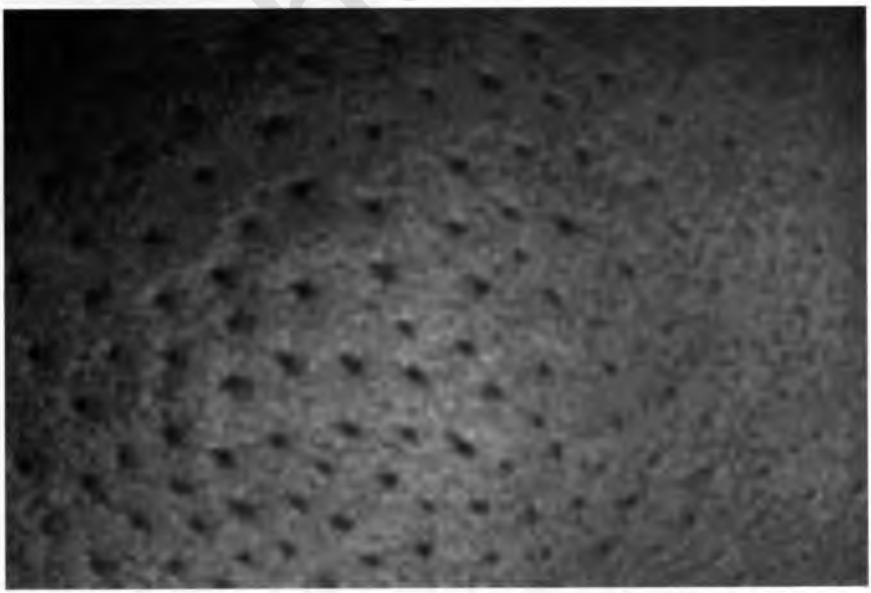

Figure 29.3 Photograph of "peau d'orange"

Source: Courtesy of David Edmonson, MD, Department of Obstetrics and Gynecology, Women and Infants Hospital.

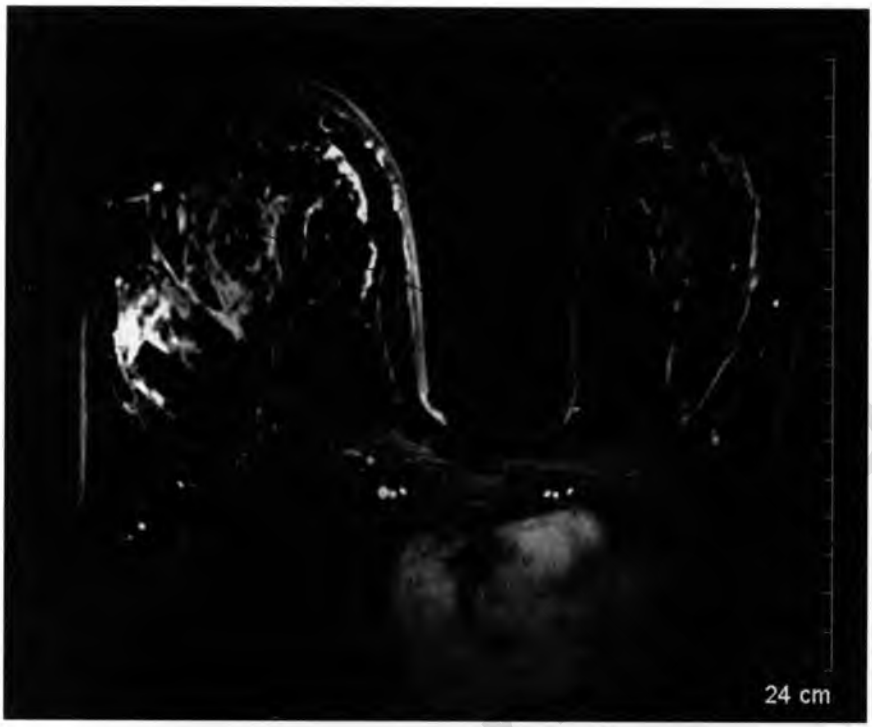

Figure 29.4 MRI of inflammatory breast cancer

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

of symptoms, but also to promote continued breastfeeding during treatment. Although one study showed that probiotics may be a useful alternative to antibiotics in the management of women with lactational mastitis (Arroyo et al., 2010), antibiotics remain the standard of care at present. In the absence of severe infection, abscess, or risk factors for MRSA, outpatient therapy is directed primarily against *S. aureus*. A 10- to 14-day course of dicloxacillin or cephalexin is first line, with clindamycin preferred for women with beta-lactam hypersensitivity. If there is concern for MRSA infection, trimethoprim-sulfamethoxazole or clindamycin are recommended. Table 29.2 lists the recommended antibiotic regimens. Re-evaluation is recommended if improvement is not noted within a few days of initiating therapy, or if full resolution is not present upon completion of therapy. In severe cases, defined as such by progressive erythema despite empiric therapy or hemodynamic instability indicative of sepsis, hospitalization and intravenous vancomycin are recommended. In such cases, culture and sensitivity results from a midstream milk culture can be used to direct the ultimate antibiotic regimen/therapy.

Continued breastfeeding throughout treatment for mastitis is strongly recommended. Regular emptying of the breast, by preventing engorgement and milk stasis, can significantly decrease duration of symptoms as well as prevent abscess formation (Jahanfar et al., 2013). Cold compresses/ice packs and anti-inflammatory agents such as ibuprofen can provide symptomatic relief of pain and swelling and may increase the ability to comply with this recommendation. Improved breastfeeding techniques can also be helpful, as can treatment of traumatized nipples, as previously mentioned. If, despite all

of these measures, breastfeeding is too difficult or painful, breast pumps or hand expression may facilitate emptying and maintain milk supply until it can be resumed. Finally, rest and increased fluid intake are advised. Of note, bromocriptine, a dopamine agonist used in the past to suppress lactation in postpartum women, is no longer recommended due to reports of serious adverse reactions including stroke, myocardial infarction, seizures, and severe hypertension (Department of Child and Adolescent Health and Development, 2000). If discontinuation of breastfeeding becomes necessary, natural suppression is endorsed as the best method.

When an abscess is present, standard management is drainage of the contents in addition to the antibiotic therapy described previously. Consultation with a surgeon with expertise in breast disease is recommended in these cases. Traditionally, drainage was by incision and drainage (I&D). However, needle aspiration has been shown to be equally effective (Eryilmaz, Sahin, Hakan Tkelioglu, & Daldal, 2005). Particularly in the presence of normal-appearing overlying skin, aspiration with a medium to large bore needle under local anesthesia is now recommended as the initial approach. This results in decreased incisional prominence and pain, thereby optimizing the likelihood of ongoing lactation. Ultrasound guidance is advised in order to completely drain the contents of the abscess cavity, since the collection may not be detectable by physical exam alone, or more than one loculation may be present, as in Figure 29.5. Serial evaluations and aspirations are then performed, approximately every 2 to 3 days, until no further purulent material is obtained. It has been estimated that greater than 90% of lactational abscesses can be treated in this manner, thereby avoiding surgery (Degnim, 2011).

In cases where an abscess persists despite standard antibiotic regimens and serial aspirations, surgical drainage is indicated (Christensen et al., 2005). This is more common when there is a delay in initial treatment, when the

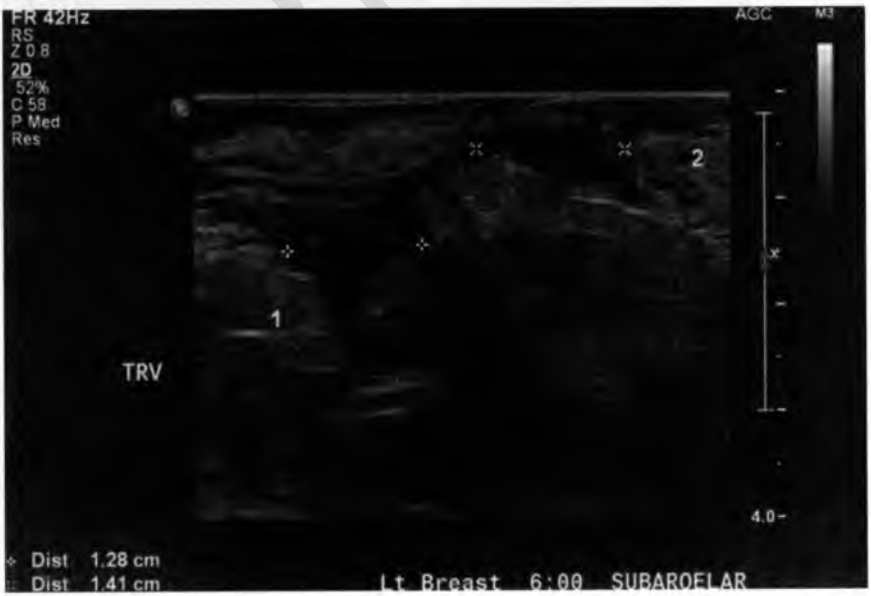

Figure 29.5 Ultrasound appearance of a multi-loculated breast abscess

Source: Courtesy of the Department of Radiology, Women & Infants Hospital, Providence, RI.

infection is more severe, or when the abscess is greater than 5 cm in diameter (Eryilmaz et al., 2005). Skin changes such as thinning, excessive tension, and/or devascularization generally mandate I&D as well. If skin necrosis is present, the affected skin is excised and the cavity irrigated to drain the pus, and then the site is intervally reinspected to resolution. Packing and/or drains are generally not implemented (Dixon, 2007), and may increase the risk of formation of a milk or a mammary duct fistula, a communication between the skin and a lactiferous duct or major subareolar duct, respectively. Both types result in milk draining through the skin of the breast. While a milk fistula generally resolves with cessation of breastfeeding, a mammary duct fistula requires additional surgical intervention for correction (Degnim, 2011). Poor cosmetic outcome is rare, though it may result from the initial I&D of a breast abscess or from the attempts to correct any subsequent complications. Diagnostic imaging is recommended approximately 3 months after resolution of any lactational abscess, in order to evaluate for any residual mass or signs of malignancy.

CLINICAL PEARLS

- Worldwide research has consistently demonstrated significant benefits to both infant and mother as a result of breastfeeding.
- The key to the management of generalized engorgement without infection, plugged ducts, nipple trauma, and mastitis is prevention.
- When a presumed mastitis does not respond to the standard treatments, it is crucial to consider a diagnosis of inflammatory breast cancer in the differential.

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Secondary Postpartum Hemorrhage and Endometritis

30

Rachel Shepherd and Martha Pizzarello

In the postpartum period, secondary postpartum hemorrhage (SPPH) and endometritis are two conditions that frequently present to an obstetric triage unit. These complications may coexist and can occur from 24 hours postpartum to 6 weeks postdelivery. SPPH is typically not as severe as a primary bleeding episode. Only 10% of the time will the hemorrhage be significant enough to cause a change in vital signs (Neil & Thorton, 2002). Likewise, postpartum women ultimately diagnosed with endometritis are generally stable, but less commonly can present in septic shock. In the obstetric triage or emergency setting, continual monitoring of vital signs is essential as healthy, young women frequently maintain their vital signs, only to quickly decompensate as the hemorrhage or infection continues.

SECONDARY POSTPARTUM HEMORRHAGE

Secondary postpartum hemorrhage is diagnosed following 0.5% to 2% of deliveries in developed countries (Lu et al., 2005). There are no randomized controlled trials to guide the evaluation and treatment as in primary postpartum hemorrhage, but guiding principles for managing hemorrhage remain the same.

PRESENTING SYMPTOMATOLOGY

The postpartum woman often presents with a sudden increase in bleeding, after having experienced a tapering of normal lochia. Pain may or may not be present. Fever and uterine tenderness may be present if an infection coexists.

HISTORY AND DATA COLLECTION

The initial history includes quantifying the amount of bleeding. Symptoms of clinically significant anemia, such as shortness of breath, lightheadedness, heart racing, or syncope, are solicited. A determination of the specific cause of the hemorrhage may assist in forming the treatment plan. Therefore, a thorough history includes prior obstetric procedures, fertility treatments, and other surgeries that have been associated with specific conditions such as an

intrauterine aneurysm or placental abnormalities (Kovo, Behar, Friedman, & Mailinger, 2007). Any history of bleeding in the initial postpartum period is significant since two-thirds of women with SPPH will have experienced a primary hemorrhage. In these cases, the pace of the evaluation must be prioritized, as significant anemia may already precede the second bleeding episode. Details about bleeding disorders are solicited as one-third of women who experience a SPPH have Von Willebrand's disease (Barbarinsa, Hayman, & Draycott, 2011). The delivery record is reviewed and the following are noted: length of rupture of membranes, length of labor, augmentation of labor, any diagnosis of chorioamnionitis, and blood counts available prior to the time of initial discharge. In addition, there is a review of how the placenta was delivered, especially noting if manual removal of the placenta was required or if any abnormalities were observed on inspection of the placenta. The mode of delivery is another key piece of history, since retained products as a cause for the hemorrhage is less likely with cesarean birth. The mean time between delivery and SPPH was 13.4 days in a recent cohort study (Dossou, Debost-Legrand, Dechelotte, Lemery, & Vendittelli, 2015).

PHYSICAL EXAMINATION

In obstetric triage, vital signs need to be noted immediately. It is critical to remember that in a healthy woman, over 1 L of estimated blood loss can occur before there is a significant change in vital signs. Therefore, vital signs will need to be trended regularly and monitored for increasing tachycardia, hypotension, and decreasing oxygen saturation. A fever is suggestive of a coexisting infection. Skin color and capillary refill are helpful physical indicators of hemoglobin levels. Abdominal palpation of the postpartum uterus for tenderness and size is informative. An enlarged uterus may suggest that retained products of conception are a factor in the bleeding. A pelvic examination is performed to examine the vagina and cervix for lacerations. The presence of foul smelling lochia in the vagina and notation as to whether or not the woman is still actively bleeding are additional key findings on pelvic examination.

LABORATORY AND IMAGING STUDIES

Essential laboratory tests include a complete blood count, coagulation profile, type and screen, and/or cross match, if indicated. A radiology ultrasound is indicated if the woman is clinically stable. If there is hemodynamic instability, a bedside ultrasound can be useful in quickly determining a cause for the SPPH. If the uterine cavity is distended and full of heterogeneous material, especially if blood flow is seen when the color Doppler function is applied, then retained products of conception is the likely diagnosis. Figure 30.1 represents a sonographic image of retained products of conception, subsequently confirmed at the time of dilatation and curettage.

It may be normal to see fluid and mixed echogenicity within the uterine cavity while performing ultrasonography on an involuting, postpartum uterus, depending on how much time has elapsed since delivery. The maximum thickness of the intrauterine contents is noted. Hematometra and clots will not typically demonstrate blood flow on ultrasound color Doppler flow. If flow to the intrauterine contents is noted, it is more likely to represent retained products of conception (Multic-Lutvica & Axelsson, 2006). Additional pathologic findings that can be diagnosed by ultrasound include fibroids or intrauterine vascular malformations.

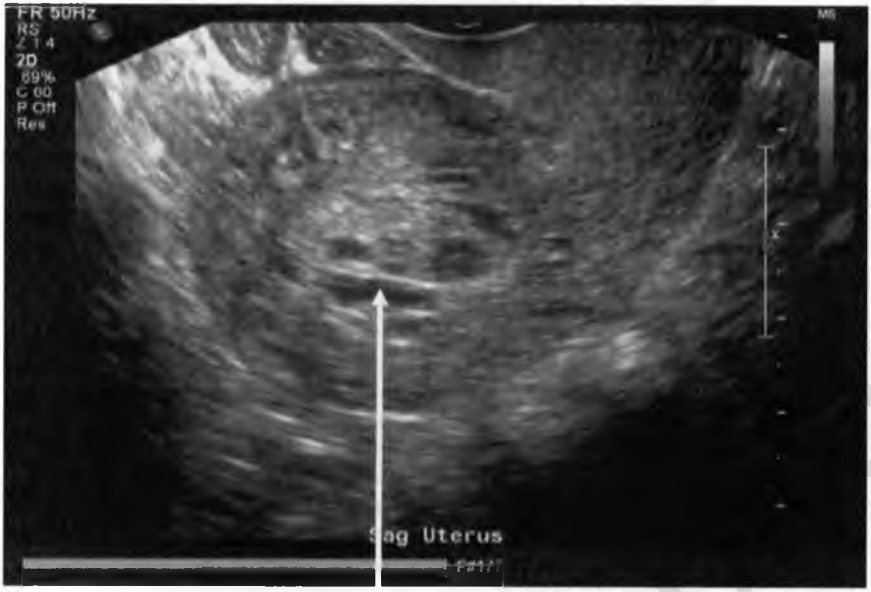

Figure 30.1 Retained products of conception

Source: Courtesy of Department of Radiology, Women & Infants Hospital, Providence, RI.

EXHIBIT 30.1

Causes of Secondary Postpartum Hemorrhage

- Idiopathic subinvolution of the uteroplacental vessels
- Retained placental tissue
- Endometritis
- Placenta accreta, increta, or percreta
- Von Willebrand's disease
- Fibroids
- Vascular malformation of the uterus including A-V malformations and uterine artery aneurysms

Source: Adapted from Barbarinsa et al. (2011).

DIFFERENTIAL DIAGNOSIS

The primary differential in SPPH is menses and secondarily postpartum bleeding that is within the normal range, but bothersome to the woman. Rarely, cancers can present as late postpartum bleeding both with an acute bleed or persistent postpartum bleeding (Riggs, Zaghami, Najid, Haber, & Schreffler, 2010). If SPPH is diagnosed, the determination of the cause of the hemorrhage will assist in formulating an appropriate treatment plan. Exhibit 30.1 lists the causes of SPPH, appearing in order of decreasing incidence (Barbarinsa et al., 2011).

Clinical management is driven by the initial assessment. If vital signs are abnormal and there is active bleeding, stabilization is the primary goal. Clinical management is initially similar to primary postpartum hemorrhage. Intravenous access with two large bore lines and crystalloid fluid boluses will be the first step. Anesthesia assistance may be necessary to secure intravenous lines and the airway. Blood transfusions, intravenous antibiotics, and medical versus surgical treatment are the next decision points. A stat bedside ultrasound will reveal information to drive the next steps. Review of the literature indicates that there is no single management protocol that is proven to have better outcomes than any other (Alexander, Thomas, & Sanghera, 2002). Figure 30.2 outlines one management protocol based on evidence in the literature, but it remains unproven.

Surgical procedures performed for a woman who is experiencing significant postpartum hemorrhage carry increased risks. The woman must be made aware of these risks at the time of consent. If the uterus is atonic or infected, then the risk of uterine perforation at the time of dilatation and curettage is increased significantly. Disseminated intravascular coagulation (DIC) may result from an episode of massive hemorrhage or severely infected retained products of infection. If DIC occurs, surgical attempts may be unsuccessful, and a hysterectomy will need to be considered. Hysterectomy will be indicated if a placenta accreta or percreta is diagnosed at the time of curettage.

Ninety percent of the time, the woman's condition will not be critical and there is time for more options to be considered. In a 2001 study of 132 women with SPPH, 75 women (57%) were initially treated with surgical dilatation and curettage, which was successful 90% of the time. Of the 57 women initially managed medically, treatment was successful in 41 (72%) women, but 12 of 16 women with continued symptoms ultimately went on to require

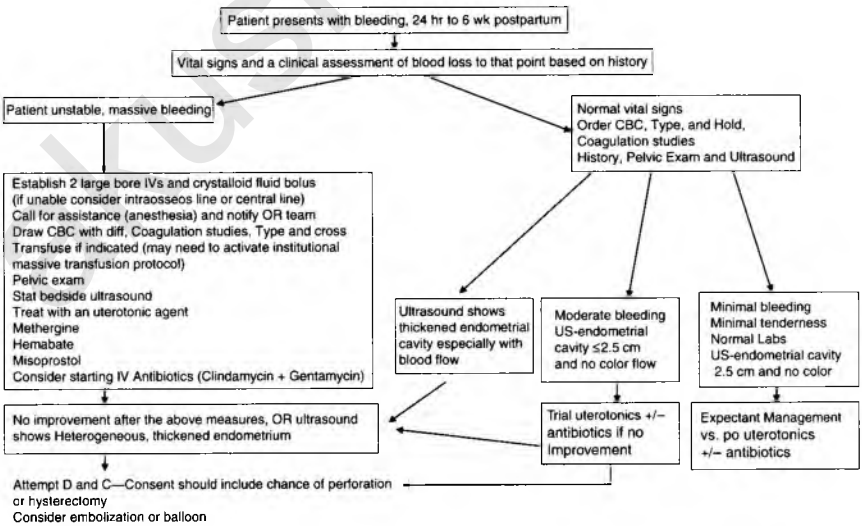

Figure 30.2 Management plan for secondary postpartum hemorrhage

CBC, complete blood count; IV, intravenous; OR, operating room; US, ultrasound.

Source: Used with permission, D. LaFontaine MD.

surgery. In the cases that submitted tissue for pathology, retained products of conception were documented in one-third of the women (Hoyveda & MacKenzie, 2001). So, if retained products are not identified on ultrasound, the literature indicates that surgery may still be helpful. If bleeding continues or if an arteriovenous malformation or pseudoaneurysm is considered, then embolization by interventional radiology may be indicated. Placement of a balloon tamponade may also be considered, especially as a temporizing measure, until either surgery or an interventional procedure by radiology can be pursued as a definitive treatment.

Medical management consists of intravenous antibiotics and uterotonic medications. Again, no specific uterotonic agent has proven more beneficial than any other in the setting of SPPH. In the clinically stable patient without ultrasound findings of retained placental tissue, medical management may be attempted initially. The Cochrane Review on treatments for SPPH suggests the need for a well-designed randomized controlled trial to compare the various therapies (Alexander et al., 2002).

POSTPARTUM ENDOMETRITIS

Postpartum endometritis refers to infection of the decidua or myometrium and parametrial tissues after the first 24 hours postpartum. Endometritis is most commonly a polymicrobial infection involving both aerobes and anaerobes from the female genital tract. Rare, but lethal causes of endometritis include group A *Streptococcus and Clostridium* leading to toxic shock-like syndrome. Group A *Streptococcus* typically presents with endometritis very early in the postpartum period with high fever (Jorup-Ronstrom, Hofling, Lunberg, & Holm, 1996). Postpartum endometritis infections caused by *Clostridium sordellii* are likely to present during the first postpartum week, and are notable for rapid decompensation of the patient, leading to septic shock (Bitti et al., 1997).

PRESENTING SYMPTOMATOLOGY

The most common presenting symptom in cases of postpartum endometritis is fever, typically 38°C to 39°C. Abdominal pain is another common presenting symptom. The postpartum woman may also note a foul odor to the lochia or an increase in vaginal bleeding. The diagnosis is a clinical one and is based on the combination of abdominal pain and fever in the absence of other causes of pathology. To make a correct diagnosis of postpartum endometritis, the following conditions must be excluded: urinary tract infection, mastitis, wound infection, pulmonary embolism, viral illness, appendicitis, or other obvious infectious etiologies. Endometritis must be high in the differential of the postpartum patient who presents in septic shock.

HISTORY AND DATA COLLECTION

The mode of delivery is a key piece of information, since the single most critical risk factor for endometritis is route of delivery (Burrows, Meyn, & Weber, 2004). The risk for endometritis following a surgical delivery is much higher than that of a vaginal delivery. Other risk factors are solicited during the history and these include prolonged labor, prolonged rupture of membranes, multiple cervical exams, internal monitoring, and manual removal of the placenta.

A lower abdominal examination may elicit significant tenderness over the uterine fundus and parametria. If the abdominal examination is equivocal, a pelvic exam may be more specific in identifying uterine and parametrial tenderness. Speculum examination may demonstrate foul smelling lochia, but this finding is neither sensitive nor specific (Lasley, Eblen, Yancey, & Duff, 1997).

LABORATORY AND IMAGING STUDIES

The diagnosis of postpartum endometritis is a clinical one. An elevated white blood count will support the diagnosis of infection. Blood cultures are typically negative and are unlikely to help determine management, unless the patient appears septic. An ultrasound may identify the presence of retained products of conception. If retained products are present, these must be evacuated to ensure successful antibiotic treatment. Endocervical and vaginal cultures are not recommended in the routine postpartum woman with fever and pain, since it is difficult to obtain a specimen uncontaminated by cervical or vaginal flora. If microbiology of the organism is necessary, consider an endometrial biopsy under sterile conditions. The specimen is submitted to microbiology in normal saline for gram stain, culture, and sensitivity. Results will be available later in the hospital course and can inform the choice of antibiotics.

CLINICAL MANAGEMENT

For moderate to severe infections, intravenous therapy with broad-spectrum antibiotics is indicated. A commonly used regimen, with a reported 90% to 97% success rate, is clindamycin plus gentamicin. A meta-analysis comparing clindamycin plus an aminoglycoside with other regimens found that the treatment failure was higher with all other regimens. Daily dosing of gentamicin is as efficacious and safe as every 8-hour dosing of gentamicin (Livingston et al., 2003). Improvement is generally seen in 48 hours. A recent Cochrane Review confirmed preferential treatment with clindamycin and gentamicin (Mackeen, Packard, Ota, & Speer, 2015). For mild cases in resource-limited areas, oral or intramuscular antibiotics may be considered; however, there is no current evidence-based recommendation to treat postpartum endometritis in this manner (Meaney-Delman, Bartlett, Gravett, & Jamieson, 2015).

Persistent fever or incomplete resolution of tenderness on examination, despite antibiotic treatment, dictates the need for further radiologic imaging studies to assess for the presence of an abscess, infected hematoma, and septic pelvic thrombophlebitis. If an inadequate response is seen to clindamycin and gentamicin, then antibiotic coverage should be broadened with the addition of ampicillin. In the penicillin allergic woman, vancomycin can be added. Antibiotics are continued until the woman is afebrile for 24 to 48 hours. At that time, antibiotics can be discontinued. In the case of proven bacteremia, oral antibiotics can be administered for a total of 14 days and the choice of outpatient antibiotics is guided by sensitivity results. In cases where retained products of conception are identified as the nidus for infection, it is recommended to administer one dose of clindamycin and gentamicin before proceeding to dilatation and curettage. Antibiotic regimens, the recommended doses, and potential effects on breastfeeding are noted in Table 30.1.

TABLE 30.1 Antibiotic Regimens for Postpartum Endometritis

PARENTERAL DRUG REGIMENS	DOSES	SAFETY IN BREASTFEEDING (AMERICAN ACADEMY OF PEDIATRICS)
Gentamicin *plus*	4–7 mg/kg/d 900 mg q 8 hr	Yes
Clindamycin *may add*	2 g q 6 hr	Yes
Ampicillin		Yes
Ampicillin-sulbactam	3 g q 6 hr	Yes
Ceftriaxone	2 g q 12 hr	Yes
Levofloxacin *plus*	500 mg q 24 hr	Unknown
Metronidazole	500 mg IV or po q 8 hr	Yes
Ticarcillin-clavulanate	3.1 mg q 6 hr	Yes

q, every.

Source: Adapted from AAP (2001) and Cunningham et al. (2014).

CLINICAL PEARLS

- Prompt treatment of both SPPH and postpartum endometritis can reduce maternal morbidity and mortality.
- SPPH is managed with the same guiding principles as primary postpartum hemorrhage.
- Initial treatment for postpartum endometritis is intravenous clindamycin and gentamicin.

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31 *Psychiatric Complications in the Postpartum Period*

Susie M. Adams

Women are most likely to develop a mood disorder during the childbearing years, and the postpartum period represents a particularly high-risk time for new onset of psychiatric illness as well as exacerbation or recurrence of preexisting psychiatric conditions (Munk-Olsen, Laursen, Pedersen, Mors, & Mortensen, 2006; Stuart-Parrigon & Stuart, 2014; Yonkers et al., 2009). Because of the frequency and regularity of obstetric visits during pregnancy, the impact of the birth experience, and the unique provider–patient relationship, most women seek consultation from obstetric providers when experiencing psychiatric symptoms throughout childbearing years as well as during pregnancy and postpartum periods. For women with no prior psychiatric history, mood disorder symptoms can be experienced as both unfamiliar and distressing. Recognition of an initial episode of depression may be challenging as women will often attribute psychiatric symptoms such as anxiety, fatigue, decreased energy, low mood, and anhedonia to the labor and birth experience, or simply new motherhood (Beck & Driscoll, 2006).

Since psychiatric symptoms can emerge with relative suddenness in the postpartum period, it is not uncommon for these women to present to obstetric triage or emergency settings. However, due to multiple societal messages that motherhood is synonymous with fulfillment and joy, many women feel a sense of shame and guilt and may be reluctant to disclose mood symptoms or negative thoughts. It is imperative that key personnel in the triage setting be familiar with psychiatric symptoms most likely to emerge during peripartum, prepared to assess the acuity of psychiatric symptoms, and able to identify the need for immediate psychiatric care versus a referral for psychiatric consultation at a subsequent appointment. When severe postpartum psychiatric symptoms go unrecognized and untreated, the consequences for both mother and infant can be dire. Obstetric providers, as primary medical caregivers for perinatal women, are uniquely positioned to intervene when psychiatric complications are detected. Like all medical conditions, early detection and intervention can greatly improve outcomes for both mothers and infants (Vesga-Lopez et al., 2008).

POSTPARTUM DEPRESSION

Postpartum depression (PPD) is the most common psychiatric complication of the prenatal and postpartum periods, affecting approximately 10% to 15% of women

(Gavin et al., 2005; Robertson, Grace, Wallington, & Stewart, 2004; Sit & Wisner, 2009). Although this prevalence rate is similar for depression among nonpregnant women, the rates of first onset and severity of depression are increased threefold (Stewart, Robertson, Dennis, Grace, & Wallington, 2003). Major depressive disorders regardless of onset during, after, or unassociated with pregnancy have high rates of recurrence. At least 50% of individuals who recover from an initial episode of depression will have one or more additional episodes during their lifetime (5th ed.; *DSM–5*; American Psychiatric Association [APA], 2013), which usually occurs within 5 years of the initial episode (Burcusa & Iacono, 2007). Approximately 80% of those with a history of two episodes of depression will have another recurrence (APA, 2013) and, on average, individuals with a history of depression have five to nine depressive episodes during their lifetime (Burcusa & Iacono, 2007).

According to the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (*DSM-5*; American Psychiatric Association, 2013), PPD is formally classified as a major depression, either recurrent or single episode, with a range from mild to severe. The specifier "peripartum onset" is now used when symptoms occur during pregnancy or in the 4 weeks following childbirth. Although the *DSM-5* specifies onset of symptoms within the first 4 weeks of childbirth to be categorized as PPD, many women don't recognize PPD symptoms until much later in the first year. The *DSM-5* notes that 50% of "postpartum" major depressive episodes actually begin prior to delivery. These episodes are now collectively referred to as peripartum episodes and are often associated with severe anxiety and even panic attacks. Postpartum mood episodes with psychotic features occur in 1 in 500 to 1 in 1,000 deliveries and may be more common in primiparous women (APA, 2013). Once a woman has had a postpartum episode with psychotic features, the risk of recurrence with each subsequent delivery is between 30% and 50% (APA, 2013). When unrecognized and untreated, PPD causes profound suffering for the mother and, although rare, can result in suicide. PPD can compromise mother–infant interactions and care practices; the long-term deleterious impact of untreated maternal depression on infant/child development is well-documented (Field, 2010).

Postpartum mood disorders are typically categorized as: postpartum blues, PPD, and puerperal (postpartum) psychosis. The prevalence, onset, duration, symptom, and treatment of these three types of postpartum mood disorders are summarized in Table 31.1 (APA, 2013; Robertson et al., 2004).

RISK AND PROTECTIVE FACTORS

PPD occurs in women of all socioeconomic, cultural, ethnic, and age groups. Antenatal risk factors that render a woman more vulnerable to PPD in order of effect size include: depression during pregnancy, anxiety during pregnancy, stressful life events during pregnancy or the early puerperal period, poor social support, and previous history of depression (Robertson et al., 2004). Moderate risk factors predictive of PPD include child-care stress, low self-esteem, maternal neuroticism, negative attribution style, and difficult infant temperament (Stewart et al., 2003). Neuroticism is a lifelong tendency or personal trait characterized by anxiety, fear, moodiness, worry, envy, anger, and depressed mood. Women who identified as "being nervous," "shy, self-conscious," or a "worrier" through questionnaires and women who had negative cognitive attributional styles of "pessimism," "anger," and "ruminations" were more likely to develop PPD (Robertson et al., 2004). Single marital status, poor relationship with partner, and lower socioeconomic status, including income, were weaker predictors of PPD (Beck, 2001; Stewart et al., 2003). Pregnancy-related complications such as preeclampsia, hyperemesis, premature labor, and delivery-related complications such as premature delivery,

TABLE 31.1 Postpartum Affective Disorders: Summary of Onset, Duration, Symptoms, and Treatment

DISORDER	PREVALENCE (%)	ONSET	DURATION	SYMPTOMS	TREATMENT
Baby or maternity blues	30–75	3 or 4 days after delivery	Hours to days, never more than 2 weeks. Mild, spontaneously remits.	Irritability, anxiety, fluctuating mood, and increased emotional reactivity.	No treatment required other than reassurance. Not considered a psychiatric disorder.
PPD	10–15	Within 4 weeks after delivery;* identified up to 6 months after delivery†	Weeks to months, often prolonged course.	Excessive guilt, anxiety, anhedonia, depressed mood, insomnia/ hypersomnia, suicidal ideation, and fatigue.	Treatment with medication and counseling usually required by mental health specialist.
Puerperal (postpartum) psychosis	0.1–0.2	Within 2 weeks after delivery	Weeks to months, often prolonged course.	Mixed or rapid cycling, agitation, delusions, hallucinations, disorganized behavior, cognitive impairment, and limited insight.	Severe symptoms considered psychiatric emergency: hospitalization usually required. Ongoing outpatient treatment by mental health specialist.

PPD, postpartum depression.

Adapted from *APA (2013); Stewart, Robertson, Dennis, Grace & Wailington (2009).

instrumental delivery, and emergency caesarean section also have a small yet significant effect in the onset of PPD (Stewart et al., 2003; Verreault et al., 2014). No relationship has been found for ethnicity, maternal age, level of education, parity, or gender of child in Western societies in predicting PPD (Stewart et al., 2003). A more recent study identified adolescence, poverty, and recent immigrant status as additional predictors of PPD (Pearlstein, Howard, Salisbury, & Zlotnick, 2009). Far less is known about protective factors associated with PPD beyond the absence of identified risk factors (Robertson et al., 2004; Verreault et al., 2014). One recent notable study reports that women experiencing a supportive couple relationship are less likely to report PPD symptoms even when they have a history of depression or a prior PPD episode (Banker & LaCoursiere, 2014).

A systematic review of risk factors for depressive symptoms during pregnancy identified maternal anxiety, life stress, history of depression, lack of social support, unintended pregnancy, Medicaid insurance, domestic violence, lower income, lower education, smoking, single status, and poor relationship quality were associated with greater likelihood of antepartum depressive symptoms (Lancaster et al., 2010). These antepartum risk factors need to be considered in conjunction with prenatal depression screening recommended by the American

College of Obstetricians and Gynecologists (ACOG) at the initial prenatal visit and at each trimester (ACOG, 2015). A similar systematic review of risk factors associated with PPD included anxiety and depression during the pregnancy, experiencing stressful life events during pregnancy or the early postpartum period, traumatic birth experience, preterm birth/infant admission to neonatal intensive care, low levels of social support, previous history of depression, and breastfeeding problems (ACOG, 2015).

PRESENTING SYMPTOMATOLOGY

The diagnosis of PPD is challenging due to inherent changes in sleep, appetite, and energy during the early postpartum weeks. Similarly, fatigue, emotionality, irritability, and worry over the infant's well-being are common postpartum and typically referred to as the "baby" or "postpartum blues." While not a true disorder, postpartum blues respond well to support, reassurance, and adequate sleep and resolve by week 3 postpartum.

Postpartum depression, on the other hand, is a serious disabling condition and is characterized by sad, depressed mood and loss of interest or pleasure persistent for at least 2 weeks. Additional symptoms include sleep disturbance, most typically insomnia (e.g., unable to sleep when the infant sleeps); lack of energy; feelings of worthlessness or guilt, often with the belief of being a "bad mother"; difficulty thinking, concentrating, and making decisions; and thoughts of suicide or "everyone would be better off without me." Other hallmark symptoms of PPD include anxiety, lack of attachment to the infant, and intrusive and unwanted thoughts of harm befalling the infant. Research substantiates clinical observation that there is no correlation between the presence of intrusive harming infant thoughts and acting on them (Barr & Beck, 2008). Rather, these thoughts are experienced as highly distressing to the mother, can result in avoidance of the infant, and signal the severity of the depression.

HISTORY AND DATA COLLECTION

In the triage setting, a brief, easily administered and scored self-report screening measure is an optimal first step in detecting depression (Gjerdingen & Yawn, 2007). The most widely used and well-studied depression screening tool for perinatal women is the 10-item Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1987), which has demonstrated validity, sensitivity (80%–90%), and specificity (80%–90%) in screening for the presence of PPD (Agency for Healthcare Research and Quality [AHRQ], 2013). Scores 13 or greater are generally indicative of depression. The EPDS is a 10-item measure with a 0–3 Likert scale response set with a range of 0–30 points (see www.sadag.org/images/brochures/edinburghscale.pdf). A cut-point of 10 is suggestive of depression and scores of 12.5 or greater are considered indicative of depression (Cox et al., 1987).

The nine-item Patient Health Questionnaire-9 (PHQ-9; Kroenke, Spitzer, & Williams, 2001) is a general depression screen commonly used in adult primary care settings and may be more familiar to primary care providers (see Exhibit 31.1). Comparative performance of the EPDS and the PHQ-9 in pregnant and postpartum women seeking mental health services found both measures had comparable sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for detecting depression (Flynn,

EXHIBIT 31.1

Patient Health Questionnaire (PHQ-9)

Name: _____ Date: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?
(use "✓" to indicate your answer)

	NOT AT ALL	SEVERAL DAYS	MORE THAN HALF THE DAYS	NEARLY EVERY DAY
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
	Add Columns	____ +	____ +	____

Health care professional: For interpretation of TOTAL, please refer to accompanying scoring card.

TOTAL: _____

10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all	____
	Somewhat difficult	____
	Very difficult	____
	Extremely difficult	____

Source: Kroenke et al. (2001). PHQ-9 is available in the public domain.

Sexton, Ratliff, Porter, & Zivin, 2011). The PHQ-2 (Kroenke, Spitzer, &Williams, 2003) consists of the first two questions of the PHQ-9, has 100% sensitivity and 44.5% to 65.7% specificity in screening for depression, and may be appealing in a busy obstetric triage setting as a brief screening measure (AHRQ, 2013). If the response is "yes" to either question, consider administering the PHQ-9, the EPDS, or asking more questions about possible depression. If the response to both questions is "no," the screen is negative.

The EPDS, PHQ-9, and PHQ-2 perform similarly in screening for depression in postpartum women (Flynn et al., 2011; Gjerdingen, Crow, McGovern, Miner, & Center, 2009). Positive screens can be followed by careful additional inquiry about mood state, sleep, appetite, concentration, anxiety, intrusive negative thoughts, hedonic capacity, degree of attachment to infant, and presence of suicidal thoughts. Symptom onset, intensity, and duration are critical as well as information regarding the woman's degree of functional impairment and whether or not adequate social support is present. History of prior episodes of depression, anxiety or other mood disorders, substance use, and interpersonal or environmental stress must also be obtained to determine comorbidities and inform treatment planning.

A distinct advantage of the PHQ-9 is that the self-report measure includes diagnostic and symptom severity items that can be used for screening, diagnosis, and monitoring treatment response for depression over time (AHRQ, 2013). A PHQ-9 score of 10 or greater has a sensitivity of 88% and a specificity of 88% for major depression (Kroenke et al., 2001). PHQ-9 scores range from 0 to 27 with scores 0 to 4 indicating none to minimal depression, 5 to 9 indicating mild, 10 to 14 indicating moderate, 15 to 19 indicating moderately severe, and 20 to 27 indicating severe depression (Kroenke et al., 2001).

SUICIDE RISK ASSESSMENT

A positive depression screening score indicates the need for suicide risk assessment. Although suicide rates are lower during pregnancy and the postpartum period, perinatal women who complete suicide do so by more violent and lethal means than nonperinatal women (Lindahl, Pearson, & Colpe, 2005). Risk factors for suicide include comorbid psychiatric and substance abuse disorders and having a stillbirth or infant death within the first postpartum year. It is recommended that when assessing suicidality in the pregnant or postpartum woman, specific inquiry must be made about suicide risk factors such as prior suicide attempts, previous trauma, current domestic violence, substance abuse, and access to firearms. Further inquiry about current suicidal thoughts, a suicide plan, access or means to carry out the plan, and intent to act on the plan warrant timely psychiatric consultation and likely hospitalization (Johannsen et al., 2016).

OTHER POSTPARTUM PSYCHIATRIC CONDITIONS

PPD is a term that is universally recognizable among obstetric providers, yet other postpartum psychiatric conditions exist that, while not as common as depression, are equally debilitating and just as likely to be encountered in the triage setting. These include postpartum psychosis and postpartum anxiety disorders and subtypes.

POSTPARTUM PSYCHOSIS

Postpartum psychosis, although not part of the formal psychiatric diagnostic nomenclature, is a widely used term to describe a severe and relatively uncommon psychiatric condition that occurs in one to two per 1,000 live births (Munk-Olsen et al., 2006). It requires immediate attention, likely inpatient psychiatric hospitalization, and has a rapid onset, with symptoms evident in the first 2 to 4 weeks after delivery. Women with postpartum psychosis may present to the obstetric triage unit exhibiting confusion, disordered thinking, mood lability, and delusions. Disorganized, bizarre behavior may be witnessed as well as flat or inappropriate affect.

Women with psychotic symptoms are frequently accompanied by family members who may additionally report paranoia, suspiciousness, grandiosity, and evidence of auditory or visual hallucinations. There are likely to be reports of poor judgment and impaired functioning. Sleeplessness and other hypomanic symptoms such as agitation and irritability are common prodromal states, emerging within 72 hours of childbirth. Unrecognized postpartum psychosis can have serious consequences including infanticide, suicide, and infant abuse/neglect. Women with postpartum psychosis may have command auditory hallucinations telling them to kill the infant or delusional beliefs that the infant or they are, for instance, possessed by demons and can only be saved through death. Risk factors include a previous episode of postpartum psychosis, previous hospitalization for a manic or psychotic episode, current or past bipolar disorder diagnosis, family history of bipolar disorder, primiparity, and recent discontinuation of mood stabilizers (Doucet, Jones, Letourneau, Dennis, & Blackmore, 2011).

POSTPARTUM ANXIETY DISORDERS

Worry is common in new mothers and is often regarded as an adaptive and protective response in the early postpartum period. When anxious worrying becomes excessive, occurs in multiple settings/situations, does not respond to reassurance, inhibits normal functioning, or interferes with self-care or care of the infant, it has moved along the continuum from "normal" to "disordered." Subtypes of anxiety disorders include generalized anxiety disorder (GAD), obsessive compulsive disorder (OCD), and panic disorder and posttraumatic stress disorder (PTSD). Because anxiety disorders and major depression are highly comorbid in the postpartum period, it is essential to screen for both (Austin et al., 2010).

Panic Disorder

Panic disorder is characterized by unpredictable, discrete episodes of intense anxiety and includes symptoms of fear, heart palpitations, shortness of breath, chest pain, dizziness, numbness or tingling, nausea, sweating, choking, fear of dying, or losing control. Postpartum women who experience an episode or more of panic will frequently present to the emergency department believing they are having a heart attack or other catastrophic medical crisis. There has been some evidence that weaning may precipitate or exacerbate panic symptoms (Ross & McLean, 2006).

PTSD develops in response to a traumatic event, which is either witnessed or experienced and involves actual or threatened death, serious injury, or threat to physical integrity. The response to the traumatic event includes intense fear, helplessness, or horror. Women who have undergone traumatic deliveries and/or women with histories of prior trauma are susceptible to PTSD during the postpartum period. Symptoms include hypervigilance, fear, irritability, poor concentration, sleeplessness, heightened anxiety, intrusive recollections of the traumatic event, flashbacks or "re-living" of the experience, and psychologic and physiologic reactivity when exposed to stimuli associated with the traumatic event. Additional symptoms include emotional numbing, avoidance of stimuli reminiscent of the event or evocative of the feelings, or thoughts associated with the traumatic event. Women who have been victims of childhood or adult sexual assault may become "triggered" and experience PTSD symptoms during childbirth procedures, examinations, and delivery (*APA*, 2013).

BIPOLAR DISORDER

Bipolar disorders are characterized by mood swings with periods of elevated, expansive, or irritable mood and increased energy or activity with major depressive episodes characterized by depressed mood or loss of interest, significant weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished concentration or indecisiveness, and recurrent thoughts of death or suicidal ideation with or without a specific plan (*APA*, 2013). Bipolar I disorder must include at least one full manic episode of abnormal and persistently elevated, expansive, or irritable mood and abnormally increased activity or energy lasting at least 1 week and present nearly every day. Symptoms include inflated self-esteem or grandiosity, decreased need for sleep (e.g., feeling rested after only 3 hours of sleep), talkative or pressured speech, distractibility, and excessive involvement in activities that have high potential for painful consequences (*APA*, 2013). Bipolar II disorder is characterized by hypomanic episodes, never a full manic episode, episodes of depression, and often a history of chronic irritability.

Diagnosis of bipolar disorder is often missed in women with PPD, which has significant clinical implications (Sharma, Khan, Corpse, & Sharma, 2008). Misdiagnosis of symptoms as PPD can result in pharmacologic intervention with antidepressants, typically selective serotonin reuptake inhibitors (SSRIs) or serotonin norepinephrine reuptake inhibitors (SNRIs; Connolly & Thase, 2011). Antidepressants can trigger psychotic symptoms, cause a full manic episode, contribute to rapid-cycling, and result in a more difficult course of clinical treatment (Stahl & Grady, 2011). The woman's mental health history, family psychiatric history, careful questioning about episodes of high energy with little sleep, mood swings, risky behaviors, and using reliable and valid assessment measures are critical to make an accurate differential diagnosis. The 17-item Mood Disorder Questionnaire (MDQ; Hirschfeld et al., 2000) is a valid, psychometrically sound measure to screen for bipolar disorder (MDQ available at www.dbsalliance.org/pdfs/MDQ.pdf).

OBSESSIVE COMPULSIVE DISORDER

Intrusive, short-lived thoughts of causing accidental harm to the infant are a common and relatively normative experience among new mothers, while 50%

of new mothers report unwanted, intrusive thoughts of intentionally harming the infant (Fairbrother & Woody, 2008). Compared with intentional harm thoughts, accidental harm thoughts are more frequent and time consuming, yet less distressing to new mothers (Fairbrother & Woody, 2008). Obsessive compulsive disorder (OCD), however, is an extreme form of recurring intrusive thoughts and interferes with a woman's ability to care for herself and/or the infant. Obsessive compulsive disorder is characterized by intrusive, unwanted images, thoughts, or impulses either with or without accompanying compulsions. The most common obsessions experienced by postpartum women include contamination, intentionally or accidentally harming the infant, need for order/symmetry, and catastrophic images. Compulsions are goal-directed, driven, and repetitive or ritualized behaviors; engagement in them results in temporary reduction of anxiety associated with the obsessive thoughts or beliefs. Compulsions include cleaning, checking (often resulting in sleep deprivation due to incessant checking on infant), washing, praying, counting, repeating certain phrases, or other ritualized behaviors. The postpartum period represents a time of increased vulnerability to the onset of OCD and a time of symptom exacerbation in women with preexisting OCD (Zambaldi et al., 2009).

ASSESSMENT AND MANAGEMENT OF POSTPARTUM MENTAL HEALTH DISORDERS

PHYSICAL EXAMINATION

Typically, mental illnesses are not conceptualized as resulting in abnormal physical findings as one would expect in detecting illnesses such as high blood pressure or gestational diabetes mellitus. While all mental health disorders are linked to neurobiology and brain dysfunction, it is important to appreciate the context of the biologic, psychologic, and social interactions that underlie mental health disorders. Certainly, the perinatal and postpartum periods with inherent physiologic, psychologic, and social role changes create a critical period of vulnerability for the emergence or exacerbation of mental health disorders. Understanding common physiologic signs and symptoms as well as mental status findings is helpful in early identification of common psychiatric disorders for this population. Table 31.2 differentiates mental status and physical examination findings for depression, anxiety, postpartum psychosis, and bipolar disorders. It is important to conceptualize these disorders as interrelated, resulting in symptom overlap.

DIFFERENTIAL DIAGNOSIS

Postpartum women will likely present to an emergency department or an obstetric triage setting if they experience mental status changes. A family member or friend may be the first to notice or first to bring attention to these changes, as women may attribute these changes to expected postpartum experiences, have limited insight to describe the symptoms, or may be too ashamed to verbalize what they are experiencing. There are multiple medical conditions that can either be mistaken for or result in psychiatric symptoms; therefore, ruling out differential diagnoses is imperative.

Medical conditions such as anemia, vitamin deficiencies, alcohol abuse, gestational diabetes, and thyroid dysfunction may produce symptoms of fatigue that mimic depression. Hypertension, anemia, and thyroid dysfunction may also result in symptoms of anxiety and panic. Use of illicit substances, thyroid

TABLE 31.2 Mental Status and Physical Examination Findings

	AFFECTIVE	COGNITIVE	BEHAVIORAL	PHYSIOLOGIC	SYMPATHETIC	PARASYMPATHETIC
Depression	Depressed mood Flat Overwhelmed Irritability Hopelessness Uncertainty	Guilt Worthlessness Thought blocking Decreased insight Poor judgment Thoughts of death	Anhedonia Fatigue/ decreased energy Poor grooming Tearfulness	Psychomotor agitation or retardation Appetite change ↑↓ Weight ↑↓ Sleep ↑↓	Anorexia Weakness	Constipation Decreased blood pressure Decreased pulse
Anxiety	Apprehensive Distressed Fearful Overexcited Worried	Preoccupation Rumination Heightened awareness Intrusive thoughts Ego-dystonic thoughts that something awful may happen	Fidgeting Glancing about Restlessness Repetitive actions Avoidance	Facial tension Perspiration Muscle tension Shakiness Trembling	Cardiovascular excitation Diarrhea Dry mouth Facial flushing Increased reflexes Increased respiration Shortness of breath Vasoconstriction	Abdominal pain Faintness Nausea Tingling in extremities Urinary frequency, hesitancy, or urgency
Psychosis	Guarded Blank Bizarre	Delusions Hallucinations Paranoia Ego-dystonic thoughts of harming infant	Disorganized speech Mood swings Agitation Sleeplessness	Hypomania		
Bipolarity **Type I*** **Type II**†	Elevated, expansive, or irritable mood Distractibility Mood swings	Inflated self-esteem Grandiosity Racing thoughts Flight of ideas Increased Risky behaviors (sexual indiscretions, unrestrained buying sprees, foolish investments/ventures	Increased energy or activity More talkative Pressured or rapid speech Mood swings Agitation	Manic episode* Hypomania† Decreased need for sleep		

Sources: Adapted from APA (2013); Sadock, Sadock, and Ruiz (2015).

disease, autoimmune disease, HIV, Sheehan's syndrome, tumors, preeclampsia, and/or post-eclamptic episodes must be ruled out given their association with mental status changes congruent with psychosis (Basraon & Constantine, 2011; Ebeid, Nassif, & Sinha, 2010).

LABORATORY FINDINGS

Evaluation of specific laboratory studies can assist in uncovering contributing factors of the etiology of symptom presentation. Thus, the recommended laboratory studies in Table 31.3 will provide evidence of possible differential diagnoses.

CLINICAL MANAGEMENT

Once diagnosis has been determined, the next step is to consider treatment options. In most situations, the obstetric triage provider can identify mental health problems and seek psychiatric consultation. The consultant can recommend or initiate psychopharmacologic interventions and collaborate with the health care team to develop an individualized plan of mental health care. If symptoms of psychosis are identified, then immediate psychiatric consultation is warranted to initiate a psychopharmacologic intervention and plan of care. Pharmacotherapy is the first-line treatment recommendation for treating PPD and especially if psychotic symptoms occur within an episode of depression or bipolar disorder (ACOG, 2009 reaffirmed 2014). Initiation of psychotropic

TABLE 31.3 Postpartum Laboratory Tests

Thyroid function tests: TSH and free thyroxine	• Hyperthyroidism, most common cause during pregnancy being Graves' disease, is associated with dysphoria, anxiety, restlessness, mania, depression, and impaired concentration. More severe symptoms include psychosis, delirium, and hallucinations.
	• Hypothyroidism, most common cause for women of reproductive age being Hashimoto thyroiditis, is associated with psychomotor slowing, poor sleep, appetite changes, apathy, and poor concentration.
Vitamin B_{12}	• Deficiency associated with symptoms of depression, mood lability, and psychosis.
Complete blood count	• Anemia is associated with depression, reduced cognitive function, fatigue, and emotional lability.
Folate	• Utilized by the brain to synthesize norepinephrine, serotonin, and dopamine.
	• Deficiency can be associated with symptoms of depression.
Electrolytes	• Imbalances resulting from inadequate nutritional intake.
	• Imbalances may cause delirium.
Vitamin D	• Deficiency associated with depressive symptoms.
Drug toxicology	• Substances may induce symptoms of depression, anxiety, and psychosis.

TSH, thyroid stimulating hormone.

Source: Adapted from Fischbach and Dunning (2014); Basraon and Constantine (2011).

medication, even at lower starting doses, can be crucial in managing and preventing further exacerbation of symptoms. Alternative treatment options such as support groups and psychotherapy will require referral to a mental health provider. Psychiatric partial (or day) hospitalization in a specialized mother-baby unit is an optimal and effective form of treatment for postpartum women with severe symptoms. One such model is the Women & Infants Hospital PPD Day hospital in Providence, Rhode Island, and consists of intensive 2- to 3-week daily (up to 6 hours/day) multidisciplinary/multimodal psychiatric intervention in a setting, which allows mother and infant to remain together for the duration of treatment (Howard, Battle, Pearlstein, & Rosene-Montella, 2006).

When initiating treatment in the postpartum period, it is necessary to weigh the difference of the risk of treatment versus the risk of untreated symptoms (ACOG, 2009). The symptoms of depression, anxiety, and psychosis have been outlined earlier in this chapter and are critical to consider when presenting treatment options to women. Women typically have heard about medication risks to them and/or the breastfeeding infant, but unfortunately the source of information is unlikely to be systematic and evidence based. As obstetric providers, this is a unique opportunity to adequately inform women of the risks and benefits of treatment versus no treatment or undertreatment.

Although data are limited, evidence-based research continues to gain momentum, providing a broader base of knowledge and understanding of the risks and benefits of psychotropic treatment in the peripartum period. The following paragraphs discuss the most commonly chosen psychotropic medications for postpartum women.

Antidepressants

The first-line treatments for depression and anxiety symptoms currently are selective serotonin reuptake inhibitors (SSRIs) for their effectiveness and low side effect profile for women (Cooper, Willy, Pont, & Ray, 2007; Meltzer-Brody, 2011). While there is limited evidence of teratogenic effects from the use of SSRIs in pregnancy or adverse effects from exposure during breastfeeding, there are two reports of congenital cardiac malformations (atrial and ventricular septal defects) associated with first-trimester exposure to paroxetine (ACOG, 2008). The 1.5- to 2-fold increased risk for congenital cardiac malformations associated with paroxetine exposure in the first trimester resulted in the manufacturer changing the drug's United States Food and Drug Administration (FDA) pregnancy category from C to D (www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm051731.htm). Exposure to SSRIs late in pregnancy has been associated with the following transient neonatal side effects: jitteriness, mild respiratory distress, transient tachypnea of the newborn, weak cry, decreased muscle tone, irritability, and neonatal intensive care unit admission (Hale, 2004; Moses-Kolko et al., 2005). Sertraline (Zoloft) and fluoxetine (Prozac) are the most well-studied SSRIs. Sertraline has not been associated with adverse infant response and has a relatively low amount that is actually transferred through breast milk (Hale, 2004). Fluoxetine, however, has the highest amount transferred through breast milk, a longer half-life, and has been associated with adverse infant response including fussiness, drowsiness, and decreased weight gain. Of the two, sertraline is usually favored for breastfeeding mothers. Citalopram (Celexa) and escitalopram (Lexapro) have shown a moderate percentage in breast milk. Second-line treatment for depression and anxiety symptoms are serotonin

TABLE 31.4 Safety of Psychiatric Medications During Pregnancy and Lactation

ANTIDEPRESSANT	FDA PREGNANCY CATEGORY*	LACTATION RISK CATEGORY†	AVERAGE RID (%)‡
Bupropion XL	B	L3	0.7
Paroxetine	D	L2	2.1
Sertraline[1]	C	L2	2.2
Citalopram/ escitalopram	C	L3	3.6
Fluoxetine	C	L2 older infants; L3 neonates	6.8
Venlafaxine	C	L3	6.4
Mirtazapine	C	L3	1.9

FDA, Food and Drug Administration; RID, relative infant dose.
*The FDA classifies drug safety using the following categories: A = controlled studies show no risk; B = no evidence of risk in humans; C = risk cannot be ruled out; D = positive evidence of risk; X = contraindicated in pregnancy.
†Lactation risk categories are as follows: L1 = safest; L2 = safer; L3 = moderately safe; L4 = possibly hazardous; L5 = contraindicated.
‡RID is the percentage of active drug metabolite that transfers through maternal breast milk.
[1]Often first choice of antidepressants in treating postpartum depression (PPD).

Sources: American College of Obstetricians and Gynecologists (ACOG) guidelines on psychiatric medication use during pregnancy and lactation (2008); Hale (2004).

norepinephrine reuptake inhibitors (SNRIs; ACOG, 2008; Armstrong, 2008). Table 31.4 summarizes pregnancy and lactation risks and the relative infant dose of active drug metabolite that transfers through maternal breast milk for commonly used antidepressants in the peripartum period.

Benzodiazepines

When initiating treatment, benzodiazepines are effective in acute treatment of anxiety disorders for short time periods. However, all benzodiazepines have been classified as FDA pregnancy risk category D (positive evidence of risk) or X (contraindicated in pregnancy) and lactation risk category L3 (moderately safe), indicating the need for caution and individualized assessment or risk/benefit ratio to mother and fetus or breastfeeding infant (ACOG, 2008). Although early studies of prenatal exposure to diazepam, a benzodiazepine, identified an increased risk of oral clefts (Arakog, 1975; Saxen, 1975), a more recent population-based case-control teratologic study did not find an association of congenital anomalies, including oral clefts to five different benzodiazepines (Eros, Czeizel, Rockenbauer, Sorensen, & Olsen, 2002). The relative risk for breastfeeding infants is low; however, caution should be taken to watch for sedation and withdrawal effects in infants (ACOG, 2008; Hale, 2004). Maternal benzodiazepine use shortly before delivery is associated with floppy infant syndrome (ACOG, 2008). Benzodiazepines are not intended for long-term use due to the potential for psychologic and physiologic dependence, especially short-acting benzodiazepines. Buspirone (FDA pregnancy risk category B and lactation risk category L3) is the only available non-benzodiazepine anxiolytic for chronic anxiety, and offers a safer risk/benefit ratio to mother and breastfeeding infant (ACOG, 2008).

Hypnotics

The limited available systematic data regarding sleep aids indicates that hypnotics have an FDA pregnancy risk category C and lactation risk category L3, except for zolpidem, which has FDA pregnancy risk category B (ACOG, 2008). However, since insomnia is a significant precursor to worsening depression, anxiety, and psychosis, the risk/benefit ratio may be warranted when weighing against symptomatology. Teaching sleep hygiene, progressive muscle relaxation, guided imagery, and other nonpharmacologic interventions are recommended before relying on hypnotics for insomnia.

Mood Stabilizers

Mood instability can occur postpartum. In fact, the postpartum period may be the first hypomanic/manic episode for women and is closely linked to the risk of psychosis. There may be several depressive episodes prior to a bipolar spectrum disorder emerging. Valproate exposure in pregnancy is associated with increased risk of fetal anomalies, including neural tube defects, fetal valproate syndrome, and long-term adverse neurocognitive effects and should be avoided in pregnancy, especially during the first trimester (ACOG, 2008). Similarly, carbamazepine exposure in pregnancy is associated with fetal carbamazepine syndrome and should be avoided in pregnancy, especially during the first trimester (ACOG, 2009). Lithium (FDA pregnancy risk category D) requires systematic monitoring and transfers to breast milk at high percentages (L4; ACOG, 2008). Lamotrigine (Lamictal; FDA pregnancy risk category C) is an effective mood stabilizer as well, but also has a high transfer through breast milk (L3; ACOG, 2008). It may be difficult to distinguish between benign infant rashes and severe life-threatening lamotrigine rash. However, neither lithium nor lamotrigine are completely contraindicated during breastfeeding; therefore, close monitoring of the infant is prudent.

Antipsychotics

The second-generation antipsychotics (SGAs) are not only a preferred choice for psychotic symptoms, but there is clinical evidence to support that SGAs are useful as alternative options for treatment of anxiety and insomnia (ACOG, 2008). All of the first and second generation antipsychotics have been placed in pregnancy risk category C with the exception of clozapine in category B (ACOG, 2008). However, clozapine, even in nonpregnant women, is limited to use for individuals with schizophrenia who do not respond to other antipsychotics due to weekly lab monitoring and risk for lowered white blood cell counts. Little data exists on antipsychotics during breastfeeding (most categorized L3-L4; ACOG, 2008). The main symptom to watch for is sedation in both mother and infant (ACOG, 2008). Due to the risk of sedation, starting at unconventionally low doses may assist in compliance and adherence.

Considerations for Psychotropic Use

Questions to consider when prescribing include the following: Will the mother be breastfeeding? Will the mother be too sedated from medication choice to tend to infant? Will the mother be more troubled by risk of weight gain, coupled with existing pregnancy weight? Will sexual side effects be more problematic since postpartum women typically have a low sexual drive?

When assessing the risks and benefits of medication choice, choosing a treatment that has been effective in the past may outweigh the risks of trying a new, better-studied medication. Remitting symptoms in the postpartum period is time sensitive in order not to prevent decline of a woman's ability to care for self and infant.

Finally, noting the limitations of the FDA pregnancy risk categories is imperative. No psychotropic medications are yet FDA approved for use during pregnancy. Psychotropic medications all cross the placenta so they are never "no risk." Adverse medication effects do not generalize from one species to another, and drugs can get "demoted" the more they are studied in humans. The most reliable data are systematic, prospective, controlled studies.

General ACOG recommendations when psychotropic medications are used during pregnancy or in breastfeeding mothers include:

1. Multidisciplinary management involves the patient's obstetrician, mental health provider, primary health care provider, and pediatrician.
2. Use of a single medication at a higher dose is favored over the use of multiple medications for the treatment of psychiatric illness during pregnancy.
3. Physiologic alterations of pregnancy may affect the absorption, distribution, metabolism, and elimination of lithium, and close monitoring of lithium levels during pregnancy and postpartum is recommended. Treatment with all SSRIs during pregnancy needs to be individualized.
4. Fetal assessment with fetal echocardiogram needs to be considered in pregnant women exposed to lithium in the first trimester (ACOG, 2008).

FOLLOW-UP

The best approach to treatment and follow-up with postpartum women is multidisciplinary utilizing physicians, nurses, social workers, and community resources within medicine and psychiatry. The algorithm in Figure 31.1 assists as a guide for decision making.

Postpartum mood changes significantly impact not only the mother but the children and family as well. Early detection and treatment initiation

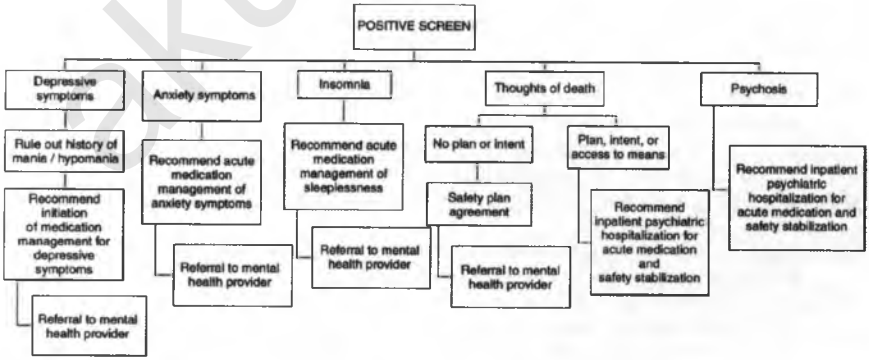

Figure 31.1 Guide for management of postpartum mood symptoms

Adapted from American College of Obstetricians and Gynecologists guidelines on psychiatric medication use during pregnancy and lactation (2008); American College of Obstetricians and Gynecologists (ACOG) & American Psychiatric Association (APA) guidelines for treatment of depression during pregnancy (2009); and Meltzer-Brody (2011).

by providers that come in contact with postpartum women will reduce the detrimental effects of symptoms, promoting healthier mothers, infants, and families. Nonpharmacologic interventions such as interpersonal psychotherapy (IPT), cognitive behavioral therapy (CBT), peer-to-peer support, and partner support have demonstrated favorable outcomes in treating PPD (Fitelson, Kim, Baker, & Leight, 2011). However, the strongest support is for the combination of these psychotherapy and social support strategies with antidepressants for safe and effective treatment of women with PPD (Wisner, Parry, & Piontek, 2002).

CLINICAL PEARLS

- Women are most likely to develop a mood disorder during the childbearing years, and the postpartum period represents a particularly high-risk time for new onset of psychiatric illness as well as exacerbation or recurrence of preexisting psychiatric conditions.
- Unrecognized postpartum psychosis can have serious consequences including infanticide, suicide, and infant abuse/neglect.
- Diagnosis of bipolar disorder is often missed in women with PPD, which has significant clinical implications.

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Critical Postpartum Medical Complications

Courtney Clark Bilodeau and Srilakshmi Mitta

The postpartum woman who presents to triage can be a clinical challenge. Common postpartum complaints can result from benign causes in the postpartum course or from a serious, potentially life-threatening complication. For example, a postpartum woman complaining of fatigue and dyspnea may be mildly anemic and sleep deprived or could be symptomatic due to a pulmonary embolism (PE) or congestive heart failure. Triage clinicians must be thorough in both history taking and physical examination, and quickly determine the appropriate clinical management. Some of the most critical postpartum conditions that a triage clinician may face include cardiomyopathy, deep vein thrombosis (DVT), and PE.

PERIPARTUM CARDIOMYOPATHY

Maternal hemodynamics change rapidly after delivery. Cardiac output temporarily increases immediately following birth, secondary to a decompression of the vena cava from the gravid uterus and auto transfusion of utero-placental blood to the intravascular space. Over several days, the cardiac output and maternal heart rate decrease to prepregnancy levels. Postpartum diuresis peaks by the fifth postpartum day and lasts for several weeks (Davies & Herbert, 2007). A postpartum woman without underlying cardiac disease can typically handle these cardiovascular changes without difficulty. In cases of a more complicated course, such as with preeclampsia and diastolic dysfunction, symptomatic pulmonary edema can occur. Postpartum heart failure can also be caused by the rare idiopathic condition of peripartum cardiomyopathy (PPCM). PPCM is defined as a dilated cardiomyopathy causing heart failure at the end of pregnancy or within 5 months postpartum. The diagnosis requires no other identifiable cause of heart failure or recognizable heart disease and echocardiographic findings of left ventricular (LV) systolic dysfunction with an LV ejection fraction (EF) less than 45%. The workshop held by the National Heart Lung and Blood Institute and the Office of Rare Diseases in 2000 strictly defined the onset of PPCM in the last month of pregnancy or later (Pearson et al., 2000). A more recent definition proposed by the 2010 European Society

EXHIBIT 32.1

Risk Factors for the Development of Peripartum Cardiomyopathy

- Advanced maternal age
- Multiparity
- Multifetal pregnancy
- Maternal cocaine use
- African descent
- Preeclampsia, eclampsia, and postpartum hypertension
- Prolonged tocolytic therapy with beta-agonists

Sources: Bello, Rendon, and Arany (2013); Elkayam et al. (2005); Gentry et al. (2010); and Mendelson and Chandler (1992).

of Cardiology (ESC) Working Group on Peripartum Cardiology uses more general timing of heart failure as "toward the end" of pregnancy; the reduced LVEF is "nearly always" less than 45%, with LV dilation not always being found on echocardiograph (Sliwa et al., 2010).

There are numerous proposed etiologies of PPCM and multiple factors may contribute to its pathogenesis. Some proposed hypotheses include apoptosis (Sliwa et al., 2006), oxidative stress (Hilfiker-Kleiner, Sliwak, & Drexler, 2008), maternal immune response to fetal antigens (Nelson, 1998; Pearson et al., 2000), and altered prolactin processing (Hilfiker-Kleiner et al., 2007). Genetic factors may also play a part in PPCM development (Morales et al., 2010; van Spaendonck-Zwarts et al., 2010, 2014). Risk factors for the development of PPCM are listed in Exhibit 32.1.

PRESENTING SYMPTOMATOLOGY

The clinical presentation of PPCM is highly variable. Symptoms can often be confused with benign peripartum complaints. The most common presenting symptoms of PPCM are noted in Exhibit 32.2.

HISTORY AND DATA COLLECTION

The woman suspected of having PPCM warrants a thorough history taking regarding the pregnancy as well as the labor and delivery. If recorded, the woman's fluid balance during labor and delivery admission should be reviewed. Family medical history should be obtained, especially regarding cardiac diseases including dilated cardiomyopathy and sudden cardiac death. Social history includes activity level prior to and during pregnancy to contrast with current exercise capacity. Questions regarding illicit drug and alcohol use are also imperative. It is recommended that the time course for the woman's complaints be clearly recorded.

PHYSICAL EXAMINATION

There is a wide range of objective findings that can help to diagnosis PPCM. Increased heart rate and respiratory rate and a decreased pulse oximetry may

EXHIBIT 32.2

Common Symptoms of Peripartum Cardiomyopathy

- Dyspnea
- Decreased exercise tolerance
- Pedal edema
- Orthopnea
- Paroxysmal nocturnal dyspnea
- Dizziness
- Chest pain
- Palpitations
- Cough
- Hemoptysis
- Fatigue
- Abdominal pain

Source: Sliwa et al. (2010).

be found. Blood pressure can vary, including postural hypotension (Sliwa et al., 2010). The jugular venous pressure may be increased. Cardiac auscultation findings include systolic ejection murmurs and a prominent pulmonic valve component of the second heart sound and a third heart sound. If there is cardiomegaly, the point of maximal impulse (PMI)/apical impulse can be displaced laterally and/or inferiorly. Pulmonary auscultation may reveal wheezes and rales. Peripheral edema, ascites, and hepatomegaly may also be found. Preeclamptic women are commonly hyperreflexive.

LABORATORY AND IMAGING STUDIES

Electrocardiograms (EKGs) are frequently obtained in suspected cases of PPCM. Exhibit 32.3 lists potential findings on EKG.

EXHIBIT 32.3

Potential Electrocardiogram Findings in Peripartum Cardiomyopathy

- Normal (no abnormalities)
- Tachycardia
- Atrial fibrillation
- Low voltage
- Anterior precordium Q waves
- PR and QRS interval prolongation
- Voltage criteria consistent with left ventricle hypertrophy
- ST-T wave abnormalities

Source: Sliwa et al. (2010).

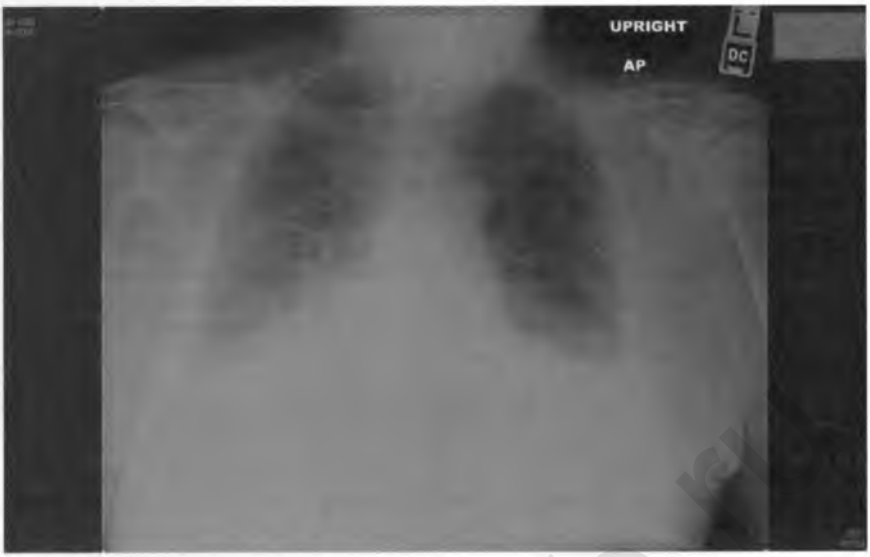

Figure 32.1 Chest radiograph: Cardiomegaly and pulmonary congestion
Source: Courtesy of Radiology Department, Women & Infants Hospital, Providence, RI.

Laboratory values of brain natriuretic peptide (BNP) and troponin-I may be elevated in PPCM. Preeclampsia is both a risk factor for the development of cardiomyopathy and can cause non-PPCM symptomatic pulmonary edema. It is critical to exclude the diagnosis of preeclampsia when determining if a woman has PPCM. In addition to history and physical examination, laboratory studies used to diagnose preeclampsia include creatinine, hemoglobin, platelets, liver enzymes, urine protein, and uric acid.

Chest radiography in women with PPCM may show enlarged cardiac silhouette, patchy lower lung infiltrates, vascular cephalization, and pleural effusions. Figure 32.1 shows cardiomegaly, as well as pulmonary congestion.

An echocardiograph is recommended for all peripartum women suspected of having PPCM. An immediate ("bedside") echocardiograph can be useful to rapidly diagnose and evaluate the severity of cardiac dysfunction. The echocardiography findings may include reduction in contractility, LV enlargement, reduction in LVEF, regional abnormalities in systolic wall thickening, pericardial effusion, left atrial enlargement, and mitral and tricuspid valve regurgitation (Blauwet & Cooper, 2011; Elkayam et al., 2005; Modi, Illum, Jariatul, Caldito, & Reddy, 2009; Sliwa et al., 2010).

Incidence of venous thromboembolism (VTE) is increased in women with PPCM. If indicated, evaluation for embolic phenomena is performed (see the following section on DVT/PE).

DIFFERENTIAL DIAGNOSIS

The differential diagnoses for PPCM include preexisting cardiomyopathy, hypertensive heart disease, congenital heart disease, myocardial infarction, and PE. Noncardiogenic pulmonary edema, most commonly secondary to

preeclampsia, tocolytics, or sepsis, must be ruled out as an alternative diagnosis (Sliwa et al., 2010).

CLINICAL MANAGEMENT AND FOLLOW-UP

The initial management goals for postpartum PPCM are to stabilize the woman's cardiovascular status and provide symptomatic relief. The woman is placed on continuous cardiac and pulse oximetry monitoring and supplemental oxygen is administered. Intravenous access is obtained and a urinary catheter is placed to monitor urine output. Consultation with specialists may include an obstetric internist (internist with special training in the care of medical illness in pregnancy), pulmonary critical care specialist, cardiologist, and maternal fetal medicine specialist.

Pharmacologic therapy in postpartum PPCM is similar to nonobstetric congestive heart failure treatment plans (Johnson-Coyle, Jensen, & Sobey, 2012; Sliwa et al., 2010). In suspected preeclamptic women, who are frequently intravascularly depleted and have decreased renal function, the medication dose and frequency of administration may need to be adjusted. Morphine can be cautiously administered for anxiety and pain control. Diuresis with loop diuretics (furosemide with a starting dose of 10 mg) is a first-line treatment. Angiotensin-converting enzyme inhibitors (ACEIs) are used for afterload reduction and are preferred over the vasodilators, such as hydralazine, which are typically used instead of ACEIs during pregnancy. Beta-blockers help to improve systolic function in the long term and are typically given after the acute decompensation of heart failure has resolved and the patient is euvolemic. Digoxin and inotropes may be used in select cases for acute heart failure management. Thromboprophylaxis is frequently considered due to the high risk for thrombus formation, especially in the postpartum state. Other agents that may be used when indicated include spironolactone and antiarrhythmics (Givertz, 2013). Once stabilized, the postpartum woman with PPCM is transferred to the appropriate inpatient service for further management.

POSTPARTUM DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

Pregnancy and the puerperium (the 6–8 week postpartum period between childbirth and the return of the uterus to its normal size) are times of increased risk for venous thromboembolism (VTE) secondary to fulfilling Virchow's Triad of hypercoagulability, venous stasis, and vascular injury (Bagot & Arya, 2008). While VTE is relatively rare in otherwise healthy young women, it can be up to 10 times more common in pregnant women of similar age. In fact, VTE has been recognized for many years as a leading cause of maternal morbidity and mortality worldwide, especially among developed and developing nations (Andersen, Steffensen, Sorensen, Nielsen, & Olsen, 1998; CMACE, 2011).

Population-based studies have shown an increasing incidence of VTE in pregnancy, which may be due in part to increasing vigilance on the part of clinicians as well as improved diagnostic techniques and standards (Andersen et al., 1998; Heit et al., 2005). In addition to this, the postpartum period has been identified as a time of even greater risk, with one study showing that the annual incidence was five times higher among postpartum women than pregnant women (Heit et al., 2005). New data has shown that there is an increased risk up to 12 weeks postpartum, though the highest risk period is still within the first

EXHIBIT 32.4

Risk Factors for Postpartum Venous Thromboembolism

- Past history of venous thromboembolism
- Family history of venous thromboembolism
- Thrombophilia
- Obesity
- Age >35 years
- Tobacco use
- Cesarean section
- Preeclampsia
- Prolonged bed rest or immobility

Source: RCOG (2009).

6 weeks after delivery (Kamel et al., 2014; Tepper et al., 2014). Additional risk factors for postpartum VTE are essential determinants for diagnoses, treatment, and outcomes and can be found in Exhibit 32.4.

PRESENTING SYMPTOMATOLOGY

A deep vein thrombosis (DVT) can cause various symptoms including lower extremity swelling, pain, erythema, warmth, or induration. It is critical to remember that DVT during pregnancy and the postpartum period may develop in uncommon locations such as pelvic or abdominal veins. Therefore, women may present with atypical complaints such as abdominal, groin, thigh, buttock, or flank pain.

A PE can present with nonspecific symptoms, making the diagnosis in both pregnant and nonpregnant patients difficult. PE needs to be considered if the presenting complaint includes chest pain or heaviness, shortness of breath, dyspnea (at rest and on exertion), hemoptysis, palpitations, or syncope. Most of these symptoms are common in normal pregnancy and some are present postpartum, making the diagnosis even more challenging.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for DVT includes cellulitis, superficial thrombophlebitis, lymphedema, musculoskeletal strain, ruptured Baker's cyst, or trauma. PE has a wider differential and can include any other cardiopulmonary processes such as pulmonary edema (both cardiogenic and noncardiogenic), pneumothorax, pneumonia, pleurisy, myocardial infarction, and pericarditis.

HISTORY AND DATA COLLECTION

The diagnosis of VTE starts with a detailed history, which will then guide the clinician with further options for future workup and management. Thorough information about the woman's presenting complaints and pregnancy course is critical. Personal history of a past VTE, superficial thrombophlebitis, pregnancy loss, or any inherited or acquired thrombophilias can further narrow the

differential. Finally, it is imperative to ask about a family history concerning thromboses and social history regarding smoking and daily activities.

PHYSICAL EXAMINATION

DVT can present with lower extremity edema (pitting and nonpitting), erythema, warmth, and palpation of a cord or induration. Physical examination findings such as Homan's sign (pain with forced dorsiflexion of the ankle) has traditionally been recommended; however, this maneuver has been shown to have low specificity and sensitivity when diagnosing DVT.

As opposed to DVT, PE can present with a variety of symptoms including fever, tachypnea, tachycardia, hypoxia (at rest and exertion), pleuritic chest pain, rales, loud second heart sound, cough, arrhythmia, syncope, or cardiopulmonary collapse.

LABORATORY AND IMAGING STUDIES

DVT is largely diagnosed with a combination of history, examination, and a confirmatory imaging study. The gold standard for the diagnosis is venography; however, because of ready availability, lack of radiation, and high specificity, compression ultrasound (CUS) has become the initial test of choice. Ultrasound is useful in detecting femoral and popliteal venous thrombi. Serial ultrasounds (over a 2-week period) to identify a clot as it progresses may be necessary to detect a possible thrombus. However, if clinical suspicion for DVT is high or if a more proximal vessel is suspected, further imaging, such as an MRI, is warranted (Cogo et al., 1998).

D-Dimer, a fibrin degradation product, can be elevated in the setting of an acute clot. It is, however, also elevated in many situations including trauma, postsurgery, malignancy, pregnancy, and the puerperium. D-Dimer testing, using an enzyme-linked immunosorbent assay (ELISA), is highly sensitive with a good negative predictive value, which, in conjunction with a low clinical suspicion for PE, can help rule out PE in nonpregnant patients. D-Dimer use in pregnancy and the puerperium has not been sufficiently studied and can be misleading since elevation is not indicative of acute thrombosis.

When PE is suspected, it is crucial to accurately make the diagnosis, but also exclude other potential etiologies for the woman's complaint. Initial assessment needs to be thorough and comprehensive. Workup includes an arterial blood gas, EKG, and chest x-ray, although none of these tests can be used to definitively rule in or rule out a PE (Rodger et al., 2000). In nonpregnant patients, the incidence of sinus tachycardia and evidence of right heart strain (i.e., right bundle branch block [RBBB]) was found to be slightly increased in patients with PE. Chest x-rays are not helpful in diagnosing a PE but rather can be used to help exclude other possible diagnoses such as pneumothorax, pulmonary edema, or pneumonia.

The biggest challenge for a clinician when trying to diagnose a pregnant woman with PE is determining what imaging test will be most useful and also minimize fetal radiation exposure. The scope of this chapter will focus on postpartum diagnosis of VTE; therefore, fetal exposure other than via breast milk is not an issue.

Both ventilation perfusion (V/Q) scan and computed tomography pulmonary angiogram (CTPA) are acceptable options for use in the postpartum period, and the decision to use one over the other can vary based on institution.

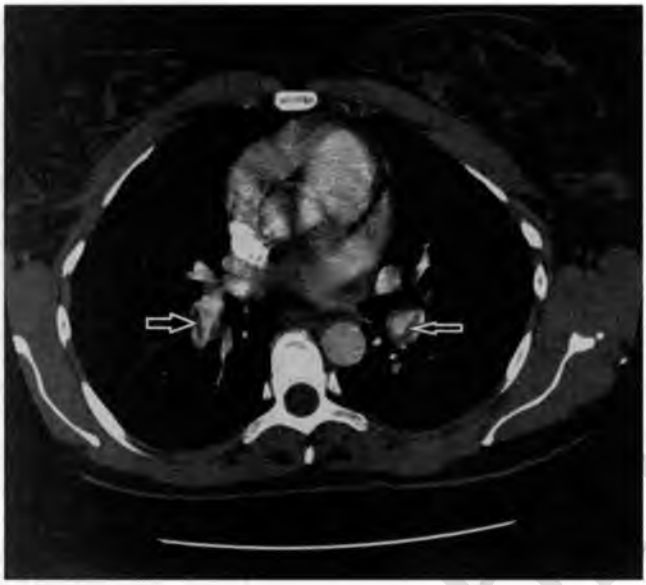

Figure 32.2 Computed tomography pulmonary angiogram of pulmonary embolism (arrows pointing to embolism in pulmonary arteries).

Source: Courtesy of Radiology Department, Women & Infants Hospital, Providence, RI.

CTPA, however, is being used more frequently due to ease of testing and a higher sensitivity and specificity over V/Q scans (Rathbun, Raskob, & Whitsett, 2000). Figure 32.2 depicts filling defects in segmental branches of the pulmonary arteries, consistent with the diagnosis of PE.

Another advantage of CTPA is its ability to detect other possible cardiopulmonary diagnoses such as pulmonary edema or even aortic dissection. In spite of all its benefits, CTPA does confer an increased amount of radiation to lactating breast tissue and is relatively contraindicated in the setting of renal failure, at which point V/Q scan may be a more suitable alternative.

Finally, it is critical to ask whether the woman is breastfeeding or not, as this can be of great concern to a new mother. Small amounts of iodinated or gadolinium-based contrast agents reach breast milk. The American College of Obstetricians and Gynecologists and the American Association of Family Physicians both support continued breastfeeding without interruption in lactating women who receive iodinated contrast or gadolinium. If a mother feels uncomfortable, an alternative option is to discard pumped milk for 24 hours postprocedure (Ito, 2000; Webb, Thomsen, Morcos, & Members of Contrast Media Safety Committee of European Society of Urogenital Radiology, 2005).

CLINICAL MANAGEMENT AND FOLLOW-UP

Once a diagnosis of VTE has been established, initial care can be started in either an inpatient or outpatient setting and is mostly dependent on clinical stability. For many postpartum women, being away from their newborn can cause distress and anxiety. Therefore, whenever clinically possible, outpatient care is considered.

Therapeutic anticoagulation can last for 3 to 6 months and the most commonly used treatment options include low-molecular-weight heparin (LMWH) and warfarin. Unfractionated heparin (UH) is rarely used in the postpartum period, unless the woman is deemed at high risk of bleeding, and therefore, the potential rapidity of reversal of UH may be an advantage. Due to the ease of administration, pharmacokinetic predictability, and decreased risk of heparin-induced thrombocytopenia (HIT) and osteopenia, LMWH is an ideal and preferred choice for initial outpatient therapy of postpartum VTE (Greer & Nelson-Piercy, 2005). LMWH can be continued for the complete duration of therapy; however, transition to warfarin for the long term is another option. Newer direct oral anticoagulants have not yet been properly studied (both in efficacy and in a breastfeeding population) so to fully advocate for their use in treating postpartum VTE may be premature (Rudd, Winans, & Panneerselvam, 2015; Wiesen et al., 2016).

At baseline, laboratory studies include a complete blood count (CBC) and coagulation studies including prothrombin time (PT) and activated partial thromboplastin time (aPTT). Close outpatient follow-up with a hematologist or the patient's primary care doctor is essential to ensure proper monitoring of anticoagulation levels and for potential complications such as bleeding or HIT. Thrombophilia workup is debatable and not all tests are useful in the setting of recent pregnancy and/or recent thrombus, thereby warranting good follow-up with a specialist in the field. Postpartum VTE can be a difficult diagnosis to make; however, better care for new mothers can be given with increased education and awareness by providers as well as improving laboratory and imaging studies.

CLINICAL PEARLS

- D-Dimer use in the diagnosis of VTE in pregnancy and the puerperium has not been sufficiently studied and can be misleading since elevation is not indicative of acute thrombosis.
- DVT during pregnancy and the postpartum period may develop in uncommon locations such as pelvic or abdominal veins.
- Both V/Q scan and CTPA are acceptable options for use in the postpartum period.

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