The Diagnosis and Management of the Acute Abdomen in Pregnancy

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This textbook is dedicated to the memories of the late Lt. Col. Reynold S. Greenspan, DO, MS, USAF, my dad, and the late James P. Youngblood, MD, FACOG, my other dad.

Foreword

Dr. Greenspan is the author of an excellent textbook on an important subject that has had very little recent update. It comprises 14 sections covering important and current information that very accurately involves the diagnosis of the acute abdomen. Each section by Dr. Greenspan, and by physicians with special interests and expertise in various components, is well organized and has helpful information for those involved in the practice of obstetrics.

This textbook is well written and easily readable. It provides prompt access to information on a subject that may at times require expedited action.

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Harry S. Jonas, MD, FACOG

Preface

An acute abdomen is defined as "an abnormal condition characterized by the acute onset of severe pain within the abdominal cavity" [1]. Although rare, it represents a potentially life-threatening emergency that necessitates immediate diagnosis and competent intervention. The management, however, can be highly challenging as acute abdominal pain is multi-etiologic and can originate from any of the multiple intraabdominal organs. Acute abdomen in pregnancy elevates these challenges to a higher level of complexity. Thus, the pregnancy-induced maternal physiological and anatomical changes, the considerations for two patients – the mother and the fetus – and the addition of obstetrical sources of an abdominal emergency compound the diagnostic and therapeutic challenges in a pregnant mother. Ensuring an optimal maternal and fetal outcome would necessarily require an integrated multidisciplinary expertise. Responding to a dearth of any practical up-to-date single reference source for managing this life-threatening condition, Dr. Peter Greenspan has assembled a team of extraordinarily talented and accomplished contributors to address the various aspects of managing an acute abdomen in pregnancy in this practical and highly useful textbook.

A spectrum of chapters deals comprehensively with the various aspects of the subject. The initial chapters discuss the relevant aspects of maternal anatomical and physiological changes in pregnancy, fetal development, general diagnostic principles of the acute abdomen, and the diagnostic imaging and laboratory investigations. Subsequent chapters present state-of-the-art reviews on the management of specific etiologies – obstetrical, gynecological, cardiopulmonary, gastrointestinal, urological, and trauma. The concluding chapters discuss the surgical and gynecological principles in managing a pregnant patient and the relevant liability considerations. As evident, the book admirably fulfils its promise.

Dr. Greenspan should be congratulated for this worthy undertaking. As a distinguished academic obstetrician gynecologist in excellent standing with years of expertise and experience as a practitioner and a teacher, he certainly has the

appropriate credentials. I am highly confident that the book will be well received and highly valued by all who are involved in providing professional care for pregnant mothers afflicted with this dire emergency.

Reference

1. Mosby's Medical Dictionary. 9th ed. Elsevier; 2009.

Kansas City, MO, USA Dev Maulik, MD, PhD, FACOG

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The daunting task of editing and contributing to a medical textbook is a humbling experience. Such an undertaking would not have been possible without the advice, assistance, encouragement, and patience of numerous individuals.

I owe an enormous amount of gratitude to Gwen Sprague, MLS, our medical librarian at Truman Medical Center who, while undergoing radiation and chemotherapy, gave me excellent support and counsel. Gwen was always available for me to discuss graphics, tables, and copyright issues and to assist me in organizing and optimizing the chapters. At the time of this writing, Gwen is cured and stronger than ever.

I am very grateful for the advice and suggestions of a dear friend, colleague, and mentor, Roger P. Smith, MD, FACOG, the author of over 40 books on topics from obstetrics and gynecology to gumball machine collecting. Dr. Smith referred me to Bonita Allen and Jennifer Jones, of Elsevier, who were instrumental in assisting me in obtaining many of the graphical materials used in this textbook.

The foreword and introduction were written by Harry S. Jonas, MD, FACOG, and Dev Maulik, MD, PhD, FACOG, FRCOG, respectively, who have been my colleagues and mentors for my entire career. Their guidance in this project is greatly appreciated.

Many thanks to Glenn Talboy, MD, FACS, a close friend and colleague, to whom I am indebted for his advice and clinical acumen.

I thank Johan P. Suyderhoud, MD, and Kara Settles, MD, of the UMKC School of Medicine Department of Anesthesia, for providing assistance in enlisting contributors for the project.

Richard Hruska, the executive editor of this textbook for Springer US, has been very patient with our production delays but has always been gracious and welcoming ever since he approached me to edit this work. Colton Coreschi, his assistant, has been diligent in moving the project continually toward publication.

Connie Walsh, however, deserves particularly special gratitude, as the developmental editor. Her involvement, on a daily basis with advising, suggesting, and hand-holding, as this textbook went from the outline stage to the finished project, has been quintessential. Without her encouragement and patience, this textbook would never have been concluded.

I am greatly indebted to my professional associates and personal friends, Kristin J. Kruse, MD, FACOG, and Sarah E. Sudduth, MD, FACOG, for their forbearance

and cooperation over the period of time that my favorite excuse for any reason was "sorry, I have to work on the book."

Additionally, I would be remiss if I didn't extend my sincerest appreciation to Joy Hobick, our administrative assistant, without whom, the three of us would be helpless in the day-to-day operation of our clinical and academic services.

Lastly, I want to acknowledge my ever-encouraging and enthusiastic children for their support, but my deepest appreciation and the most thanks go to my soul mate and pilot, the love of my life, Kim Greenspan, who has been an endless source of suggestions, encouragement, support, and sacrifice during the entirety of the enterprise of creating this textbook.

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Maternal Anatomical and Physiological Adaption to Pregnancy

1

Peter Bogach Greenspan

Anatomical Changes

Introduction

Pregnancy is not a pathological state. However, maternal and/or fetal diseases can rapidly transform a normal pregnancy into a serious condition, requiring meticulous diagnosis and management to avoid catastrophes to the mother, the fetus, or both.

Conditions that arise in pregnancy are often associated with the acute abdomen. Several of these conditions can be managed medically, while other conditions require surgical intervention. Pregnant women are also subject to serious traumatic injuries, such as may occur in vehicular accidents or violent crimes, among other causes.

The modern practice of medicine and surgery allows the caregivers of sick and injured pregnant women to vastly improve maternal and fetal outcome with interventions that are safe for both.

The diagnosis and management of disease and injury in pregnancy are complicated by several factors such as changes in maternal anatomy and physiology as well length of gestation and consideration of the trimesters of pregnancy, which may inform the provider as to what options are available for the safest outcome in each case.

When confronted with a gravid female who presents to the clinic or the labor suite with signs and symptoms of an acute abdomen, the clinician must be well

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educated in the anatomical and physiological adaptations and alterations that occur normally in pregnancy to be able to make the most accurate diagnosis.

Uterine Enlargement

The implantation of a gestation produces physiological effects on the uterine musculature that allows for the myometrium to soften and expand. These changes are palpable to the examiner by 5–6 weeks of pregnancy. The nonpregnant uterus is located in the pelvic cavity between the bladder anteriorly and the rectum posteriorly [1].

Usually, the gravid uterus is not palpable above the pubic ramus until about 12 weeks of gestation. The inferior portion of the anterior uterine wall, called the lower uterine segment, is united to the posterior wall of the bladder by a well-defined loose connective tissue layer – the vesicouterine peritoneum. During cesarean delivery, the peritoneum of the vesicouterine pouch is often sharply incised, and the vesicouterine space is entered. This is referred to as the bladder flap.

The majority of the uterus, with the exception of the cervix, is muscle. The inner surfaces of the anterior and posterior walls are closely approximated, and the cavity between these walls forms a mere slit. The nulligravid uterus measures 6–8 cm in length compared with 9–10 cm in multiparous women. The uterus averages 60 g and typically weighs more in parous women [2, 3].

A gestation stimulates remarkable uterine growth due to hypertrophy of the muscle fiber. The uterine fundus, a previously flattened convexity between tubal insertions, now becomes dome shaped. Furthermore, the round ligaments appear to insert at the junction of the middle and upper thirds of the organ. The fallopian tubes elongate, but the ovaries grossly remain the same.

The growth of the uterus is initially cephalad, but by 14–16 weeks of gestation, the fundus also protrudes anteriorly thus creating a visible bulge in the abdominal wall. In healthy gravidas, the fundus is at the level of the umbilicus by 20 weeks of gestation.

In normal pregnancy, the fundus grows at a rate of about 1 cm per week and can be documented as “MacDonald’s Measurement.” Deviation in expected growth, either less or more than expected, should arouse suspicion in the examiner of potential maternal/fetal problems.

As the gravid uterus expands, it naturally displaces other viscera. Furthermore, the expansion may produce compression of surrounding organs, which in turn, may compromise the functions of those structures. This accounts for increased urinary frequency in pregnancy, as well as constipation. In the latter third trimester, the displacement of the intestines and stomach often encroach on the diaphragm of the gravid woman, often producing shortness of air and difficulty with breathing. Palpitations are also common, as the abdominal viscera push up on the diaphragm, allowing the gravida to sense her beating heart. Gastrointestinal reflux and nausea are often associated with compression of the stomach. Biliary function may be compromised, as well. Upward displacement of the appendix can make the diagnosis of

appendicitis very difficult. Uterine enlargement combined with other natural physiological alterations in pregnancy must be understood to accurately evaluate and treat the acute abdomen in the pregnant woman.

Physiological Changes

Cardiovascular System

Gestation produces significant physiological changes in the cardiovascular system. Several adaptive mechanisms are initiated as early as 5 weeks' gestation to maximize oxygen delivery to maternal and fetal tissues [4].

Most pregnant women tolerate these physiological changes. In cardiac diseases, however, maternal morbidity and even mortality may occur.

Heart

Displacement of the diaphragm and the effect of pregnancy on the shape of the rib cage shift the heart cephalad and to the left. In addition, the heart rotates on its long axis, moving the apex somewhat laterally, causing an increased cardiac silhouette on radiographic studies, without an actual change in the cardiothoracic ratio. Other radiographic findings include an apparent straightening of the border of the left side of the heart and increased prominence of the pulmonary conus. Diagnosis of cardiomegaly by chest x-ray should be confirmed by echocardiogram if clinically appropriate [5].

Actual cardiomegaly in pregnancy is rare; however, physiological myocardial hypertrophy of the heart is observed as a result of expanded blood volume in the first half of the pregnancy and progressively increasing afterload in the latter part of the pregnancy. These structural changes in the heart are similar to the findings in response to exercise and result in eccentric hypertrophy as opposed to concentric hypertrophy that is observed with disease states such as hypertension or aortic stenosis. The eccentric hypertrophy facilitates enhanced pumping capacity in response to increased demand, producing greater mechanical efficiency [6, 7].

These physiological alterations commence early in the first trimester and peak by 30–34 weeks' gestation. Left ventricular end-diastolic dimension increases 12% over preconceptional values by M-mode echocardiography. Concurrently, left ventricular wall mass increases by 52% (mild myocardial hypertrophy), and atrial diameters increase bilaterally, peaking at 40% above nonpregnant values [7].

Pulmonary capillary wedge pressures are stable, as a result of a combination of decreased pulmonary vascular resistance and increased blood volume. Multiple gestations increase myocardial hypertrophy, atrial dilation, and end-diastolic ventricular measurements even further [8]. Following delivery, the pregnant heart slowly regresses in size and may take up to 6 months to return to prepregnant dimensions [9].

Evaluation of left ventricular contractility is difficult in pregnancy because it is strongly influenced by changes in heart rate (HR), preload, and afterload. Despite

the increase in stroke volume (SV) and cardiac output (CO), normal pregnancy is not associated with hyperdynamic left ventricular function during the third trimester, as measured by ejection fraction, left ventricular stroke work index, or fractional shortening of the left ventricle. However, some studies have shown that contractility might be slightly increased in the first two trimesters, whereas other literature reports no change throughout the pregnancy, and some report a decline toward term [7]. A recent study demonstrated that in the third trimester, the cardiac systolic function declines as demonstrated by a decrease in the ejection fraction and the systolic myocardial velocities compared with the first trimester. The study results are consistent with impaired contraction and relaxation of the left ventricle at the end of pregnancy suggesting that a decline in cardiac function at term is normal in pregnancy and that an exaggeration of this decline may explain the etiology for peripartum cardiomyopathy [10].

Clinicians and researchers have concentrated on abnormalities of diastolic function as significant contributors to cardiac disease and symptom severity, especially in the setting of normal or near-normal systolic function [11].

One review noted that diastolic dysfunction was highlighted as a leading cause of cardiac failure in pregnancy [12].

The effects of pregnancy on diastolic function have been exhaustively investigated using pulsed-wave Doppler echocardiography [7].

In young healthy women, the left ventricle is elastic; therefore, diastolic relaxation is swift, and ventricular filling occurs almost completely by early diastole with minimal contribution from the atrial kick. The E/A ratio compares the peak mitral flow velocity in early diastole (E) to the peak atrial kick velocity (A); although both velocities increase in pregnancy, the overall ratio falls because of a greater rise in the A-wave velocity. The rise in the A value, which begins in the second trimester and increases throughout the third trimester, indicates the increased importance of the atrial contraction in left ventricular filling during pregnancy [7].

Veille et al. found that in healthy women, pregnancy did not adversely affect baseline diastolic function, however at maximal exercise, diastolic function was impaired. This impairment was attributed to increased left ventricular wall stiffness. The authors also speculated that this change may be the limiting factor for exercise in pregnancy [13].

Cardiac Output

The tremendous increase in CO is one of the most remarkable changes in pregnancy. Van Oppen and coworkers performed a meta-analysis of 33 cross-sectional and 19 longitudinal studies and found greatly divergent results on when CO peaked, the magnitude of the rise in CO before labor, and the effect of the third trimester on CO [14].

All of the studies agreed that CO increased significantly beginning in early pregnancy, peaking in between 30% and 50% above preconceptional values. In a longitudinal study by Robson and associates using Doppler echocardiography, CO increased by 50% at 34 weeks from a prepregnancy value of 4.88–7.34 L/min [15, 16] (Fig. 1.1).

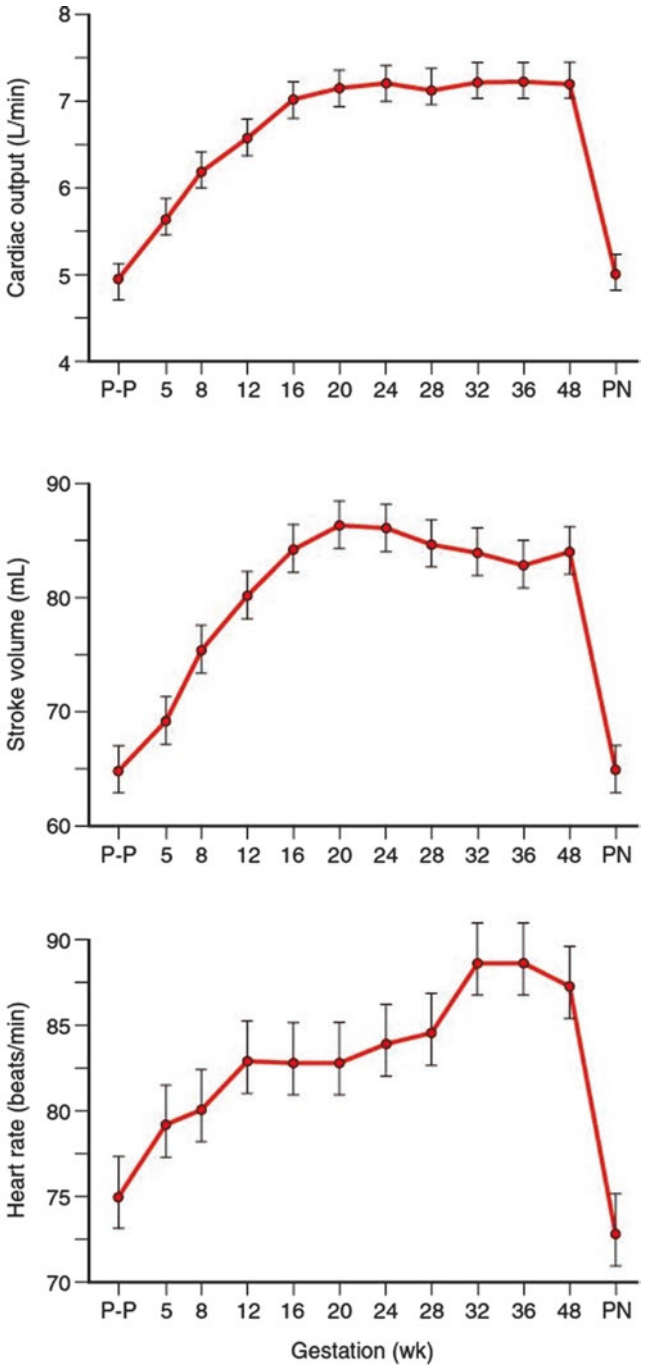

Fig. 1.1 Cardiac output in pregnancy. Increase in cardiac output, stroke volume, and heart rate from the nonpregnant state throughout pregnancy (From Gabbe [17]. Reprinted with permission from Elsevier)

The CO in twin gestations incrementally increases an additional 20% greater than that of singleton pregnancies [8]. Robson et al. showed that by 5 weeks' gestation, CO has already risen by more than 10%. At 12 weeks, the rise in output is 34–39% above nongravid levels, accounting for about 75% of the total increase in CO during pregnancy. There is no literature consensus as to the exact gestation when CO peaks, but most studies point to a range between 25 and 30 weeks [18].

The data on whether the CO continues to increase in the third trimester are very divergent, with equal numbers of good longitudinal studies showing a mild decrease, a slight increase, or no change [14].

These study discrepancies are not explained by differences in investigative techniques, position of the women during measurements, or study design. This apparent discrepancy appears to be explained by the small number of individuals in each study and the probability that the course of CO during the third trimester is determined by factors specific to the individual [14].

Desai and coworkers reported that CO in the third trimester is significantly correlated with fetal birthweight and maternal height and weight [19].

Increases in CO are mostly directed to the uterus, placenta, and breasts. The uterus receives 2–3% of CO in the first trimester as well as in the nongravid state. The breasts receive 1%. CO going to the kidneys (20%), skin (10%), brain (10%), and coronary arteries (5%) remains at similar nonpregnant percentages. However, because of the overall increase in CO, this results in an increase in absolute blood flow of about 50% [15]. At term, the uterus receives 17% (450–650 mL/min) and the breasts 2%, mostly at the expense of a reduction of the fraction of the CO going to the splanchnic bed and skeletal muscle. The absolute blood flow to the liver is not changed, but the overall percentage of CO is significantly decreased.

CO is the product of SV and HR (CO = SV × HR). Both are increased during pregnancy and contribute to the overall rise in CO. Maternal HR initially rises at 5 weeks' gestation and peaks at 32 weeks' gestation at 15–20 beats above the nongravid rate, an increase of 17%. The SV starts to rise by 8 weeks' gestation reaching its maximum at about 20 weeks, which is 20–30% above nonpregnant values. In the third trimester, it is primarily variations in the SV that determine whether CO increases, decreases, or remains stable, as described earlier.

Maternal position influences CO in pregnancy. One study in 10 normal gravid women in the third trimester, using pulmonary artery catheterization, CO was noted to be highest in the knee–chest position and lateral recumbent position at 6.6–6.9 L/min. CO decreased by 2.2–5.4 L/min in the standing position. The decrease in CO in the supine position compared with the lateral recumbent position is 10–30%. In both the standing and the supine positions, decreased CO results from a fall in SV secondary to decreased blood return to the heart. The enlarged uterus compresses the inferior vena cava in the supine position, reducing venous return. However, this effect is not observed before 24 weeks. Importantly, in late pregnancy, the inferior vena cava is completely occluded in the supine position, with venous return from the lower extremities occurring through the dilated paravertebral collateral circulation [16].

Most supine women are not hypotensive or symptomatic because of the compensated rise in systemic vascular resistance (SVR), despite decreased CO. However, 5–10% of gravidas experience supine hypotension with symptoms of dizziness, lightheadedness, nausea, and occasional syncope. The women who are symptomatic have a greater decrease in CO and blood pressure (BP) and a greater increase in HR when in the supine position than do asymptomatic women [20]. It has been proposed that the determination of whether women become symptomatic depends on the development of an adequate paravertebral collateral circulation. Interestingly, with engagement of the fetal head, less of an effect on CO is seen [16].

Maintaining a normal BP in the supine position may be lost during epidural or spinal anesthesia because of the inability to increase SVR. The clinical significance of the effects of maternal position on CO are especially important when the gravida is clinically hypotensive or in the setting of a category II or III fetal heart rate tracing. The observation of decreased birthweight and placental infarctions in working women who stand for prolonged periods may be associated with findings of a decreased CO in the standing position.

Arterial Blood Pressure and Systemic Vascular Resistance

Blood Pressure (BP) is the product of CO and resistance (BP = CO × SVR). Even with the large increase in CO, typically the maternal BP is decreased until later in pregnancy because of a decrease in SVR that peaks in midpregnancy, followed by a gradual rise until term. The SVR remains 21% lower than prepregnancy values in pregnancies not affected by gestational hypertension or preeclampsia, even at full term. Progesterone-mediated smooth muscle relaxation is the most obvious cause for the decreased SVR. However, the precise mechanism for the fall in SVR is not well understood. Increased nitric oxide (NO) also contributes to decreased vascular resistance by direct actions and by blunting the vascular responsiveness to vasoconstrictors such as angiotensin II and norepinephrine. During conception, the expression and activity of NO synthase is elevated and the plasma level of cyclic guanosine monophosphate, a second messenger of NO and a mediator of vascular smooth muscle relaxation, is also increased [21]. Consequently, despite the overall increase in the renin–angiotensin–aldosterone system (RAAS), the normal gravida is resistant to the vasoconstrictive effects of angiotensin II. Gant et al. showed that nulliparous women who developed preeclamptic continue to respond to angiotensin II before the appearance of clinical signs of preeclampsia [22].

Initial decreases in BP manifest at 8 weeks' gestation or earlier paralleling the falling SVR. Current studies did not include preconception BP or frequent first-trimester BP sampling and, therefore, cannot determine the exact time course of hemodynamic alterations. Menstruation causes fluctuations in BP, which is decreased in the luteal phase. Therefore, it seems reasonable that BP drops immediately in early pregnancy. The diastolic BP and the mean arterial pressure [MAP = (2 × diastolic BP + systolic BP)/3] decrease more than the systolic BP (Fig. 1.2).

The diastolic BP and the MAP reach their peaks at midpregnancy. By term, they both return to prepregnancy levels and rarely exceed prepregnancy or postpartum values. However, some investigators have reported that at term, the BP is greater

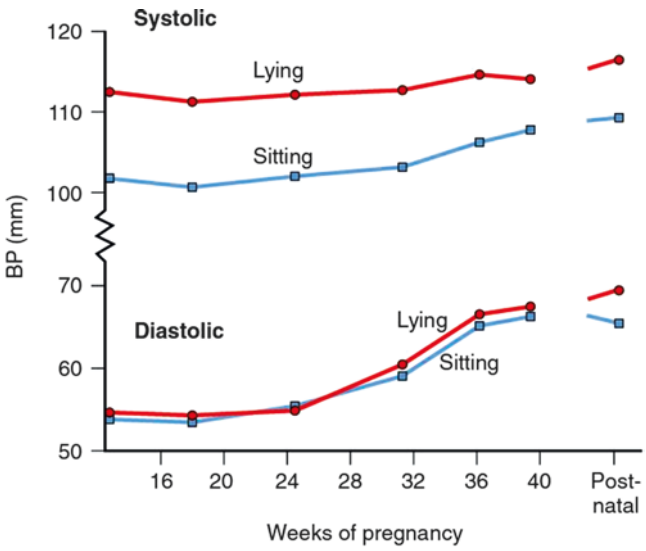

Fig. 1.2 Blood pressure in pregnancy. Blood pressure trends (sitting and lying) during pregnancy. Postnatal measures performed 6 weeks postpartum (From Gabbe [17]. Reprinted with permission from Elsevier)

than in matched nonpregnant controls and believe that in the third trimester, the BP is higher than prepregnant values. These studies are very limited by the absence of preconceptional values for comparison within individual patients.

Positioning and Korotkoff sounds are important when the BP is taken to determine the diastolic BP. BP is lowest in the lateral recumbent position, and the BP of the superior arm in this position is 10–12 mm Hg lower than the inferior arm. Clinically, BP should be taken in the sitting position and the Korotkoff 5 sound should be used. This is the diastolic BP when the sound disappears as opposed to the Korotkoff 4, when there is a muffling of the sound. One study of 250 gravidas showed that the Korotkoff 4 sound could only be identified in 48% of patients, whereas the Korotkoff 5 sound could always be determined. The Korotkoff 4 should only be used when the Korotkoff 5 occurs at 0 mm Hg [23].

When compared with mercury sphygmomanometry during pregnancy, automated BP monitors tended to overestimate the diastolic BP. However, the overall results were similar in normotensive women. Automated monitors appear increasingly inaccurate at higher BPs in women with preeclampsia.

Venous Pressure

Venous pressure in the upper extremities remains unchanged in pregnancy but rises progressively in the lower extremities. Femoral venous pressure increases from values near 10 cmH_2O at 10 weeks' gestation to 25 cmH_2O near term [24]. Clinically, the increase in venous pressure, as well as the obstruction of the inferior vena cava by the enlarging uterus, leads to the development of edema, varicose veins, and hemorrhoids, and increases the risk for developing deep venous thrombosis.

Pulmonary System

Upper Respiratory Tract

Pregnancy causes the mucosa of the nasopharynx to become hyperemic and edematous with hypersecretion of mucus due to increased estrogen. Marked nasal stuffiness is the result of these changes; epistaxis is also common. Insertion of nasogastric tubes may cause excessive bleeding if adequate lubrication is not used [25]. Polyposis of the nose and nasal sinuses develop in some individuals, which regress postpartum. Because of these changes, many pregnant women complain of chronic cold symptoms; however, the temptation to use nasal decongestants should be avoided because of the risk for hypertension and rebound congestion.

Mechanical Changes

The anatomic configuration of the thorax changes early in pregnancy, much earlier than can be explained by mechanical pressure from the enlarging uterus. Relaxation of the ligaments between the ribs and sternum may be responsible for these configurations. The subcostal angle increases from 68° to 103°, the transverse diameter of the chest expands by 2 cm, and the chest circumference expands by 5–7 cm. As pregnancy progresses, the diaphragm rises 4 cm; however, diaphragmatic excursion is not impeded and actually increases 1–2 cm. Respiratory muscle function is not affected by pregnancy, and maximal inspiratory and expiratory pressures are unchanged [26].

Lung Volume and Pulmonary Function

The anatomic changes in chest wall configuration and the diaphragm lead to changes in static lung volumes. In a review of studies with at least 15 subjects compared with nonpregnant controls, Crapo found significant changes [25] (Fig. 1.3 and Table 1.1).

The elevation of the diaphragm decreases the volume of the lungs in the resting state, thereby reducing total lung capacity and the functional residual capacity (FRC). The FRC can be subdivided into expiratory reserve volume and residual volume, and both decrease.

Spirometric measurements evaluating bronchial flow are unchanged in pregnancy. The forced expiratory volume in 1 second (FEV_1) and the ratio of FEV_1 to forced vital capacity are both unchanged, implying that airway function remains stable. Additionally, peak expiratory flow rates measured using a peak flow meter seem to be unaltered in pregnancy at rates of 450 ± 16 L/min [28]. Harirah and associates performed a longitudinal study of the peak flow in 38 women from the first trimester until 6 weeks postpartum [29]. They reported that the peak flows had a statistically significant decrease as the pregnancy progressed; however, the amount of the decrease was minimal enough to be of questionable clinical significance. Similarly, a small decrease in the peak flow was noted in the supine position versus the standing or sitting position. Therefore, during gestation, both spirometry and peak flow meters can be used in diagnosing and managing respiratory illnesses, but the clinician should ensure that measurements are performed in the same maternal position [29].

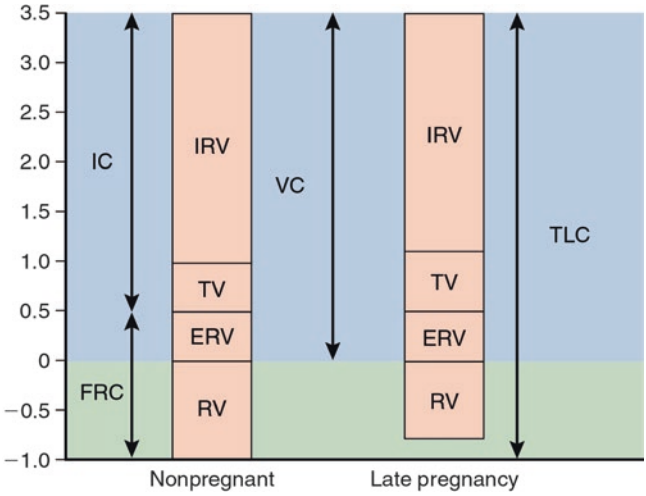

Fig. 1.3 Lung volumes in pregnant and nonpregnant women. *ERV* expiratory reserve, *FRC* functional residual capacity, *IC* inspiratory capacity, *IRV* inspiratory reserve, *RV* residual volume, *TLC* total lung capacity, *TV* tidal volume, *VC* vital capacity (From Gabbe [27]. Reprinted with permission from Elsevier)

Table 1.1 Lung functions in pregnancy

Lung volumes and capacities in pregnancy		
Measurement	Definition	Change in pregnancy
Respiratory race (RR)	Number of breaths per minute	Unchanged
Vital capacity (VC)	Maximal amount of air that can be forcibly expired after maximal inspiration (IC + ERV)	Unchanged
Inspiratory capacity (IC)	Maximal amount of air that can be inspired from resting expiratory level (TV + IRV)	Increased 5–10%
Tidal volume (TV)	Amount of air inspired and expired with a normal breath	Increased 30–40%
Inspiratory reserve volume (IRV)	Maximal amount of air that can be inspired at end of normal inspiration	Unchanged
Functional residual capacity (FRC)	Amount of air in lungs at resting expiratory level (ERV + RV)	Decreased 20%
Expiratory reserve volume (ERV)	Maximal amount of air that can be expired from resting expiratory level	Decreased 15–20%
Residual volume (RV)	Amount of air in lungs after maximal expiration	Decreased 20–25%
Total lung capacity (TLC)	Total amount of air in lungs at maximal inspiration (VC + RV)	Decreased 5%

From Cruickshank et al. [27], Gabbe [17]. Reprinted with permission from Elsevier

Gas Exchange

Rising progesterone levels drive a state of chronic hyperventilation, as noted by a 30–50% increase in tidal volume by 8 weeks' gestation. In turn, increased tidal volume results in an overall parallel rise in minute ventilation, regardless of a stable respiratory rate (minute ventilation = tidal volume × respiratory rate). The rise in minute ventilation, combined with a decrease in FRC, leads to a larger than expected increase in alveolar ventilation (50–70%). Chronic mild hyperventilation produces an increase in alveolar oxygen (PaO_2) and a decrease in arterial carbon dioxide ($PaCO_2$) from normal levels (Table 1.2).

The drop in the $PaCO_2$ is extremely important because it drives a more favorable carbon dioxide (CO_2) gradient between the fetus and mother, facilitating CO_2 transfer. The low maternal $PaCO_2$ results in a chronic respiratory alkalosis. The increased excretion of bicarbonate, as a result of partial renal compensation, helps maintain the pH between 7.4 and 7.45 and lowers the serum bicarbonate levels. In early pregnancy, the arterial oxygen (PaO_2) increases (106–108 mm Hg) as the $PaCO_2$ decreases; however, by the third trimester, a slight decrease in the PaO_2 (101–104 mm Hg) occurs as a result of the expanding uterus. This decrease in the PaO_2 late in pregnancy is even more pronounced in the supine position, with a further drop of 5–10 mm Hg and an increase in the alveolar-to-arterial gradient to 26 mm Hg, and up to 25% of women exhibit a PaO_2 of less than 90 mm Hg [25, 32].

A simultaneous but smaller increase in oxygen uptake and consumption occurs as the minute ventilation increases. Most investigators have found maternal oxygen consumption to be 20–40% above nonpregnant levels. This increase is a result of the oxygen requirements of the fetus, the placenta, and the increased oxygen requirement of maternal organs. With exercise or during labor, an even greater rise in both minute ventilation and oxygen consumption takes place [25]. Oxygen consumption can triple during contractions. Increased oxygen consumption and decreased FRC results in a lowering of the maternal oxygen reserve. Therefore, pregnant women are more susceptible to the effects of apnea, for example, during intubation when a more rapid onset of hypoxia, hypercapnia, and respiratory acidosis is seen.

Table 1.2 Lung volumes in pregnant and non-pregnant women

Blood gas values in third trimester of pregnancy		
	Pregnant	Nonpregnant
Pao_2 (mm Hg)[a]	101.8 ± 1	93.4 ± 2.04
Arterial Hgb saturation (%)[b]	98.5 ± 0.7%	98 ± 0.8%
$Paco_2$ (mm hg)[a]	30.4 ± 0.6	40 ± 2.5
pH[a]	7.43 ± 0.006	7.43 ± 0.02
Serum bicarbonate (Hco_3) (mmol/L)	21.7 ± 1.6	25.3 ± 1.2
Base deficit (mmol/L)[a]	3.1 ± 0.2	1.06 ± 0.6
Alveolar-arterial gradient [$P(A\text{-}a)O_2$ (mm Hg)][a]	16.1 ± 0.9	15.7 ± 0.6

[a]Data from Templeton and Kelman [30]. Data present as mean ± SEM
[b]Data from McAuliffe et al. [31]. Data presented as mean ± SD
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Gastrointestinal System

Appetite

The appetite of most women increases throughout pregnancy. At the end of the first trimester, food intake increases by about 200 kcal/day, in the absence of nausea. An additional 300 kcal/day is recommended, but the majority of gravidas compensate for this by decreasing their activity. Depending on the population being studied, energy requirements vary. More active women and teenagers show a greater increase in the need for calories. Cultural folklore about dietary cravings and aversions during gestation abound. These may be the result of an individual's perception of which foods aggravate or ameliorate symptoms such as nausea and heartburn. Some women experience a decrease in taste thus producing an increased desire for highly seasoned food. Bizarre cravings for strange foods, Pica, are relatively common among gravidas. Women with anemia or poor weight gain should be evaluated for a history of pica. Pica examples include the consumption of clay, starch, toothpaste, and ice [33].

Mouth

The pH and the production of saliva remain unchanged during gestation. Ptyalism, considered an unusual complication of pregnancy, usually occurs in women suffering from nausea. Women with ptyalism may secrete 1–2 L of saliva per day. Many experts believe that ptyalism actually represents an inability of the nauseated woman to swallow normal amounts of saliva as opposed to a true increase in the saliva production. Decreasing the ingestion of starchy foods may help to lower the amount of saliva. There is no evidence to support that pregnancy produces or accelerates dental caries. The gums, however, swell and may bleed after tooth brushing, thus causing "gingivitis of pregnancy". Tumorous gingivitis may occur occasionally, presenting as a violaceous pedunculated lesion at the gum line that may bleed profusely. This is called epulis gravidarum or pyogenic granulomas. These lesions consist of granulation tissue and an inflammatory infiltrate [33].

Stomach

The tone and motility of the stomach are decreased because of the smooth muscle–relaxing effects of progesterone and estrogen. The scientific evidence regarding delayed gastric emptying, however, is inconclusive [34]. Macfie et al. studied acetaminophen absorption as an indirect measure of gastric emptying. But they were unable to demonstrate a delay in gastric emptying when comparing 15 nonpregnant controls with 15 women in each trimester [34]. Additionally, a recent study showed no delay in gastric emptying in parturients at term who ingested 300 mL of water following an overnight fast [35]. However, an increased delay was seen in labor, with the etiology being ascribed to the pain and stress of parturition.

A decrease in peptic ulcer disease is observed in pregnancy. However, gastroesophageal reflux and dyspepsia increases by 30–50% [36]. This may be explained, in part, by physiological changes of the stomach and lower esophagus. Gestational hormones causing esophageal dysmotility play a role in gastroesophageal reflux

disease. Other factors include gastric compression from the enlarged uterus and a decrease in the pressure of the gastroesophageal sphincter. Progesterone causes the decrease in the tone of the gastroesophageal sphincter, while estrogen may be attributed to increased reflux of stomach acids into the esophagus. This may be the predominant cause of reflux symptoms. The decreased incidence of peptic ulcer disease, in theory, includes increased placental histaminase synthesis with lower maternal histamine levels, increased gastric mucin production leading to protection of the gastric mucosa, reduced gastric acid secretion, and enhanced immunologic tolerance of *Helicobacter pylori*, the infectious agent that causes peptic ulcer disease [36].

Intestines

Alterations in the motility of the small intestines and colon are common in pregnancy, thus causing an increased incidence of constipation in some and diarrhea in others. One study noted up to 34% of women experienced an increased frequency of bowel movements, possibly associated with increased levels of prostaglandin synthesis [37]. The incidence of constipation seems to be higher in early pregnancy, with 35–39% of women having constipation in the first and second trimester and only 21% in the last trimester [38]. Small intestines motility is reduced in pregnancy, with increased oral–cecal transit times. Progesterone has been thought to be the primary cause of the decrease in gastrointestinal motility, but newer studies showed that the actual etiology may be due to estrogen. Estrogen affects the increased release of NO from nerves in the gastrointestinal tract that subsequently cause relaxation of the gastrointestinal tract musculature. Absorption of nutrients from the small bowel is unchanged aside from the exception of increased iron and calcium absorption, but the increased transit time provides more efficient absorption. Parry and colleagues documented an increase in both water and sodium absorption in the colon [39].

The enlarging uterus produces intestinal displacement, and most importantly, the position of the appendix changes. Thus, the management of appendicitis regarding presentation, physical signs, and type of surgical incision are affected. An increase in portal venous pressure leads to dilation wherever there is portosystemic venous anastomosis such as at the gastroesophageal junction and the hemorrhoidal veins resulting in the common complaint of hemorrhoids.

Gallbladder

Gallbladder function is markedly altered because of the effects of progesterone. Starting in the second trimester, the fasting and residual volumes are double, and the rate of gallbladder emptying is much slower. Furthermore, the biliary cholesterol saturation is increased, and the chenodeoxycholic acid level is decreased [40]. As a result of this change, the composition of the bile fluid favors the formation of cholesterol crystals, and with incomplete emptying of the gallbladder, the crystals are retained, and enhanced gallstone formation ensues. One third of pregnant women develop biliary sludge. At the time of delivery, 10–12% of women have gallstones on ultrasonographic examination. Postpartum, biliary sludge disappears in essentially all women, but only about one third of small stones disappear.

Liver

Pregnancy does not change the size or the histology of the liver. There are, however, many clinical and laboratory signs present that may be associated with liver disease. Spider angiomata and palmar erythema, resulting from elevated estrogen levels, are normal and resolve at the conclusion of the gestation. The serum albumin and total protein levels fall progressively during pregnancy. Albumin levels are 25% lower than nonpregnant levels at term. Hemodilution causes a decrease in total protein and albumin concentrations despite an overall increase in total body protein. Furthermore, serum alkaline phosphatase levels rise during the third trimester to that of two to four times those of nongravid women. This increase is explained by placental production of the heat-stable isoenzyme and not from the liver [41]. Many protein serum concentrations produced by the liver increase. Other elevations occur in serum fibrinogen, ceruloplasmin, transferrin, and the binding proteins for corticosteroids, sex steroids, and thyroid hormones [41].

Other "liver function tests" remain unchanged by pregnancy, including serum levels of bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyltransferase, 5′-nucleotidase, creatinine phosphokinase, and lactate dehydrogenase, with the exception of alkaline phosphatase. The mean levels of ALT and AST are often mildly elevated but still within normal values [42]. Creatinine phosphokinase and lactate dehydrogenase levels can increase during labor. Further, pregnancy may cause some changes in the production and secretion of bile acid. Pregnancy may be associated with mild subclinical cholestasis resulting from the high concentrations of estrogen. Reports differ on serum bile acid concentrations, with some studies showing an increase and others no change. The fasting levels are unchanged. The measurement of a fasting level appears to be the best test for diagnosing cholestasis of pregnancy [42]. Cholestasis is caused by elevated levels of bile acids and is associated with significant pruritus. It is also noted to produce mild increases of ALT/AST and an increased risk for poor fetal outcomes.

Nausea and Vomiting of Pregnancy

Seventy percent of pregnancies are complicated by nausea and vomiting, or "morning sickness." Usually, the onset is between 4 and 8 weeks' gestation. Most women improve before 16 weeks. As many as 10–25% of women still experience symptoms at 20–22 weeks' gestation, and some women experience symptoms throughout the gestation [43]. In most patients, simple morning sickness rarely leads to significant weight loss, ketonemia, or electrolyte disturbances. In very few pregnant women, pernicious nausea and vomiting can be life-threatening. The cause is still poorly understood, although relaxation of the smooth muscle of the stomach probably plays a role. Elevated levels of human chorionic gonadotropin (hCG) have been implicated, although a good correlation between maternal hCG concentrations and the degree of nausea and vomiting has yet to be demonstrated. Correspondingly, little data exist to confirm that the etiology is related to higher levels of estrogen or progesterone. It has been observed that pregnancies complicated by nausea and vomiting generally have a more favorable outcome than do those without such symptoms [43]. Management is generally supportive, consisting of reassurance,

avoidance of foods found to prompt nausea, and consuming frequent small meals. Ingesting dry toast or crackers before getting out of bed may be helpful. The American College of Obstetricians and Gynecologists has endorsed the use of either vitamin B_6 alone or in combination with doxylamine (Unisom) as a safe and effective treatment and should be considered a first line of medical treatment. A recent review of alternative therapies to antiemetic drugs found that acupressure, wristbands, or treatment with ginger root may be helpful.

Hyperemesis gravidarum is a form of nausea and vomiting that is more pernicious and is associated with weight loss, ketonemia, electrolyte imbalance, and dehydration. It affects 1–3% of women, with persistence often throughout pregnancy. Rarely does it result in significant complications, but may include Wernicke encephalopathy, rhabdomyolysis, acute renal failure, and esophageal rupture. The clinician must rule out other pathologies such as pancreatitis, cholecystitis, hepatitis, and psychiatric disease. In some cases, hospitalization with intravenous replacement of fluids and electrolytes is needed. Several options of antiemetics include the phenothiazines: promethazine (Phenergan), chlorpromazine (Thorazine), and prochlorperazine (Compazine) or metoclopramide (Reglan), or ondansetron (Zofran) [44]. When hospital admission is inevitable, the patient should be given intravenous hydration and treated with one of the aforementioned medications (intravenously or intramuscularly initially). The clinician should not combine the phenothiazines with metoclopramide because of the additive risks for causing extrapyramidal reactions (tardive dyskinesia). Chlorpromazine given rectally (25–50 mg every 8 h) may be highly effective in the more refractory patients. The use of oral methylprednisolone, 16 mg three times daily for 3 days and then tapered over 2 weeks, has been shown to be more effective than promethazine, but several subsequent trials did not demonstrate benefit from the use of steroids [44].

There is currently no single therapy that works in all women. Occasionally, multiple different medications must be tried prior to having effective success. There are potential risks of parenteral caloric replacement, and this option should only be used as a last resort following multiple antiemetic treatments and attempts at enteral tube feedings.

Musculoskeletal System

Calcium Metabolism

In the past, pregnancy was believed to be a state of "physiologic hyperparathyroidism" with maternal skeletal calcium loss occurring to supply calcium to the fetus. It was also thought that this could produce long-term maternal bone loss. Now it is known that the majority of fetal calcium needs are provided by a series of physiological changes in calcium metabolism devoid of long-term consequences to the maternal skeleton [45]. This allows the fetus to accumulate 21 grams (g) (range 13–33 g) of calcium, 80% of this amount during the third trimester, when fetal skeletal mineralization is at its peak. Calcium is actively transported across the placenta. Interestingly, calcium is excreted in larger amounts by the maternal kidneys so that, by term, calciuria doubles.

There is a decline of maternal total calcium levels throughout pregnancy. Reduced serum albumin levels cause the fall of total calcium that result in a decrease in the albumin-bound fraction of calcium. However, the physiologically important fraction, serum ionized calcium, is unchanged and constant [45] (Fig. 1.4).

Consequently, maternal serum calcium levels are maintained, and the fetal calcium needs are met largely through increased intestinal calcium absorption. Calcium absorption occurs in the small intestines, and its absorption doubles by 12 weeks gestation; maximal absorption occurring in the third trimester [45, 46]. The early increase in absorption possibly allows the maternal skeleton to accumulate calcium in advance of the peak third-trimester fetal demands. Although the majority of fetal calcium needs are met by increased absorption of calcium, accumulating data confirm that at least some calcium resorption from maternal bone occurs to assist in meeting the increased fetal demands in the third trimester. These data are compatible with the hypothesis that physiological mechanisms exist to ensure an adequate supply of calcium for fetal growth and milk production without sole reliance on the maternal diet [46]. In similar fashion, maternal serum phosphate levels are unchanged [45].

In five recent prospective studies of maternal parathyroid hormone (PTH) levels, all using modern assays, maternal levels of PTH were not elevated and essentially remained in the low-normal range throughout gestation [45]. Hence, pregnancy is not concomitant with relative hyperparathyroidism.

The prohormone vitamin D is derived from cholesterol and occurs in two main nutritional forms: D3 (cholecalciferol), which is produced in the skin, and D2 (ergocalciferol), which is derived from plants and absorbed in the gut. Serum levels of 25-hydroxyvitamin D (25[OH]D) increase in proportion to vitamin D synthesis and intake. The best indicator of vitamin D status is levels of 25[OH]D. 25[OH]D is further metabolized to 1,25-dihydroxyvitamin D or active vitamin D. Levels of 1,25-dihydroxyvitamin D increase overall in pregnancy, with prepregnancy levels doubling in the first trimester and peaking in the third trimester [47]. Unless vitamin D intake or synthesis is changed, levels of 25[OH]D do not change in pregnancy. Increases in 1,25-dihydroxyvitamin D are secondary to increased production by the maternal kidneys and potentially the fetoplacental unit and is independent of PTH control. The increase in 1,25-dihydroxyvitamin D is directly responsible for most of the increase in intestinal calcium absorption [45]. The prevalence of vitamin D deficiency in pregnancy is 5–50%, which has recently created a great deal of interest. The recommendations to introduce universal screening during pregnancy by measuring serum levels of 25[OH]D are controversial. Levels less than 32 ng/mL indicate vitamin D deficiency. It is recommended to increase vitamin D supplementation should a deficiency be diagnosed [47]. Calcitonin levels also rise by 20% and may help protect the maternal skeleton from excess bone loss [45].

Skeletal and Postural Changes

The effect of pregnancy on bone metabolism is complex. The evidence of maternal bone loss during pregnancy has been inconsistent, with various studies reporting bone loss, no change, and even gain. A critical question is whether pregnancy

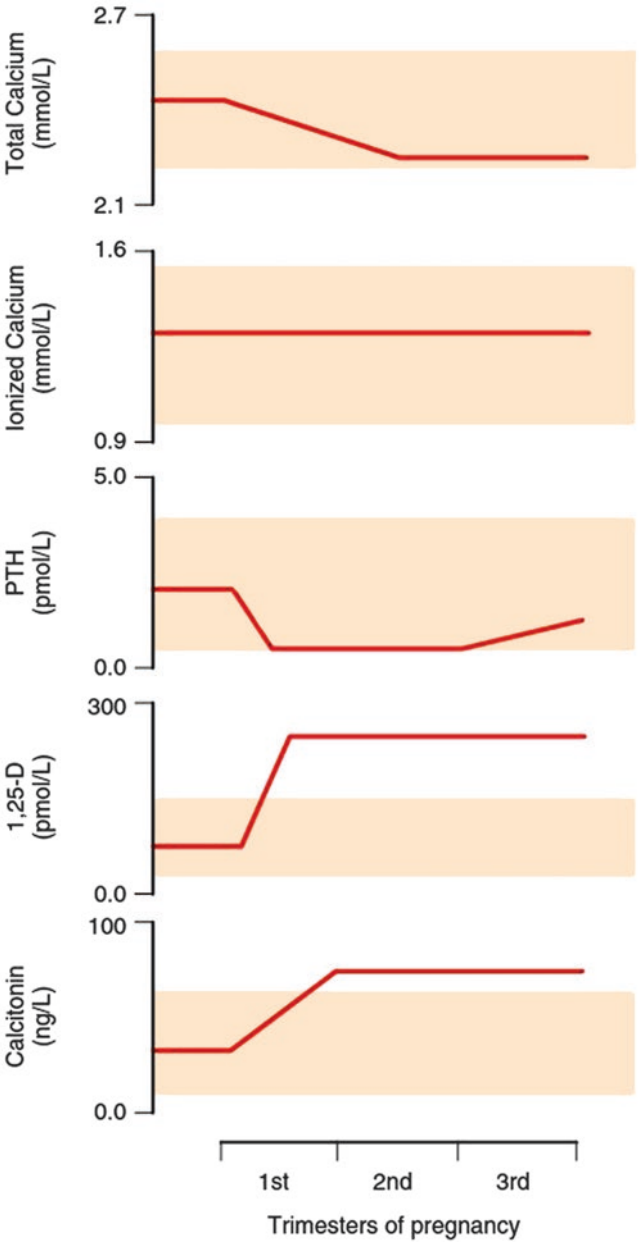

Fig. 1.4 Calcium in pregnancy. The longitudinal changes in calcium and calcitropic hormone levels that occur during human pregnancy. Normal adult ranges are indicated by the *shaded areas*. *1,25-D* 1,25-dihydroxyvitamin D, *PTH* parathyroid hormone (From Gabbe [17]. Reprinted with permission from Elsevier)

and lactation have a long-term risk for causing osteoporosis later in life [48]. A recent review of 23 studies, by Ensom and colleagues, determined that pregnancy is a state of high bone turnover and remodeling. Pregnancy and lactation can cause reversible bone loss; the loss being increased in women who breastfeed for longer intervals [48]. There is no support of an association between parity and osteoporosis later in life. Furthermore, in a comparison of female twins discordant for parity, pregnancy and lactation were found to have no detrimental effect on long-term bone loss.

Bone turnover is apparently low in the first half of gestation, but then it increases in the third trimester, corresponding to the peak rate of fetal calcium needs, and may represent turnover of previously stored skeletal calcium [45]. Markers of both bone resorption (hydroxyproline and tartrate-resistant acid phosphatase) and bone formation (alkaline phosphatase and procollagen peptides) are increased during gestation [46]. Shahtaheri and associates, in the only study of bone biopsies performed during pregnancy, noted a change in the microarchitectural pattern of bone; however, no change in overall bone mass was elucidated. This change in the microarchitectural pattern seems to result in a framework more resistant to the bending forces and biomechanical stresses needed to carry a growing fetus [49]. Multiple recent studies that support these findings have shown that bone loss occurs only in the trabecular bone and not cortical bone. Promislow et al., measured bone mineral density twice during pregnancies using dual-energy x-ray absorptiometry and showed the mean loss of trabecular bone was 1.9% per 20 weeks' gestation [50]. However, women placed on bed rest had significantly greater bone loss. In comparison, the mean bone loss in postmenopausal women rarely exceeds 2% per year. There are previous reports that indicate that the cortical bone thickness of long bones may even increase with pregnancy.

Osteoporosis during or soon after pregnancy is rare, despite the bone loss that occurs. It remains controversial whether additional calcium intake during pregnancy and lactation prevents bone loss. More recent studies indicate that calcium supplementation does not decrease the amount of bone loss, but Promislow and associates found that maternal intake of 2 g per day or greater was modestly protective [50]. This exceeds the recommended dietary allowance of 1000–1300 mg/day during pregnancy and lactation [46].

Progressively increasing anterior convexity of the lumbar spine (lordosis) occurs in pregnancy. This is a compensatory mechanism that keeps the woman's center of gravity over her legs and prevents the enlarging uterus from shifting the center of gravity anteriorly. Low back pain in two thirds of women is an unfortunate side effect of this compensation. In one third of the women, this pain is described as severe. Ligaments that support the pubic symphysis and sacroiliac joints loosen, assumed to be from the effects of the hormone relaxin. Relaxin levels increase tenfold in pregnancy. Marked widening of the pubic symphysis occurs by 28–32 weeks' gestation, with the width increasing from 3–4 mm to 7.7–7.9 mm. As a result, pain is referred down the inner thigh with standing and may result in a disturbing sensation of snapping or movement of the bones with walking.

Renal System

One of the most significant adaptations of pregnancy is the increase in total body water of 6.5–8.5 L by the end of gestation. The fetus, placenta, and amniotic fluid at term account for approximately 3.5 L of water content. Additional water is accounted for by expansion of the maternal blood volume by 1500–1600 mL, plasma volume by 1200–1300 mL, and red blood cells by 300–400 mL. The balance is attributed to extravascular fluid, intracellular fluid in the uterus and breasts, and expanded adipose tissue. Consequently, pregnancy produces chronic volume overload with active sodium and water retention secondary to changes in the osmoregulation and the renin–angiotensin system. The increase in body water content contributes to maternal weight gain, hemodilution, physiological anemia of pregnancy, and the elevation in maternal cardiac output. Inadequate plasma volume expansion has been associated with increased risks for preeclampsia and fetal growth restriction [33].

Osmoregulation

Shortly after conception, expansion in plasma volume begins, mediated partially by a change in maternal osmoregulation through altered secretion of arginine vasopressin (AVP) by the posterior pituitary. Water retention exceeds sodium retention despite an additional 900 mEq of sodium being retained during pregnancy, and serum levels of sodium decrease by 3–4 mmol/L. This is reflected by decreased overall plasma osmolality of 8–10 mOsm/kg, a change that is in place by 10 weeks' gestation and continues through 1–2 weeks postpartum [51]. Correspondingly, the threshold for thirst and vasopressin release changes early in pregnancy; during gestational weeks 5–8, an increase in water intake occurs and results in a transient increase in urinary volume but a net increase in total body water. Initial changes in AVP regulation may be due to placental signals involving NO and the hormone relaxin [52]. Following the 8th week of gestation, the new steady state for osmolality has been established with little subsequent change in water turnover, resulting in decreased polyuria. Pregnant women discern fluid challenges or dehydration normally with changes in thirst and AVP secretion, but at a new, lower "osmostat" [52].

The levels of plasma AVP remain relatively unchanged despite heightened production because of the threefold to fourfold increase in the metabolic clearance. Increased clearance results from a circulating vasopressinase produced by the placenta that rapidly inactivates both AVP and oxytocin. This enzyme increases about 300–1000-fold over the course of gestation proportional to fetal weight, with the highest concentrations occurring in multiple gestations. Increased AVP clearance can unmask subclinical forms of diabetes insipidus, presumably because of an insufficient pituitary AVP reserveand causes transient diabetes insipidus with an incidence of 2–6 per 1000. Typically presenting with polydipsia and polyuria, hyperosmolality is usually mild unless the thirst mechanism is abnormal or access to water is limited [53].

Salt Metabolism

Sodium metabolism is carefully balanced, facilitating a net accumulation of about 900 mEq of sodium. The fetoplacental unit contains 60% of the additional sodium (including amniotic fluid) and is lost at delivery. By 2 months postpartum, the serum sodium returns to preconceptional levels. Pregnancy increases the preference for sodium intake and is explained primarily by enhanced tubular sodium reabsorption. Increased glomerular filtration raises the total filtered sodium load from 20,000 to about 30,000 mmol/day; sodium reabsorption must increase to prevent sodium loss. However, the adaptive rise in tubular reabsorption surpasses the increase in filtered load, resulting in an additional 2–6 mEq of sodium reabsorption per day. Alterations in sodium handling signify the largest renal adjustment that occurs in gestation [54]. Hormonal control of sodium balance is under the opposing actions of the Renin–Angiotensin–Aldosterone System and the natriuretic peptides; both being modified during pregnancy [33].

Renin–Angiotensin–Aldosterone System

Normal pregnancy is typified by a significant increase in all components of the Renin–Angiotensin–Aldosterone System (RAAS) system. In early gestation, reduced systemic vascular tone (attributed to gestational hormones and increased NO production) results in decreased mean arterial pressure (MAP). As a result, decreased MAP activates adaptations to preserve intravascular volume through sodium retention [4]. Plasma renin activity, renin substrate (angiotensinogen), and angiotensin levels are all increased a minimum of fourfold to fivefold over nonpregnant levels. Activation of these components of RAAS leads to twofold elevated levels of aldosterone by the third trimester, increasing sodium reabsorption and preventing sodium loss. Regardless of the elevated aldosterone levels in late pregnancy, normal homeostatic responses still occur to changes in salt balance, fluid loss, and postural stimuli. In addition to aldosterone, other hormones that may contribute to increased tubular sodium retention include deoxycorticosterone and estrogen.

Atrial and Brain Natriuretic Peptide

Circulatory hemostasis is maintained by neuropeptides that are released in the myocardium. Atrial natriuretic peptide (ANP) is secreted primarily by the atrial myocytes in response to dilation, and in response to end-diastolic pressure and volume, the ventricles secrete brain natriuretic peptide (BNP). Both peptides have similar physiological actions, acting as diuretics, natriuretics, vasorelaxants, and overall antagonists to the RAAS. Elevated levels of ANP and BNP are found in both physiological and pathological conditions of volume overload and can be used to screen for congestive heart failure outside of pregnancy in symptomatic patients. As gravidas frequently present with shortness of air and many of the physiological effects of conception mimic heart disease, it is clinically significant whether pregnancy affects the levels of these hormones. Gestational alterations in ANP are controversial because some authors have reported higher plasma levels during different stages of pregnancy, whereas others have reported no change. In a meta-analysis by Castro and colleagues, ANP levels were 40% higher during gestation and 150% higher during the first postpartum week [55].

The circulating concentration of BNP is 20% less than that of ANP in normal individuals and noted to be more useful in the diagnosis of congestive heart failure. Levels of BNP are reported to increase largely in the third trimester of pregnancy compared with first-trimester levels (21.5 ± 8 pg/mL vs. 15.2 ± 5 pg/mL) and are highest in pregnancies complicated by preeclampsia (37.1 ± 10 pg/mL). The levels throughout pregnancy have been found to be higher than in nonpregnant controls. Preeclamptic pregnancies demonstrate higher levels of BNP, which are associated with echocardiographic evidence of left ventricular enlargement [56]. Although the levels of BNP are increased during pregnancy and with preeclampsia, the mean values are still lower than the levels used to screen for cardiac dysfunction (>75–100 pg/mL) and, therefore, can be used to screen for congestive heart failure [57].

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Overview of the Normal Development of the Human Embryo and Fetus

2

David C. Mundy and Gustavo Vilchez

Introduction

Although the complex mechanisms controlling human development have not yet been fully delineated, science and technology have advanced the understanding of these processes. Fertilization of the ovum by the spermatozoa initiates a transfiguration resulting in a fully formed infant, whose development continues long after the day of delivery. During gestation, numerous changes occur at the cellular level, including cell division, migration, differentiation, rearrangement, transportation, growth, and apoptosis [1]. This chapter will provide an overview of early pregnancy events and review the development of major fetal organ systems. When discussing the developing human, confusion may exist because of the differences in embryonic, fetal, and gestational age. Unless otherwise stated, gestational age will be the primary measure in this chapter.

Periods of Antenatal Human Development

By convention, human antenatal development is typically divided into two phases (Fig. 2.1) [1]:

(a) *Embryonic development phase:* The embryonic phase starts with fertilization and continues until the 10th week of gestation. Totipotent cells, which form the embryo, and extraembryonic tissue are present during the first few cell divisions

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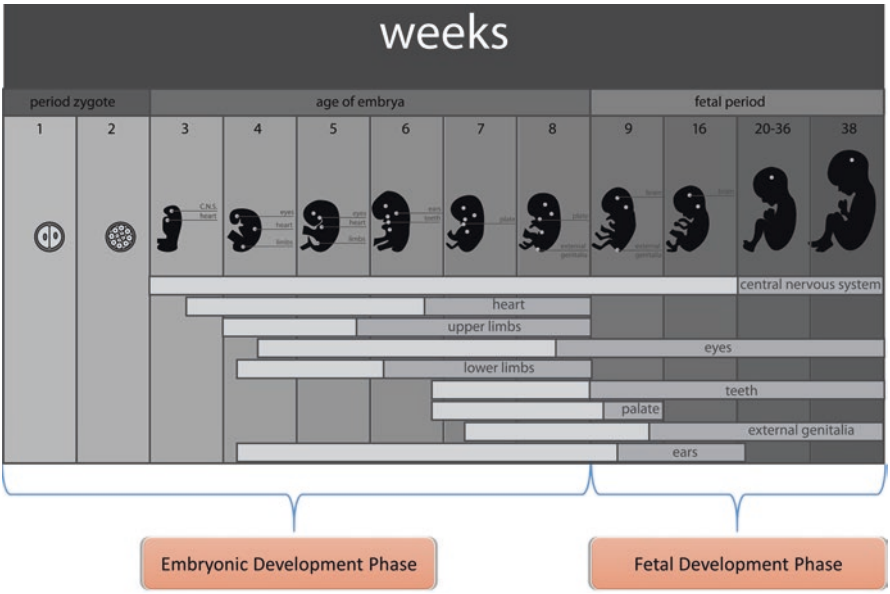

Fig. 2.1 Phases of antenatal human development (Image used under license from Shutterstock.com)

and give way to pluripotent cells that differentiate into the cells forming all components of the body.

(b) *Fetal development phase:* The fetal phase begins during the 10th gestational week and ends on the day of delivery. This period is characterized by organ differentiation and growth [1, 2].

The Embryonic Period

First Postconceptional Week

Week 1 begins at conception and typically occurs approximately 14 days after the onset of the last menstrual period. Embryonic age at week 1 therefore correlates with a gestational age of 3 weeks. Fertilization normally takes place in the ampulla of the fallopian tube (Fig. 2.2) [2, 3]. The sperm penetrates the corona radiata of the ovum, binds to, and then penetrates the zona pellucida. It then enters the oocyte membrane, fuses to the oocyte, and forms a highly specialized totipotent cell called the zygote [1]. After its formation, the zygote undergoes cleavage, which is characterized by a sequence of mitotic cell divisions into daughter cells called blastomeres [1, 2].

Cleavage starts approximately 30 h after fertilization. The mass of the blastomeres does not increase during these divisions, so the entire embryo maintains its size [2, 4].

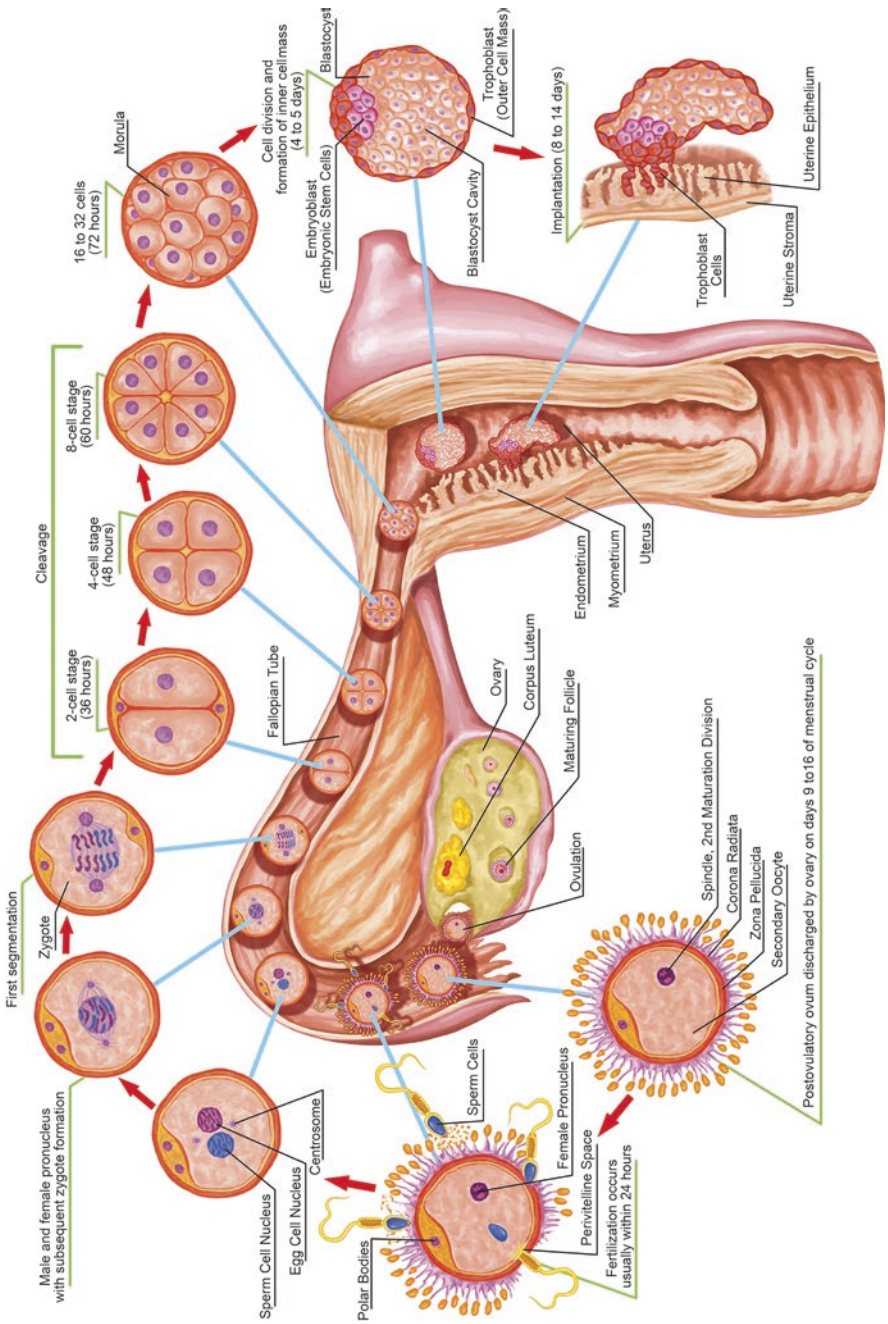

Fig. 2.2 First postconceptional week of embryonic development (Image used under license from Shutterstock.com)

Three days after fertilization the conceptus consists of 12–32 blastomeres and becomes the morula [1]. The morula enters the uterus approximately 4 days after fertilization [5]. Fluid accumulates within the morula and forms a cavity [4, 6]. At this point, the developing human is called the blastocyst. This cavity separates the conceptus into two parts (Fig. 2.2):

(a) *The trophoblast:* the thin outer cell layer formed by 53 cells [4, 5] that gives rise to the placenta, and
(b) *The embryoblast:* a group of five centrally located pluripotent cells [4, 5] that gives rise to the embryo.

Approximately 4 days after fertilization, the zona pellucida degenerates. Six to seven days after fertilization (day 20 after the first day of the last menstrual period), the blastocyst attaches to the endometrium and implantation begins [1].

Implantation typically occurs at the posterior and superior portion of the uterus, in the functional layer of the endometrium during the secretory phase of the menstrual cycle. As the blastocyst attaches to the endometrium, the trophoblast will differentiate into the cytotrophoblast and the syncytiotrophoblast [7].

Second Postconceptional Week

The process of implantation occurring during the second week can be divided into four stages: lysis or "hatching" of the surrounding zona pellucida; apposition of trophoblast cells into the decidua of endometrium; adhesion; and invasion [8]. At implantation (Fig. 2.2), the embryoblast undergoes cellular proliferation and differentiation into two layers:

(a) *The epiblast:* a dorsal layer formed by columnar cells, and
(b) *The hypoblast:* a ventral layer formed by cuboid cells.

These two layers form the primordial bilaminar embryonic disc, which will give rise to the three germ cell layers that will form all the body's tissues and organs (Fig. 2.3).

Upon implantation of the blastocyst, the syncytiotrophoblast produces human chorionic gonadotropin (hCG). Secreted hCG enters the maternal blood via the lacunae, which are small blood-filled spaces that form in the syncytiotrophoblast. These lacunae will form a primitive uteroplacental circulation to pass oxygen and provide nutrients to the embryonic disc. Production of hCG is sufficient by the end of the second week to yield a positive pregnancy test [9].

Within the epiblast, small clefts develop that subsequently coalesce and form the primordium of the amniotic cavity [2]. This primordial amniotic cavity becomes lined by a thin layer of cells from the epiblast to form the amnion [10].

Hypoblast cells migrate and line the inner surface of the cytotrophoblast to form the exocoelomic membrane, which delimits the former blastocyst cavity and forms the primary umbilical vesicle.

Connective tissue from the epiblast surrounds the amnion and umbilical vesicle, filling the space between the exocoelomic membrane and the cytotrophoblast, forming the extraembryonic mesoderm.

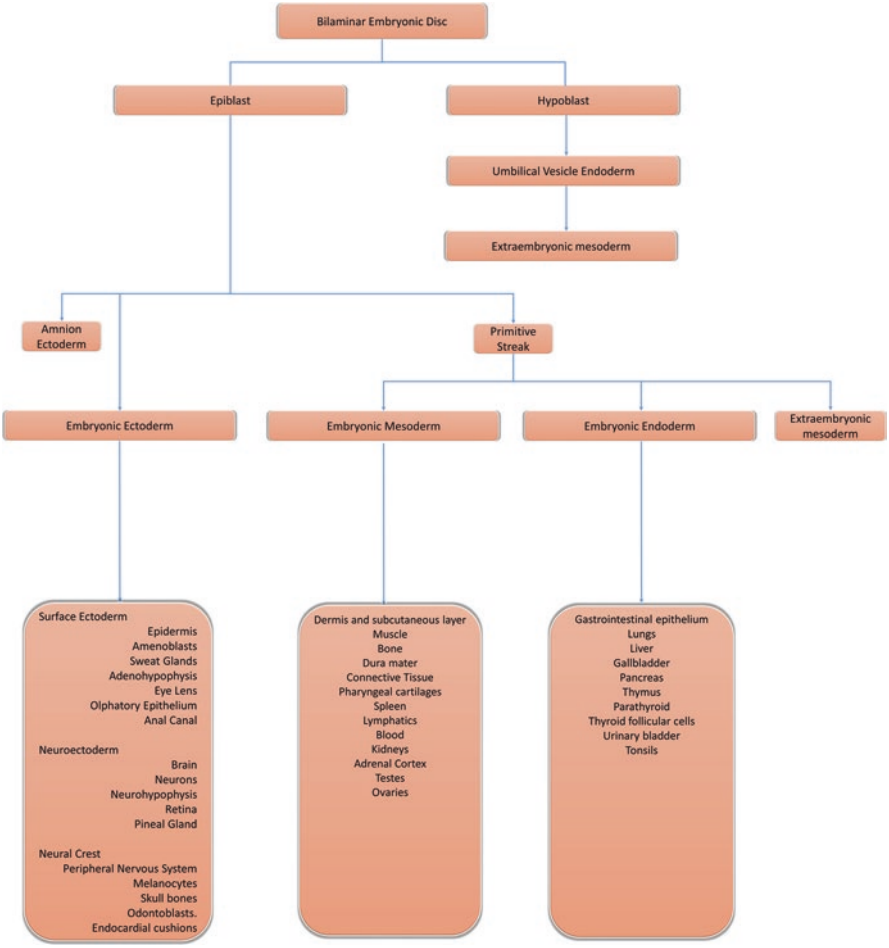

Fig. 2.3 Origin of the three germ cell layers and their derivatives

Fluid-filled spaces then appear in the extraembryonic mesoderm. These spaces will form the extraembryonic coelom or chorionic cavity surrounding the amnion and umbilical vesicle. The remaining of mesoderm, called the connecting stalk, is the structure that maintains the embryonic attachment to the trophoblast. The extraembryonic coelom divides the extraembryonic mesoderm into somatic and splanchnic layers. The somatic mesoderm will merge with the trophoblast to form the chorionic sac.

Third Postconceptional Week

During the third week, the bilaminar embryonic disc is converted into a trilaminar disc by gastrulation. These three germ layers will give rise to all the tissues and organs of the human body.

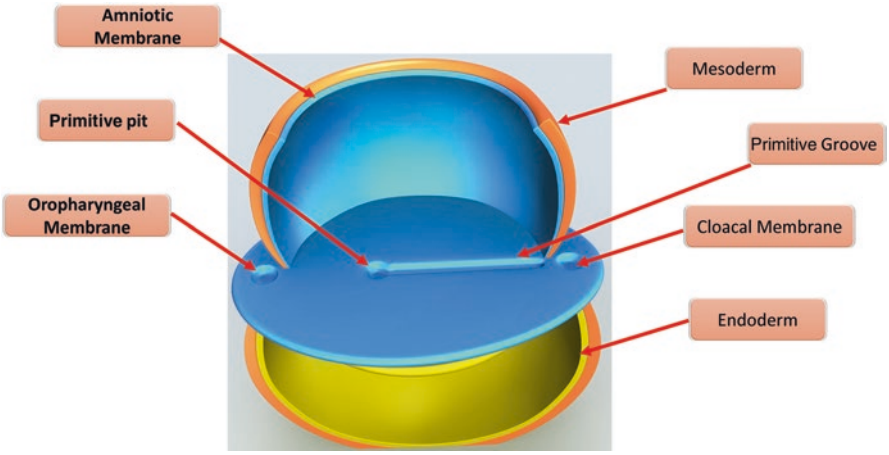

Fig. 2.4 Third postconceptional week of embryonic development (Image used under license from Shutterstock.com)

Gastrulation begins with the formation of the primitive streak, which is an indentation of the epiblastic surface in the caudal portion of the embryo (Fig. 2.4). From this primitive streak, epiblast cells migrate ventrally, laterally, and cranially between the epiblast and hypoblast. Subsequently, the epiblast transforms into embryonic ectoderm. Some epiblast cells also displace the hypoblast and form embryonic endoderm (Fig. 2.4). Mesenchymal cells occupy the area between ectoderm and endoderm, and form the intraembryonic mesoderm [11]. All three germ cell layers are derived from the epiblast [8]. These mesenchymal cells migrate between the ectoderm and mesoderm to form the intraembryonic mesoderm:

(a) The first cells that travel toward the cephalic end will form the *prechordal plate.*
(b) Mesenchymal cells that migrate cranially from the primitive node form a median cellular cord called the notochordal process. This notochordal process will merge with cells from the hypoblast to form the *notochord*. This structure extends from the primitive node to the prechordal plate.
(c) Mesodermal cells that migrate to the embryonic disc edges will join the *extraembryonic mesoderm* surrounding the amnion and umbilical vesicle.
(d) The paraxial mesoderm, a thick plate of mesoderm located at each side of the midline, will form the *somites.*
(e) The lateral mesoderm is a thin plate of mesoderm located along the lateral sides of the embryo, which develops into the *intraembryonic coelom.*
(f) Mesoderm cells traveling to the cranial end to a horseshoe-shaped region called the *cardiogenic region* will form the future heart.

The notochord is the primordium of the vertebral column. The notochord induces a thickening in the embryonic ectoderm called the neural plate. A groove along the *neural plate* forms the neural folds (Fig. 2.4). The *neural folds* fuse with the neural

plate to form the *neural tube*, which is the progenitor of the central nervous system (CNS) [9]. The *neural crest* is formed between the surface ectoderm and neural tube. Mesoderm on each side of the notochord forms longitudinal columns of paraxial mesoderm that will give rise to the somites.

The heart and great vessels are formed from mesenchymal cells in the cardiogenic area. Endocardial heart tubes fuse to form the primordial heart tube. These tubes join with the formed blood vessels to form the primordial cardiovascular system [9].

Fourth to Eighth Postconceptional Weeks

During this period, the three germ layers differentiate into various tissues that will form the primordia of most of the major organs and systems of the body [2]. Exposure to teratogens during this period may cause malformations [10].

At this stage of development, the uteroplacental circulation alone is no longer sufficient to satisfy the increasing nutritional needs of the embryo. Development of the cardiovascular system to supplement nutritional needs is critical for survival.

Differential growth rates cause the flat embryo to develop curves and folds commencing on day 22. Due to the growth of the neural tube and the amnion in the median plane (craniocaudal folding), the enlarging sheet of the embryo pushes out and over the rim of the umbilical vesicle [2]. At the cranial end, the neural tube forms, the buccopharyngeal membrane (Fig. 2.4) is positioned where the mouth will develop, and the cells that will form the heart tube are positioned in what will be the future thorax. At the caudal end, the connecting stalk is in the region of the future umbilical cord, and the cloacal membrane is positioned more caudally (Fig. 2.4).

Due to the growth of the somites, the amnion and the lateral body walls, the left and right flanks of the embryonic disc extend and curl around and underneath the embryo, squeezing the sides of the umbilical vesicle (lateral folding). The flanks meet in the midline ventrally, and the germ cell layers of both flanks fuse. The umbilical vesicle is converted to a slender vitelline duct [2]. The ectoderm fuses and forms the external surface of the embryo. The endoderm forms the primitive gut, from the buccopharyngeal membrane cranially and the cloacal membrane caudally [10].

Because of median and lateral folding, the initial trilaminar embryonic disc is converted to a c-shaped, cylindrical embryo. By the end of the eighth week, the embryo has recognizable human morphology [10]. Major organ systems have begun development even though functionality may be minimal.

The Fetal Period

The fetal period, beginning at a gestational age of 11 weeks and continuing to delivery, is characterized development that involves rapid corporeal growth and differentiation of tissues, organs, and systems (Fig. 2.1) [4]. As most of the organs are already developed, the fetus is less vulnerable to teratogens during this period. However, some agents may still interfere with growth and functional development.

There is a relative slowing in the growth of the head compared with the growth of the rest of the body [7]. By the 11th week, the face is broad, eyes are widely separated, eyelids are fused, and ears are low set. By the 12th week, swallowing can be visualized, and fingernail development commences.

By the 14th week, primary ossification centers appear in the cranium and long bones. The neck is well defined. The upper limbs have almost reached their maximum length in relation to the body. The fingers and toes have become differentiated. The liver is the major site of erythropoiesis. The intestines rotate into the abdomen [4]. Urine formation begins and is discharged through the urethra into the amniotic cavity. The external genitalia become identifiable. The fetus can be observed making spontaneous movements [12].

By 15 weeks, fetal growth accelerates. The fetal head continues to grow, but at a rate less than the fetal corpus. The fetal head measures about half the size of the fetus [4]. Scalp hair may be visualized. The position of the eyes is more anterior and no longer anterolateral. The external ears approximate to their position at term. Lower limbs lengthen, and their movements become coordinated and visible during ultrasonography. Primary ossification centers are active and developing bones are visible on ultrasound. Ovaries are differentiated and contain primordial ovarian follicles. Genitalia can be recognized [13]. Respiratory movements can be seen by 16 weeks. By the 16th–18th week, eye movement begins, coinciding with midbrain maturation [12].

By the 21st week, lanugo and head hair appear, and the skin is less transparent and coated with vernix caseosa. Substantial weight gain occurs, and the fetus becomes better proportioned [13]. Fetal movements are clearly recognized by the mother, and the fetus is active 30% of the time [12]. The skin is pink, wrinkled, and more translucent. Rapid eye movements and blinking commence. Fingernails start apparent. Type II pneumocytes begin to secrete surfactant. Fetuses born at this gestational period are usually capable of extrauterine existence, mainly because of the maturity of its respiratory system, but it will require intensive care unit care [13]. Cochlear function develops by 22nd–25th weeks [12]. Sucking movements can be seen by 24 weeks [4].

By 26 weeks, the eyes begin to open, and lanugo and head hair are well developed. Toenails are visible, and considerable subcutaneous fat develops under the skin, giving the fetus a smooth, healthy appearance [13]. The CNS is able to direct rhythmic breathing movements and control body temperature, and some sounds can be perceived by the fetus [4]. Lungs and pulmonary vasculature have developed sufficiently to provide adequate gas exchange. The neural pain system is developed [12]. The fetal spleen is an important site of erythropoiesis up to 28 weeks, and then the bone marrow becomes the major site of erythropoiesis [13]. By 28 weeks, eyes may be wide open and are sensitive to light [4].

By 30 weeks, the pupillary reflex develops. The limbs develop a chubby appearance [13]. In males, the testicles begin to descend.

By 35 weeks, there is a decrease in the growth rate as the time of birth approaches. Fetus adds 14 g of fat per day during these last weeks, being most of the time plump, and can reach 360 mm of height and 3400 grams [13]. The nervous system is mature,

and the fetus can carry out some integrative functions, such us firm grasp and orientation to light. The thorax is prominent and the breasts protrude [13]. The testicles are usually descended in full-term male neonates [13].

Important Aspects of Specific Fetal Systems Development

Nervous System

The process of formation of the neural tube is called neurulation [14]. The notochord and paraxial mesenchyme induce the thickening of ectoderm, called the neural plate, which gives rise to the CNS [15]. The neural plate invaginates to form a neural groove with neural folds on each side. The neural folds fuse and the neural tube is formed during the fourth week. The neural tube is initially open at each end (rostral and caudal neuropores) and communicates with the amniotic cavity through these neuropores. The anterior neuropore will close by day 25 and will become the lamina terminalis. The posterior neuropore will close by day 27 [11]. The notochord will form the nucleus pulposus of the intervertebral disk [14].

The neural tube has a broad cephalic portion and a long caudal portion [4]. The portion of the neural tube forming the primordial brain undergoes flexion at three points: mesencephalic flexure; cervical flexure; and pontine flexure. The first two flexures are ventral; the third flexion is dorsal [2]. Three primary brain vesicles develop during week 4 in the cranial end of the neural tube: the forebrain; the midbrain; and the hindbrain (Fig. 2.5). During week 6, five secondary brain vesicles will form. The forebrain splits into the telencephalon and diencephalon. The dorsal telencephalon will form the cerebral cortex; the ventral telencephalon will become the basal ganglia. The diencephalon will form the optic cup and stalk, the pituitary gland, thalamus, hypothalamus, and pineal body. The mesencephalon does not subdivide and becomes the adult midbrain (Fig. 2.5) [4].

The hindbrain divides into the metencephalon and myelencephalon. The metencephalon will form the pons ventrally and the cerebellum dorsally [8]. The myelencephalon will form the medulla oblongata. The caudal end of the neural tube continues to elongate and forms the spinal cord [11]. The neural canal (neurocele) forms by 9 week and differentiates into the ventricles of the brain and the central canal of the medulla and spinal cord [8]. The walls of the neural tube thicken by neuroepithelial cellular proliferation, and give rise to all nerve and macroglial cells in the CNS (Fig. 2.5). The microglia differentiates from mesenchymal cells that enter the CNS with the blood vessels [11].

Cardiovascular System

The heart and vascular systems develop from the splanchnic mesoderm by the third week after fertilization [16]. Heart progenitor cells migrate through the primitive streak to a position cranial to the neural folds where they form a horseshoe-shaped

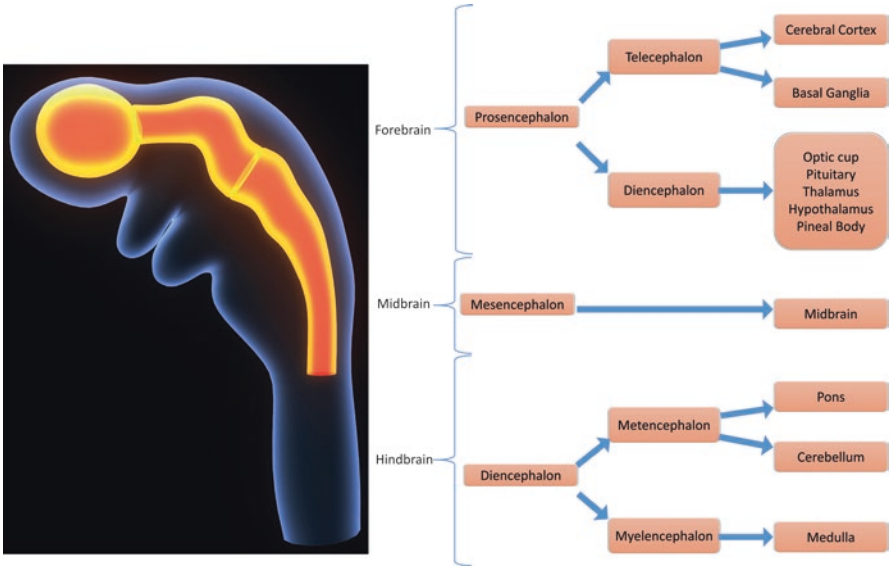

Fig. 2.5 Primordium of the nervous system and its derivatives. Sections of the primitive neural tube, vesicles, and adult derivatives (Image used under license from Shutterstock.com)

region [4]. Blood islands appear in this region and split the mesoderm into somatic and splanchnic layers, forming the pericardiac cavity [8]. As folding of the embryo occurs, the heart-forming regions fuse at midline and form a continuous sheet of mesoderm. Vascular channels form within this sheet of mesoderm, remodeling into a single endocardial tube. Progenitor cells migrate from the epiblast to become myoblasts and surround the endocardial tube. The primordial heart starts beating during the fourth week [7].

The heart primordium consists of four chambers: the bulbus cordis; primitive ventricle; primitive atrium; and sinus venosus [7]. The truncus arteriosus (primordium of the ascending aorta and pulmonary trunk) is continuous caudally with the bulbus cordis, which becomes part of the ventricles. These chambers, by looping, folding, remodeling, and partitioning [16], will give rise to the main structures of the adult heart (Fig. 2.6). As the heart grows, it starts to bend at 23 days to the right undergoing an S-shaped looping and soon acquires the general external appearance of the heart. The heart becomes partitioned into four chambers between the fourth and seventh weeks.

The critical period of heart development is from day 20 to day 50 after fertilization [7]. Numerous events occur during cardiac development, and deviation from the normal pattern at any time may produce one or more congenital defects.

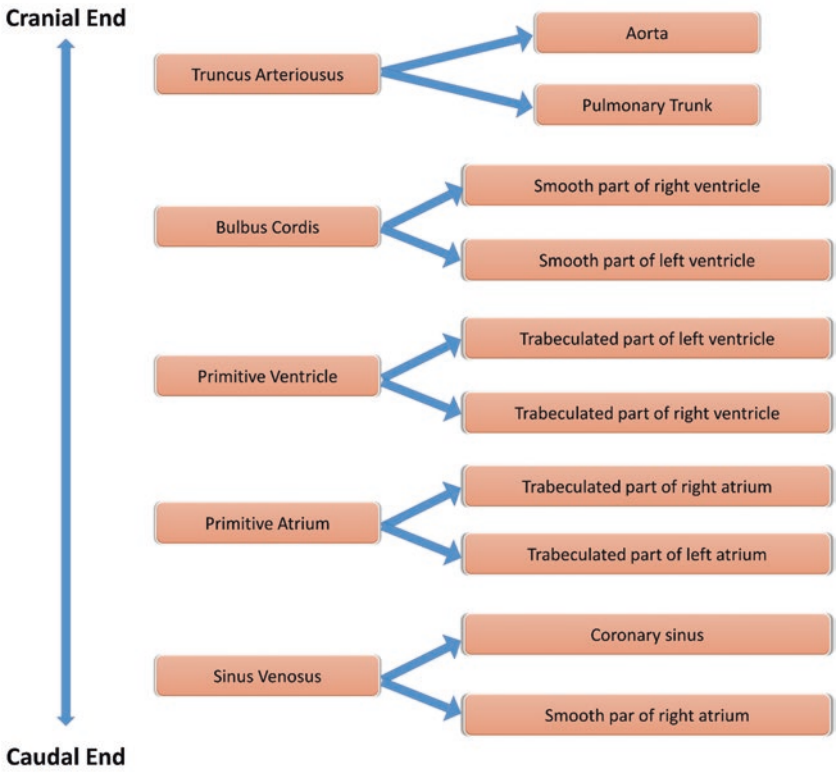

Fig. 2.6 Dilations of the heart primordium and definitive structures. Vesicles of the primitive heart and derivative structures

Respiratory System

The development of the fetal lung is divided into four stages (Table 2.1): pseudoglandular (6–16 weeks); canalicular (16–26 weeks); terminal sac (26 weeks to birth); and alveolar (32 weeks to birth). By the fourth week, a laryngotracheal diverticulum develops from the floor of the primordial pharynx at the ventral wall of the developing gut. This diverticulum becomes separated from the foregut by tracheoesophageal folds that fuse to form a tracheoesophageal septum [17]. This septum results in the formation of the esophagus and laryngotracheal tube.

The endoderm of the laryngotracheal bud gives rise to the lower respiratory organs and tracheobronchial gland epithelium. The splanchnic mesenchyme that surrounds this respiratory bud will form connective tissue, cartilage, muscle, blood, and lymphatic vessels [8]. Pharyngeal arch mesenchyme forms the epiglottis and connective tissue of the larynx. Mesenchyma from the caudal pharyngeal arches will form the laryngeal muscles. The laryngeal cartilages are derived from neural crest cells [17].

Table 2.1 Stages in the development of the respiratory system

Stage	Time	Events during development
Embryonic	3–5 weeks	Initial bud (respiratory diverticulum) Initial three rounds of branching to form the primordia of lungs, lobes, and segments Diverticulum stem forms the trachea and larynx
Pseudoglandular	5–16 weeks	Respiratory tree branching Formation of terminal bronchioles No respiratory bronchioles or alveoli are present yet
Canalicular	16–26 weeks	Terminal bronchiole divides into respiratory bronchioles Respiratory vasculatory begins to develop Differentiation of respiratory epithelium
Saccular	26 weeks to term	Respiratory bronchioles divide to produce terminal sacs Capillaries establish close contact with terminal sacs
Alveolar	8 months to childhood	Mature alveoli with well-developed blood–air barrier

During the fifth week, the distal end of the laryngotracheal diverticulum divides into two bronchial buds. Each bronchial bud enlarges to form a main bronchus, and then the main bronchus subdivides to form lobar, segmental, and subsegmental branches. Each tertiary bronchial bud with the surrounding mesenchyme represents the primordium of each bronchopulmonary segment [17].

Canals of tubes branch out from the terminal bronchioles, and each tube forms an acinus comprising the terminal bronchiole, an alveolar duct and a terminal sac, which forms the primitive alveolus. By 20–22 weeks, type II pneumocytes begin to secrete pulmonary surfactant [17]. Growth of the lungs will continue until and after birth.

Gastrointestinal System

The primordial gut forms from the dorsal part of the umbilical vesicle after it rotates into the embryo during lateral folding [8]. Endoderm will form the lining of the primordial gut, except at the cranial and caudal parts, which are derived from ectoderm of the buccopharyngeal membrane and cloacal membrane, respectively [10].

The primordial gut remains in contact with the umbilical vesicle through the vitelline duct. The cranial end of the primordial gut is sealed by the buccopharyngeal membrane, which will deteriorate during the fourth week and become the mouth. The caudal end is sealed by the cloacal membrane, which will deteriorate during the seventh week and become the anus. This opening will further connect the primordial gut with the umbilical vesicle. The mesenchyme surrounding the primordial gut gives rise to the muscular and connective tissue of the gastrointestinal track. Buds develop along the length of the tube that will form gastrointestinal and respiratory structures.

The gut is divided into three portions: the foregut; the midgut; and the hindgut. The foregut develops into the pharynx, lower respiratory system, esophagus, stomach, proximal part of the duodenum, liver, pancreas, and biliary system. The lower foregut begins to dilate by the fourth week; the dorsal side grows faster than the ventral side until the sixth week, then after that it will become the stomach [18].

An outgrowth of the endodermal epithelial lining of the foregut gives rise to the hepatic diverticulum, primordium of the liver, gallbladder, and biliary duct system [10]. The hepatic diverticulum forms epithelial cords that become the septum transversum. Primordial cells between the layers of the ventral mesentery derived from the septum transversum differentiate into hepatic tissues and linings of the ducts of the biliary system. The endodermal lining of the foregut forms the ventral and dorsal pancreatic buds [10].

When the duodenum rotates to the right, the pancreatic bud fuses to give rise to the pancreas. The ventral bud forms the head of the pancreas and the uncinate process. The dorsal pancreatic bud forms the remainder of the pancreas.

The midgut gives rise to the duodenum, jejunum, ileum, cecum, appendix, ascending colon, and right transverse colon. It forms a U-shaped umbilical loop of intestine that herniates into the umbilical cord during the sixth week because there is no room for it in the abdomen. While in the umbilical cord, the midgut loop rotates counterclockwise 90°. During the 10th week, the intestines return to the abdomen, rotating a further 180° [10].

The hindgut becomes the left transverse colon, the descending and sigmoid colon, the rectum, and the superior part of the anal canal. The anal pit gives rise to the inferior part of the anal canal. The caudal part of the hindgut divides the cloaca into the urogenital sinus anteriorly and the anorectal canal posteriorly. The urogenital sinus gives rise to the urinary bladder and urethra [10]. The rectum and superior part of the anal canal are separated from the exterior by the cloacal membrane, which will break down by the end of the eighth week, opening the gut to the amniotic cavity.

Urinary System

Production of urine by the fetus is important for maintenance of amniotic fluid volume and composition [16]. The urinary system arises from the intermediate mesoderm [18]. At the level of the abdomen, this intermediate mesoderm forms a condensation of cells called the urogenital ridge. This ridge contains the nephrogenic cord and the gonadal ridge [8].

By the fourth week, the cloaca is split by the urorectal septum into the urogenital sinus (ventrally) and the anal canal (dorsally). The top portion of the urogenital sinus, the allantois, and the surrounding splanchic mesenchyme give rise to the bladder. The middle and lower portions of the urogenital sinus will form the urethra.

The nephrogenic cord evolves into three kidney components: the pronephros; the mesonephros; and the metanephros.

The first system called the pronephros appears by the third week at the level of the embryo neck. It is a transitory, nonfunctional structure that disappears by the fifth week.

The second phase of renal development, called the mesonephros, appears by the fourth week. This system develops caudally to the pronephros by differentiation of the mesoderm in a craniocaudal sequence that forms pairs of mesonephric ducts (Wolffian ducts) and mesonephric tubules. It is a partially transitory structure, as the tubules regress, but the ducts persist and open into the urogenital sinus.

The third phase of renal development is the metanephros (primordia of the permanent kidney) and begins to form by the fifth week caudal to the mesonephros [12]. It develops from an outgrowth of the mesonephric duct to form the ureteric bud, as well as from a condensation of mesoderm within the nephrogenic cord called the metanephric blastema, and will finally become the newborn kidney.

The ureteric buds branch and give rise to the ureter, renal pelvis, calices, and collecting tubules [8]. The metanephrogenic blastema, metanephric diverticulum, and growing vascular endothelial cells within the developing metanephros will give rise to the nephrons [17]. Capillaries grow into Bowman's capsule from the dorsal aortae and convolute to form the glomeruli. The ureters insert into the posterior bladder wall. This functional renal unit will produce urine from week 12 onwards and will continue to form throughout fetal life [18].

The intricate and complex process of embryonic and fetal development informs the clinician that stresses such as diseases and conditions that may produce abdominal pain in the gravid female could easily disrupt pregnancy, yet in most cases, they do not.

Other influences such as anesthetics, radiation from imaging, and mechanical manipulations during surgery also can interfere with the developing fetus, but, surprisingly, usually do not.

Nonetheless, clinicians must appreciate the developmental process of the fetus when considering any issue that involves the patient in whom the fetus resides.

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General Principles in the Diagnosis of the Acute Abdomen

3

Peter Bogach Greenspan

Introduction

The overall antenatal hospitalization rate is approximately 10.1 per 100 deliveries [1]. One third is for nonobstetrical conditions that includes renal, pulmonary, and infectious diseases. One in every 635 pregnant women will undergo a nonobstetrical surgical procedure [2, 3].

The obstetrician may be qualified to manage many nonobstetrical disorders. Other conditions will require consultation, and others still may require a multidisciplinary team. Consultants may include maternal–fetal medicine specialists, internists and medical subspecialists, surgeons, anesthesiologists, and numerous other disciplines [4]. Obstetricians should have knowledge of a wide range of surgical disorders frequently diagnosed in women of childbearing age. Consequently, nonobstetricians who care for these women and their unborn fetuses need to be familiar with pregnancy-induced physiological changes that occur in the gravida as well as special fetal considerations. Often normal pregnancy distresses have clinically significant effects on various diseases and may cause aberrant changes in routine laboratory values.

It is obvious that a woman should never be punished because she is pregnant. Gravid women are susceptible to any of the medical and surgical maladies that can

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affect women of childbearing age. A number of questions should be addressed to assure appropriate evaluation and management:

- Would a different management plan be recommended if the woman was not pregnant?
- If the management plan is different because the woman is pregnant, can this be justified?
- What are the risks versus benefits to the mother and her fetus, and are they counter to each other?
- Are there individualized management plans that balance the benefits versus risks of any alterations?

This approach allows individualization of care for women with most surgical disorders complicating pregnancy. This may be specifically helpful for consideration by nonobstetrical consultants.

History

The foundation of the diagnostic process is the patient's history. Skilled history taking is acquired with experience and the utilization of the examiners' senses. An understanding of body language often significantly contributes to the history-taking process.

Aside from patients who are unconscious, obtaining a coherent, accurate history is often challenging. Language barriers, educational disparities, and cultural differences among other things can make obtaining a clear history very difficult. At times, even with a conscious patient, getting a coherent history is all but impossible.

Often, an emergency is pending and time for history taking can be severely curtailed. In such cases, the most essential information to be obtained includes the patients' allergies, medications, major prior medical and surgical problems, etc.

When the clinical setting allows for more time, then a general history should be ascertained on all patients with whom the examiner is otherwise, unfamiliar. This is essential in the determination of the type and urgency of the proposed surgery, if that is warranted.

The interview typically begins with the elicitation of a chief complaint from which the examiner develops the history of the present illness. Often, there is more than one chief complaint; therefore, each one should be explored, as well. In some instances, multiple complaints can be coalesced into a single history.

One should be cautious not to develop the notion of a "routine" history as each patient is entirely unique. Observation of the patient while questioning them is critical.

The examiner should sit while interviewing the patient affording him or her enormous amounts of information. Furthermore, this usually makes the suffering patient feel more at ease.

Observations of the patients' position in the bed, facial expressions, degree of stillness versus movement (such as rocking back and forth) provides very useful clues to the clinician [5, page 19].

Determining the acuteness of onset of the pain provides clues to its severity. Determination of what the patient was doing when the pain began is very useful. Was the gravida asleep and awakened by the pain? Was she standing, sitting, or lying down when the pain began? Was she walking, running, exercising, etc.? Did the pain begin during or after sexual intercourse?

Rarely, patients will develop sudden-onset severe pain that will cause them to fall down or faint. However, in pregnant women, fainting or collapse is associated with ovarian torsion and rupture of an ectopic pregnancy [5, page 21].

Characterization of pain regarding onset and distribution is greatly important. Pain that is felt throughout the abdomen is associated with sudden exposure of the peritoneum to fluids such as blood, pus, or succus entericus. When generalized pain can be further characterized to specific locations in the abdomen, this aids the clinician in focusing on the likely source. For example, if a pregnant patient has generalized abdominal pain but the greatest intensity is in the left lower quadrant, then the most likely explanation is ovarian, sigmoid or rectal pathology and not appendix or ileocecal disease.

Pain associated with small bowel obstruction or colic is first noted in the epigastrium and periumbilical regions, which corresponds to the innervation by the ninth and tenth thoracic nerves. These nerves also supply the appendix; hence, early appendicitis pain is often felt in the epigastrium. Typically, the pain from large bowel pathologies is felt in the hypogastrium [5, page 22].

An accurate description of the pain regarding severity or quality is often an indication of the seriousness of the underlying cause. For example, burning is used to describe pain from gastric ulcer, whereas pancreatitis may cause agonizing pain. Colicky pain is sharp and constricting, whereas tearing pain may be described in an aortic dissecting aneurysm, albeit rare in pregnant women. Obstructions of the bowel may be described as gripping pain, but appendicitis may produce dull aching. Pelvic abscess may also be described as dull pain as well [5, page 22].

Pain that radiates or travels along the area of distribution of the nerves from that segment of the spinal cord often provides valuable diagnostic information. The pain of biliary colic, fairly common in gravidas, typically radiates or is referred to the tip of the inferior angle of the right scapula. The pain caused by renal lithiasis is often perceived in the patients' labia.

Pain that worsens with inspiration is associated with pleuritic inflammation; however, this may also be of a musculoskeletal origin, devoid of any organic pathology [5, page 23].

Patients with an acute abdomen often present with vomiting. If the patient does not have gastritis, then the vomiting is typically due to one of the following:

1. Peritoneal or mesenteric nerve irritation
2. Luminal obstructions of a ureter, bile duct, endocervical canal, or intestines

Any irritation of the peritoneum from blood, gastric secretions, or inflammation of an organ will stimulate sympathetic nerves, which produce persistent vomiting. Similarly, as smooth muscles are stretched as in cases of torsion or bowel obstruction, this will result in vomiting.

Determining the relationship of the vomiting to the onset of the pain is very critical. The more sudden and/or severe the stimulation to the peritoneum, the earlier the vomiting occurs. Duct obstructions from renal calculi, gallstones, or pancreatic duct ranulae produce early-onset, sudden, and severe vomiting. Vomiting from small intestinal obstructions generally follow the pain onset by 4 or more hours. Large bowel obstructions do not feature vomiting in many cases, but are associated with nausea.

Pain that is produced by appendicitis usually precedes the onset of vomiting by 3–4 h or longer. It is unusual for the vomiting and pain to coincide or that the vomiting precedes pain development [5, page 21].

Vomiting frequency is variable and is often directly correlated to the severity of the underlying cause for the pain. Beware that there are numerous serious abdominal pathologies that produce minimal or no vomiting.

Whenever observable, the character of the emesis may provide clues to the causation of the pain. Simple gastritis generates undigested stomach contents with little or no bile. Bilious vomit is a sign of bile duct obstruction. Intestinal obstruction may produce various materials, but feculent emesis is pathognomonic of bowel obstruction in the later stages of the process [5, Page 22].

Anorexia that is acute in onset is significant and raises the suspicion of appendicitis. However, the loss of appetite may or may not be associated with vomiting.

Other questions regarding the patients' pain may include exploration of their bowel habits. Recent changes that include constipation or diarrhea provide important clues in diagnosing the pain. Gravidas with hypogastric pain and diarrhea followed by tenderness and constipation may have a pelvic abscess [5, Page 23]. The finding of frank blood and mucus in the rectum is often a sign of intussusception.

The pain presentation might include the O-P-Q-R-S-T mnemonic.

O-onset: When did the pain begin or first become noticeable?
P-Provocation/Palliation: What makes the pain worse? What improves the pain?
Q-Quantity: Clinicians usually offer a scale of 1–10. Observation by the examiner may render a different assessment of the pain quantity versus the patient's subjective description.
R-Radiation: Does the pain travel elsewhere or is it referred to another location?
S-Severity: How does the patient describe the pain, that is, severe, burning, sharp, shooting, etc.? How does the patient rate the pain relative to a score (1–10, etc.)?
T-Temporality: Is there a time relationship accompanying the pain, that is, morning, afternoon, only while having a bowel movement, etc.?

Other details of the history should include past surgical history, prior hospitalizations, trauma, family medical history, and prior obstetrical and gynecological problems. Social history is essential, as well, addressing nicotine use, past and present, alcohol and illicit drug consumption, and if pertinent, sexual practices. Information regarding a patient's social history helps the examiner to be alert for problems in the perioperative period such as drug or alcohol withdrawal. A history of any substance abuse including nicotine provides essential information that may have significant impact on the intraoperative and postoperative course. This is especially of concern in the gravid patient. The effects of substances on the fetus must be given appropriate consideration.

Though it is often uncomfortable for some examiners to question the patient's sexual history, there are many times, especially in the evaluation of a pain complaint, that sexual practices play a significant role in the etiology of the pain. Furthermore, sexual abuse and trauma can produce significant but unapparent internal injuries that manifest as an acute abdomen in a gravid woman.

Low-risk procedures may not need further evaluation even in the highest risk patient. Emergency surgeries should not be delayed for "medical clearance" when the risk of the procedure outweighs the benefit of postponing the intervention [6].

There are instances when clearance would be appropriate particularly in the assessment of cardiovascular and pulmonary risks. If the history warrants it and time allows for it, then "medical clearance" is a valuable undertaking to avoid significant morbidity and mortality [6]. Rudimentary screening for history of deep venous thrombosis or pulmonary embolism is preferable, and appropriate precautions and interventions should be implemented if indicated. A full coagulation panel is not necessary in a patient with a negative history of coagulopathy as these tests do not predict bleeding risk [6].

Physical Examination

A thorough, comprehensive physical examination is always preferable; however, there are instances when an emergency requires a limited exam, focusing on the problem area. In pregnant women, a digital vaginal exam may be pertinent to ascertain cervical change associated with labor, which may or may not be associated with the patient's complaint.

The general examination includes an assessment of vital signs, mental status, cardiopulmonary findings, and a minimal neurological evaluation.

The focused physical assessment, particularly in pregnant patients with abdominal pain, can be challenging due to the presence of the gravid uterus. The enlarging uterus displaces the viscera, which may render confusing findings. The examiner should consider that any pathology or condition that occurs in nonpregnant women can occur in the pregnant state, as well.

Observation

As was addressed in the section on History, observation of the patient is the initial step in the physical examination. In what position is the patient when you first greet her? Is the patient lying down, sitting up, curled into the fetal position? How easily can the patient communicate? Is there an emesis basin nearby? Has intravenous access been started by other providers? Facial expression may provide clues as to the severity of the patients' pain in many but not all cases. Grimacing and sweating can indicate greater degrees of suffering. Pallor may raise the suspicion of intra-abdominal hemorrhage. The simple application of the examiners' palm on the patients' forehead may provide clues about fever. Answers to these and other questions provide clues to the examiner about the patient's condition and disposition.

Auscultation

Auscultation of the undisturbed abdomen can provide significant clues in diagnosing the patient with an acute abdomen. The presence and quality versus the absence of bowel sounds can be correlated to many diagnoses, including bowel obstruction, appendicitis, etc. Furthermore, as one listens to the abdomen with a stethoscope, the examiner can alternate pressure with the head of the stethoscope placed on the various quadrants to see if that elicits guarding or utterances of pain from the patient. Bowel sounds are variable and may be absent in many patients with other signs and symptoms of a peritonitis.

Rarely observed, a succusion splash may suggest a bowel obstruction.

Palpation

Pregnant women with abdominal pain may be difficult to palpate due to the presence of the gravid uterus. Bear in mind, however, that the cause of abdominal pain is often directly related to the gravid uterus, itself, so care should be taken to evaluate the uterus systematically, including the use of Leopold's Maneuvers for fetal positioning.

When the patient has localized pain, it is helpful to ask her to point with a single finger to the area of maximal pain intensity. This helps to narrow the examiners area of exploration. Typically, one would palpate all other regions and quadrants of the abdomen prior to palpating the affected area last.

Gentle pressure is imperative; a hard compression of the painful site will usually elicit guarding and unnecessary discomfort for the patient. Rebound tenderness is addressed under a separate heading.

Palpation may reveal nonpain-related important findings such as masses, organomegaly, pulsatility of major vessels, etc. Such findings may or may not be related to the diagnosis.

Percussion of the abdomen has limited value, but it may help to demonstrate a fluid wave. This should also be implemented with gentleness, as the tapping over

areas of peritonitis may elicit unnecessary exacerbation of the pain. In gravid women, this technique rarely yields useful information.

The Pelvic Examination

The pelvic examination of a pregnant woman includes variously a speculum evaluation of the vaginal vault and cervix, and a bimanual digital examination of the vagina to palpate the cervix, uterine fundus, and adnexa. Adding a digital rectal exam may be warranted, especially when considering the diagnosis of appendicitis. Rectal examination, albeit generally uncomfortable to the patient, allows the examiner access to the lower pelvic peritoneum, which is cases of appendicitis or pelvic abscess will elicit significant pain on palpation. The individual components or any combination thereof depends on the clinical presentation. Evaluation of vaginal discharge is often indicated in pain assessments, as well as the collection of secretions for screening of sexually transmitted infections and to rule out rupture of membranes.

Cervical dilatation and the station of the presenting part are relevant if preterm or term labor is a concern. Furthermore, the patient with a presentation of abdominal pain may simply be in labor and should thus be managed accordingly.

Supplemental Examinations

Other examinations that complement the physical examination are addressed elsewhere in this text. These include laboratory studies and imaging options.

One must be cautioned, however to use discretion and experience when relying on evaluation technologies other than the classic history and physical examination. Hayward [7] proposed a condition described as V.O.M.I.T. syndrome. This stands for Victims Of Modern Imaging Technology. His point is worth heeding. Many times, the clinician is apt to make major decisions on the basis of a finding on CT scan or sonogram, without considering the limitations of these tools. As much as modern imaging technology has vastly contributed to the practice of medicine and surgery over the past several decades, they should not be considered a substitute for sound clinical judgment and experience.

The Use of Rebound Tenderness (Commentary)

This author agrees with the sentiments of the Late Sir Zachary Cope [8], one of the greatest surgical diagnosticians of the twentieth century:

> *If the fingers be pressed gently but deeply over an inflamed focus within the abdomen and then the pressure be suddenly released, the patient may experience sudden, sometimes severe pain on the 'rebound'. We do not recommend the performance of this test for it elicits no more than can be ascertained by careful gentle pressure and may cause unexpected and unnecessary pain.*

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Imaging the Gravid Female

4

Stephanie Anne Scott and Justin Stowell

Abbreviations

ACOG	American College of Obstetrics and Gynecology
ACR	American College of Radiology
ADC	Apparent diffusion coefficient
AFLP	Acute fatty liver of pregnancy
ART	Assisted reproductive technology
β-hCG	Serum human chorionic gonadotropin
C-section	Caesarian section
CT	Computed tomography
dB	Decibel
DWI	Diffusion-weighted imaging
FAST	Focused abdominal sonography for trauma
FDA	Food and Drug Administration
GS	Gestational sac
Gy	Gray
hCG	Human chorionic gonadotropin
HEELP	Hemolysis, elevated liver enzymes, low platelets
IBD	Inflammatory bowel disease
IUP	Intrauterine pregnancy
kV	Kilovolt
mAS	Milliampere-second

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mGy	Milligray
MR	Magnetic resonance
MRCP	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
MRU	Magnetic resonance urography
mSV	Millisievert
mW/cm^2	Milliwatt per square centimeter
OHSS	Ovarian hyperstimulation syndrome
PID	Pelvic inflammatory disease
RI	Resistive index
SAR	Specific absorption rate
SSFP	Single-shot fast spin-echo
TOA	Tubo-ovarian abscess
TV	Transvaginal
US	Ultrasound
W/kg	Watt per kilogram
YS	Yolk sac

Introduction and Background

Imaging is frequently employed in the initial workup of patients presenting with acute abdominal or pelvic complaints. As discussed, signs and symptoms of expected benign physiological changes in pregnancy often masquerade with more ominous features of an acute abdomen, leading to diagnostic uncertainty. Rapid and accurate diagnosis of the cause of the acute abdomen in pregnant patients can be achieved with the help of imaging, preventing a delay in diagnosis, and allowing for the timely initiation of appropriate treatment thereby reducing morbidity and mortality for both the patient and her developing fetus.

Utilization and selection of appropriate imaging in gravid patients present unique challenges to the clinician. The risk-to-benefit ratio, balancing the need for precise diagnostic imaging and avoiding undue risks to the patient and the fetus, must be carefully considered. Uncertainty as to the best choice of imaging modality in various clinical scenarios is common. Ultrasound (US) and magnetic resonance imaging (MR, or MRI) are preferred for the pregnant patient, as they do not expose the fetus or patient to ionizing radiation [1, 2]. Nonetheless, fear of exposure of the fetus to ionizing radiation should not delay the diagnostic workup in some critical patients, which might require the use of radiography or computed tomography (CT) [1–3]. Condition-specific imaging algorithms can be developed by individual healthcare institutions as part of a collaboration between clinicians and radiologists to help guide appropriate use of imaging [1, 3, 4].

Ionizing Radiation and Risks

In recent years, the use of radiological examinations in pregnant women has more than doubled, with the greatest increase in utilization of examinations associated with ionizing radiation (particularly CT) [5, 6]. Despite issuance of practice guidelines for the use of imaging in pregnant patients by the American College of Radiology (ACR) and American College of Obstetricians and Gynecologists (ACOG) [1, 2], generalized lack of familiarity among referring providers about the risks of radiation and inconsistent adherence to these guidelines among radiology departments exists [7–10]. As such, a working understanding of the inherent risks of ionizing radiation associated with radiography and CT is paramount for clinicians and radiologists involved in the care of pregnant patients to ensure safe and judicious use of imaging.

Two categories of radiation effects—deterministic or stochastic—are used to describe the types of biological damage incurred as a function of radiation dose and time from exposure [1, 5, 11]. Deterministic effects manifest as cell death that occurs progressively in proportion to the absorbed radiation dose at or above a threshold level, and are not encountered at doses below these tissue-specific thresholds [1]. An example of a deterministic effect is skin erythema that occurs at doses of 2–5 gray (Gy). Stochastic effects are less predictable and may occur at any dose. In other words, there is no threshold dose limit below which stochastic effects cannot occur, and unlike deterministic effects, the severity of the radiation damage is not dose dependent [1]. Stochastic effects represent sequelae of damaged chromosomal material which may lead to mutations or some malignancies [1, 12, 13]. Fetal effects of radiation (either deterministic or stochastic) take the form of radiation-induced teratogenesis or carcinogenesis, respectively.

Radiation and the Developing Fetus

Absorbed radiation dose (measured as milligray [mGy]) and gestational age are two of the primary factors which determine the potential effects of radiation on fetal development [1, 12, 13] (Table 4.1). Fetuses exposed at earlier gestational ages exhibit the highest risk of detrimental deterministic effects, attributable to relative genetic susceptibility of rapidly dividing tissues to X-ray damage during early periods of organogenesis (4th through 10th weeks) [1] (Table 4.1). Effects of radiation exposure range in severity, such as embryonic death, malformation, growth restriction, and carcinogenesis [11–13].

Teratogenic effects from radiation exposures during this period generally manifest with radiation-induced malformations and general growth restriction. The central nervous system is particularly sensitive to ionizing radiation during this period and extending to the 15th week of pregnancy, as neuronal stem cells with high mitotic activity migrate along their pathways from the ventricular zones to the cortical mantle [1, 12]. This probably explains the relative frequency of diminished IQ, mental restriction, and microcephaly found in patients exposed to sufficient fetal

Table 4.1 Threshold radiation dose limits incurring teratogenesis throughout gestation

Developmental period	Dose range (mGy)	Teratogenic effects
Any	<50	None
Preimplantation (0–2 weeks after conception)	50–100	All-or-none effect resulting in either embryonic demise or no effect
Organogenesis (2–8 weeks)	200–250	Congenital anomalies and growth restriction
Fetal period: 8–15 weeks	60–310	High risk for neurological deficits (microcephaly, intellectual deficit, or severe intellectual disability) related to accelerated neuronal proliferation and migration during this period
Fetal period: 16–25 weeks	250–280	Lower risk for severe intellectual disability as neurons become progressively neuroresistant

Data from [1, 2, 4]

doses during susceptible developmental periods. Cells of the central nervous system become progressively more radioresistant beyond the 25th week of gestation, after which there are very little, if any, neurological effects. As these malformations are deterministic effects, the threshold dose necessary to induce these effects ranges from 100 to over 200 mGy [1].

Examinations in which the fetus is positioned directly within the radiation field (e.g., abdominopelvic CT) warrant consideration of the potential risks of fetal exposure (Table 4.2), whereas CT examinations where the fetus is not directly irradiated (i.e., scatter radiation from chest, head, or neck CT) pose less of a risk [1, 14]. Direct measurement of fetal dose is not possible due to variations in beam attenuation related to maternal size (anteroposterior dimension), fetal depth, the scanned region, and CT scanner parameters (filtration, tube voltage [kV, kilovolt], current [mAs, milliampere-second], pitch, rotation time, detector configuration, and number of acquisitions) [4, 14, 15]. Estimates of absorbed fetal dose are derived from phantom models [15, 16]. Based on these and a few clinical models, estimated fetal doses from single-acquisition abdominopelvic CT have ranged from 10 to 15 mGy, well below the threshold dose associated with fetal malformations [14].

Stochastic effects of in utero exposures (namely carcinogenesis) are probably of higher concern for the patient and clinician, as these are not predictable and may occur at any dose or gestational age, with increasing probability with higher or more frequent exposures [1, 11, 12]. The risk of developing childhood cancer from in utero exposure varies from negligible to low depending on whether the exposure was a one-time, high-dose event or repeated low-dose (≥10 mGy) exposures. Comparing the lifetime risk of development of childhood malignancy (e.g., leukemia) in exposed fetuses to unexposed controls (rate 0.2–0.3%), the relative increase in risk of developing radiation-induced cancer was minimal (rate 0.3–0.7%) [1, 13].

Table 4.2 Estimated maternal and fetal exposures to ionizing radiation during abdominal and pelvic imaging

Modality	Fetal dose (mGy)	Maternal dose (mSv)
Radiography		
Abdominal	0.1–0.3	0.01–1.1
Pelvis	1.1–4	
Fluoroscopy		
Intravenous pyelography	5–10	0.7–3.7
Small bowel follow-through	1.0–20	2.0–18.0
Barium enema (double contrast)	7	3.0–7.8
CT		
Abdomen	1.3–35	3.5–25
Pelvis	10–50	3.3–10
Abdomen & Pelvis without contrast (renal stone protocol)	10–11	3–10
Abdomen & Pelvis with contrast	13–25	3–45
Nuclear medicine		
^{99m}Tc DTPA	0.35–9	1.39–3.79
^{99m}Tc MAG3	0.58–13.5	1.32–9.0
^{99m}Tc MDP	1.8–7.87	1.8–4.7
^{99m}Tc RBC in vivo	2.51–5.95	2.5–6.0

Data from [5, 13, 18, 19]
^{99m}Tc technetium 99 m, *DTPA* diethlenetriaminepentacetate, *MAG3* mercaptoacetyltriglycine, *MDP* methylene diphosphonate, *RBC* red blood cell

Radiography, Fluoroscopy, Interventional Radiology and Nuclear Medicine

Although radiography remains the most common radiation-producing imaging examination performed in pregnant patients, the total average absorbed fetal dose from this modality is far less than that of CT [6]. If exposure of the fetus to radiation from a fluoroscopic or interventional radiology procedure is necessary, ultrasonography should be used for guidance, when possible, and dose-minimizing techniques employed by the operator, including optimization of patient positioning and shielding, limiting fluoroscopic time, reducing the number of images, utilizing last-image hold technique, lowering the frame rate, applying tight collimation, and limiting use of magnification [5, 17].

In general, most nuclear medicine procedures may be delayed until the postpartum period. However, most achieve radiation exposures much below threshold doses believed to induce fetal harm [5, 13, 18, 19] (Table 4.2) For example, technetium 99 m used for most procedures delivers less than 5 mGy to the fetus. Adequate hydration and bladder catheterization may be useful to expedite the renal excretion of radiotracers, thereby limiting fetal exposures [5].

Ultrasonography

Ultrasonography has long been established as a safe modality for the first-line evaluation of both fetal and maternal wellbeing. It is preferred in the evaluation of pregnant patients as it avoids the use of ionizing radiation, is inexpensive, and easily accessible. However, limitations of ultrasonography relate to the skill of the operator (sonographer) and patient body habitus [20]. Ultrasonography operates on deposition of energy in the form of sound waves though tissues, measuring tissue composition and movement as reflections and attenuation of the sound beam. Mechanical and thermal energy produced by the ultrasound pulse waves may theoretically affect the developing fetus, although no deleterious effects have been documented in humans. Nonetheless, the Food and Drug Administration (FDA) has established limits for mechanical and thermal indices of less than 1 and energy exposure to less than 94 mW/cm^2 (milliwatts per square centimeter) [5, 20, 21]. As color, power, and spectral Doppler techniques utilize higher intensity acoustic output, these modalities are generally used only when needed throughout pregnancy and avoided in the early 1st trimester. Fetal heart rate is instead evaluated with lower energy M-mode ultrasonography [5, 21].

Computerized Tomography

In general, CT is to be avoided in pregnancy, as scans of the abdomen and pelvis deliver the most radiation to the fetus. Nevertheless, its use in pregnancy is increasing at a rate more than twice that of other imaging modalities [6, 22]. Despite the continued increase in abdominopelvic CT utilization in pregnancy, the percentage of scans positive for acute pathology has not changed [6]. The benefits of information obtained from a scan must outweigh the inherent risks to the fetus. However, these perceived fetal risks should not deter a clinician from using CT as a diagnostic tool should acquisition of adequate information about potentially life-threatening diagnoses be delayed or suboptimal by other means [1, 2, 12, 23]. CT offers the added benefit of detecting unanticipated masquerading causes of acute abdominal pain [21]. It is generally preferred to exhaust nonionizing imaging modalities (US and MR) before CT or radiography when possible. Uniquely, CT is considered a first-line modality in the evaluation of pregnant trauma patients, following initial rapid triage with focused abdominal sonography for trauma (FAST) scan to evaluate for free intraperitoneal fluid, pleural effusions, and pericardial fluid [3, 5, 21, 23, 24].

Magnetic Resonance Imaging

MRI offers the diagnostic benefits of nonionizing, cross-sectional, high soft tissue resolution evaluation of abdominopelvic pathology. MR imaging at ≤3 tesla strength is possible and safe at all stages of development [1, 2, 5]. To date, no studies have demonstrated harmful effects to the fetus from MR. However, theoretical risks to

the fetus exist related to inherent properties of the magnet. These include the static magnetic field strength, applied gradient magnetic fields, and radio frequency (RF) pulses. High magnetic field strengths are hypothesized to affect fetal neuronal migration and proliferation during early pregnancy but remain theoretical [5].

Energy deposition in tissues from the RF pulses may lead to tissue heating. This is known as the specific absorption rate (SAR) and is quantified as watts per kilogram (W/kg), with federally mandated and internally monitored upper limit of 4 W/kg. This limit is associated with a 0.6 °C increase in maternal body temperatures after 20–30 min of imaging [5]. Fetal injury may occur with maternal temperature elevations of 2–2.5 °C for 30–60 min, but the maximum SAR is deposited in the maternal surface tissues with fetal heating considerably less than the proposed detrimental levels [5, 25].

MR sequences that employ rapid gradient switching (particularly in single-shot fast spin-echo [SSFP] sequences commonly utilized in fetal imaging) lead to higher energy deposition, as well as acoustic noise in the scanner. Use of such sequences should be kept brief, as theoretical damage to the developing fetal ear may result exposure to ≥90 dB (decibel) [5].

Utilization of Intravenous Contrast in Pregnancy

In addition to the risks of ionizing radiation, intravenous contrast material utilized in diagnostic imaging poses additional risks to fetal wellbeing. Both iodine- and gadolinium-based contrast agents are known to cross the blood–placenta barrier and enter the fetoamniotic circulation [26].

Iodinated Contrast

To date, no adverse fetal or neonatal effects have been documented from administration of low-osmolality iodinated contrast media (e.g., iodinated contrast used in CT) and are thus classified by the United States FDA as Category B (no adverse effects in animal studies but controlled studies in pregnant patients do not exist) [5]. The American College of Radiologists (ACR), therefore, recommends against withholding iodinated contrast agents in pregnant patients if it is necessary for diagnosis [26]. Concerns over fetal and neonatal hypothyroidism after in utero exposure to iodinated contrast have not been validated, and neonates are generally screened for hypothyroidism at birth if there is a pertinent history [5, 26].

Gadolinium-Based Contrast

Gadolinium-based contrast agents have been labeled as Category C medications by the FDA because of documented fetal demise and malformations associated with in utero exposure in animal studies, yet these effects have not been documented in

retrospective human studies [5]. Therefore, these agents should be administered with caution in pregnant patients, and their use is generally avoided [2, 26]. The ACR does indicate that use of gadolinium-based contrast in pregnancy should occur only after carefully documented consensus decision by the radiologist, clinician, and patient, when the information obtained from its use outweighs the purported risks to the fetus from exposure to free gadolinium ions [2, 5, 26, 27]. In such cases, agents with tightly bound gadolinium-chelate complexes are advised, administered at the lowest dose, including gadobenate dimeglumine (MultiHance; Bracco Diagnostics, Monroe Township, NJ) or gadoteridol (ProHance; Bracco Diagnostics) [5]. Informed consent should be obtained from the patient and documented in the medical record prior to gadolinium administration.

Allergic Reactions

Pretreatment and treatment of allergic reactions to contrast media should follow established guidelines from the ACR, such as oral and intravenous diphenhydramine and corticosteroids (prednisone or dexamethasone) [5, 26].

Screening for Pregnancy

In allowable clinical settings, all women of potential childbearing age (defined as ages 12 through 50 years) should undergo a full determination of pregnancy status to include menstrual and surgical history (tubal ligation or hysterectomy), contraceptive use, and qualitative urine human chorionic gonadotropin (hCG) or quantitative serum human chorionic gonadotropin (β-hCG) testing, prior to the use of direct ionizing radiation [1, 2, 21]. In some patients, pelvic US may be indicated to assess the status of the pregnancy. Pregnancy status can be assessed by interview of the patient as to her likelihood of pregnancy (e.g., not sexually active, on effective birth control, or biologically incapable of pregnancy) or that she has recently completed her menstrual period within the last 4 weeks prior to imaging [1]. Pregnancy test results should not be the sole screening measure, and patients must undergo the standard interview procedure, as negative pregnancy tests do not necessarily exclude recent conception [5]. A positive pregnancy test will prompt the imaging technologist to follow appropriate pregnancy-tailored protocols. For procedures expected to deliver high doses of radiation to the uterus (e.g., pelvic interventional procedures), a pregnancy test should be obtained within 72 h proceeding [1]. The ACR and ACOG both emphasize that when pregnancy status cannot be verified in the emergent setting, a waiver should be included in the patient's medical record documenting the critical need for the study [1, 2].

Counseling the Pregnant Patient About Imaging Procedures

Patients may report anxiety surrounding the exposure of their fetuses to ionizing radiation and must be appropriately counseled. It should be emphasized in a positive light that for most imaging modalities, the risk of pregnancy loss, birth defects, mental restriction, and subsequent childhood malignancy are small [1, 21]. The risk of incurring detrimental effects from exposure to ionizing radiation of imaging examinations must be considered in light of generalized background risks associated with pregnancy, such as birth defects (3%), miscarriage (15%), prematurity (4%), growth restriction (4%), and mental restriction or neurological deficits (1%) [1, 2, 20, 22]. At the relatively low fetal doses encountered in abdomen and pelvic imaging (10–35 mGy for abdominopelvic CT), threshold limits are extremely unlikely to be met to cause deterministic effects. The main concerns therefore are those of carcinogenesis in later life, which, for examinations involving less than 50 mGy fetal exposures, are less than 0.8% with attributable lifetime risk of approximately 2% [1, 2, 5]. More clearly stated, there is a 98–99% likelihood that the fetus will be unaffected by the radiation. Useful comparisons with background radiation may highlight that differences in topographic elevation between women in Denver, Colorado, and those living at sea level result in a slight relative excess exposure to radiation levels (about 0.6 mSv, millisievert), which only theoretically place fetuses at risk for an additional attributable cancer in every 5000 births [1]. Average background radiation is estimated at 1.0–2.5 mGy. There exists no single, wellmonitored diagnostic radiology procedure which will result in a radiation dose significant enough to affect the wellbeing of the fetus. Therefore, pregnancy termination is not justified for fetal exposures to a single examination (< 100 mGy) [1, 2, 5, 11].

Nongynecological Causes of Abdominal Pain

Appendicitis

Acute appendicitis is the leading cause of acute abdominal pain in pregnancy requiring surgical intervention and complicates 1 in 2000 pregnancies [3, 21, 28, 29]. First-line imaging of the pregnant patient with right lower quadrant pain is ultrasound with graded compression. However, despite being the first-line modality for the evaluation of appendicitis, ultrasonography has a low yield, allowing visualization of the appendix only 1/3 of the time. Another study showed that the sensitivity and specificity of US in the assessment of appendicitis is only up to 78% and 83%, respectively [20]. Knowledge of variation in appendiceal location in the gravid abdomen may increase diagnostic yield. Detection of a blind-ending, tubular, nonperistaltic, noncompressible structure arising from the cecal base, with luminal diameter > 6 mm establishes the imaging diagnosis (Fig. 4.1). Use of color Doppler may reveal associated hyperemia and surrounding inflammation of the periappendiceal fat [20, 21, 28, 30]. In the setting of acute appendicitis, the patient is often exquisitely tender with direct transducer pressure over the appendix, which can help

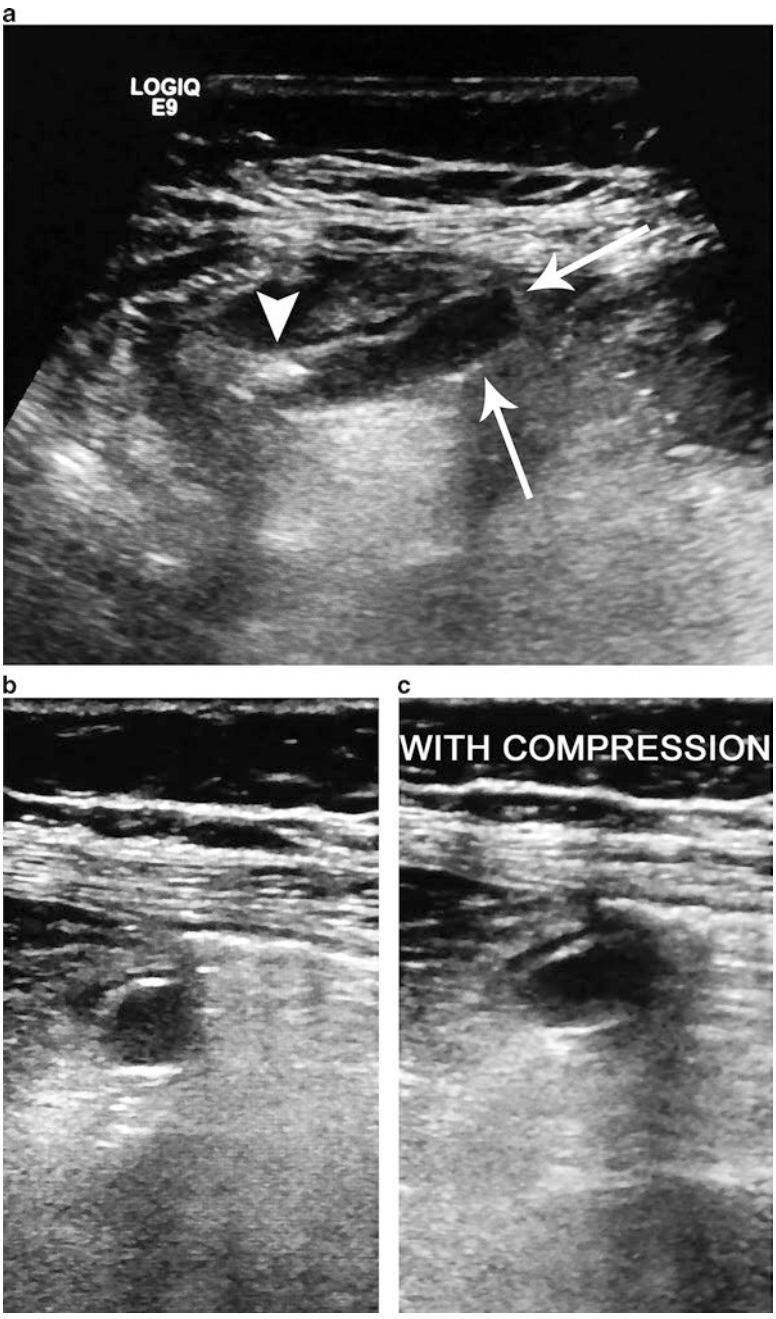

Fig. 4.1 US of acute appendicitis: acute appendicitis in a 31 y/o pregnant patient at 21 weeks' with right lower quadrant abdominal pain. (**a**) Gray scale image of the right lower quadrant demonstrates a longitudinal view of a dilated, blind ending tubular structure arising from the cecum consistent with the appendix (*arrows*). Echogenic, shadowing appendicolith (*arrowhead*) is seen within the lumen toward the base. Gray scale transverse images through the appendix without (**b**) and with compression (**c**) demonstrate an appendiceal diameter of 10 mm with no change with compression. Appendicitis was confirmed at surgery

confirm the diagnosis. When these findings are variably present, equivocal, or when the appendix is not discretely visualized, imaging with other modalities is typically warranted.

Delay in diagnosis and surgical management may lead to perforation, which is associated with up to 30% fetal loss, and occurs most frequently in later stages of pregnancy when sonographic evaluation of the appendix is technically difficult from progressive displacement of the appendix by the gravid uterus [28]. MR is a highly sensitive (100%) and specific (94%) modality for the diagnosis of appendicitis in pregnancy after targeted ultrasound examinations fail to demonstrate a normal appendix [25, 27, 31, 32]. The extremely high negative predictive value of MR (100%) is helpful in triaging patients who may potentially have a surgical abdomen [31]. As with the other modalities, the variable position of the appendix may complicate interpretation. A normal appendix is defined as one with a luminal diameter of ≤6 mm, or an air- or contrast-filled lumen (using either rectal saline or oral ferumoxil oral suspension admixed with barium sulfate) [31]. A positive exam demonstrates an enlarged, thickened appendix (>7 mm) with fluid-filled lumen with or without periappendiceal inflammation, most apparent on T2-weighted images as ill-defined increased signal in the periappendiceal fat (Fig. 4.2). Indeterminate results include luminal size between 6 and 7 mm and no surrounding inflammation [27, 31]. MR also offers the added benefit of detecting potential alternate diagnoses for the patient's complaints [32].

If ultrasonography and MRI are inconclusive or in the absence of available MRI, abdominopelvic CT with contrast may be used to evaluate for appendicitis [3]. However, dose reduction techniques should be considered [8]. Lazarus and colleagues reported CT to have a 92% sensitivity and 99% specificity for the diagnosis of appendicitis, with overall negative predictive value of 94% [29]. Furthermore, CT can detect additional pertinent diagnostic information, such as small bowel obstruction and urinary calculi, among others [29].

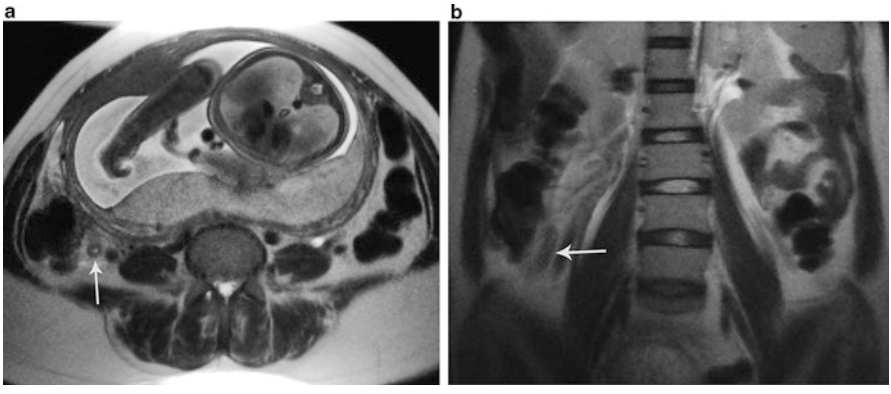

Fig. 4.2 MRI of acute appendicitis: acute appendicitis in a 29 y/o pregnant patient at 31 weeks' with right lower quadrant abdominal pain. Axial (**a**) and coronal (**b**) T2 HASTE images demonstrate a dilated, thick walled, fluid-filled appendix (*arrows*) measuring 9 mm in diameter with periappendiceal inflammation. Appendicitis was confirmed at surgery

Urolithiasis and Urinary Tract

Urolithiasis and urinary tract infections constitute the most common painful nonobstetric causes of abdominal or pelvic pain in pregnancy [21]. Urolithiasis affects as many as 1 in every 1500 pregnancies, and coexisting pyelonephritis or urinary tract infection frequently leads to hospitalization. Ultrasound is the first-line modality for evaluation of suspected renal colic in pregnancy [3, 5, 21, 22, 28, 33]. Renal sonography readily detects the presence of hydronephrosis, but a distinction must be determined between physiological hydronephrosis of pregnancy (more commonly right sided and a result of mechanical compression of the gravid uterus and hormone-related ureteral relaxation) and obstructive urolithiasis (more frequent in pregnancy due to increased urine production and stasis) [21, 28, 33]. Renal pelvis diameter measuring up to 25 mm on the right and 10 mm on the left up to 40 weeks of gestation may be physiological [34]. Smooth tapering of the distal ureter as it enters the pelvis and the absence of luminal filling defects help confirm the diagnosis. Ultrasonography is highly sensitive and specific (90% and 98%, respectively) for hydronephrosis, increased in the presence of a stone [33].

Ultrasonographic sensitivity for detection of stones is highly variable, ranging from 34–95% [35, 36]. Renal or ureteral stones manifest as foci of hyperechogenicity often with accompanying acoustic shadowing (Fig. 4.3). When color Doppler is applied, a "twinkling artifact" may result (up to 86% of urinary calculi), increasing diagnostic confidence [30, 34]. When possible, imaging should be performed with a distended bladder to better evaluate distal ureters. Transvaginal (TV) ultrasound can be performed to evaluate the presence of distal ureteral stones, distal ureteral dilatation, and ureteral jets in patients with inconclusive transabdominal examinations. In late pregnancy, ureteral jets may not be visualized, and their absence does not necessarily indicate obstructive urolithiasis. Reimaging the patient

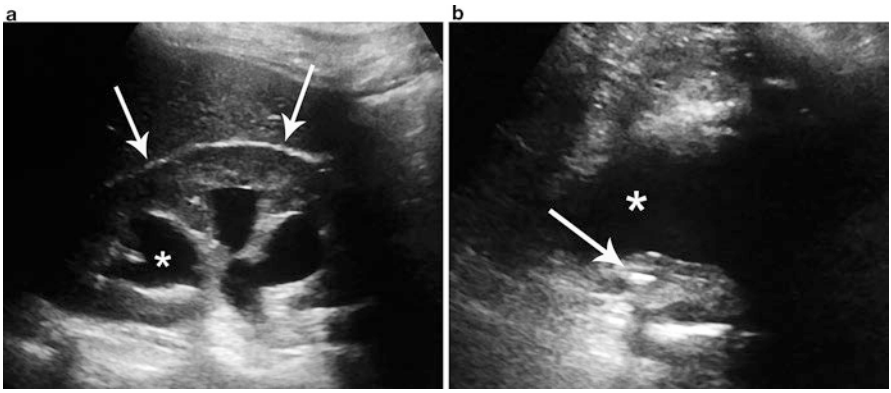

Fig. 4.3 US of obstructive uropathy: 35 y/o pregnant patient at 33 weeks' with right flank pain. (**a**) Longitudinal gray scale image of the right kidney (*arrows*) demonstrates moderate right hydronephrosis (*asterisk*). (**b**) Gray scale image at the level of the distal right ureter and bladder (*asterisk*) shows an echogenic shadowing calculus (*arrow*) in the distal right ureter at the ureterovesicular junction. This initially was not seen when the patient had a decompressed bladder. After hydration and reimaging, the calculus was able to be visualized. The patient was admitted and passed the stone the following day

in the contralateral decubitus position may elicit a ureteral jet or confirm its absence [33]. Despite conflicting evidence, differences in renal vascular resistive indices (RI) between each kidney can help to differentiate these entities, with no difference in RI between the kidneys in physiological hydronephrosis whereas RI greater than 0.70 suggests obstructive pathology, particularly if unilateral [33]. The rate of spontaneous passage of urinary stones in pregnant women reportedly ranges from 48% to 81% and persistent obstructive stones although conservative management may undergo further treatment with nephrostomy tube placement or ureteral stent placement [33]. Nephrostomy tube placement may be accomplished with ultrasound guidance to further limit exposure of the patient and fetus to fluoroscopy [17].

Low-dose noncontrast CT is a sensitive and specific test for detection of obstructive uropathy in the pregnant patient and should be considered if ultrasound is inconclusive [36, 37]. The likelihood of spontaneous stone passage is dependent on stone width, with decreasing likelihood of passage above 5 mm and a more proximal ureteral location [38]. Stone size can be readily measured by CT and is less reliable on MRI. Retained or impacted stones place the patient at risk for pyelonephritis and pyonephrosis, which can lead to untoward pregnancy complications. Thus, low-dose, noncontrast CT should be used in the setting of suspected obstructive uropathy, even in pregnant patients [37].

MR and MR urography (MRU) utilizing heavily T2-weighted images may serve as helpful adjunct modalities in evaluation of suspected urolithiasis, especially when coexistent physiological hydronephrosis and hydroureter confound US findings in the third trimester [20, 21, 25, 35, 39] (Fig. 4.4). Although, when compared to low-dose CT, MRU suffers from poor spatial resolution and lower sensitivity for detecting calcified stones, with an overall sensitivity of 80% [20, 39]. Flow-related

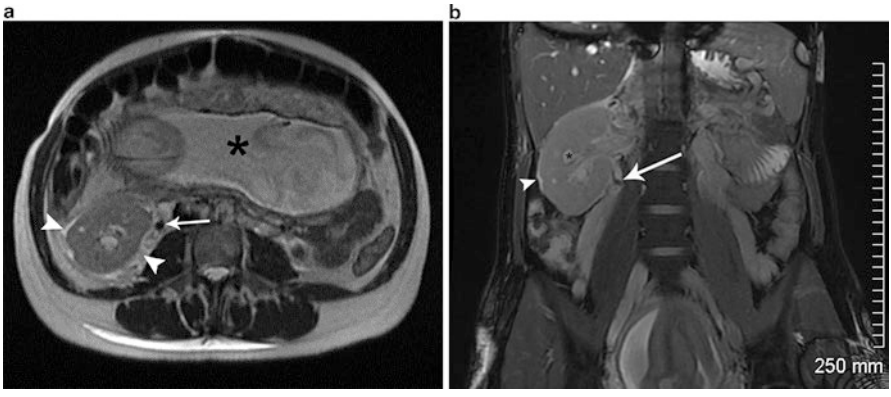

Fig. 4.4 MRI of obstructive uropathy: 28 y/o pregnant patient at 29 weeks' with right flank pain and hematuria. Renal US demonstrated right hydronephrosis but no obvious ureteral calculus (not shown). (**a**) Axial T2-weighted MR image of the abdomen demonstrates mild right hydronephrosis, perinephric-free fluid (*arrowheads*), and a 4 mm hypointense filling defect in the proximal ureter compatible with ureteropelvic junction calculus (*arrow*). Partial visualization of IUP anteriorly (*asterisk*). (**b**) Coronal T2 FIESTA fat-saturated image through the abdomen demonstrates mild right-sided hydronephrosis (*asterisk*), perinephric-free fluid (*arrowhead*), and filling defect in the proximal ureter compatible with ureteral calculus (*arrow*). Right nephroureteral stent was placed after stone extraction

artifacts may mimic calculi, resulting in false positive examinations [21]. Findings of obstructive uropathy on MR include renal enlargement, increased signal (edema) in the renal parenchyma on T2-weighted images, and perirenal fluid [25, 35, 39]. Calculi appear as focal filling defects within the ureteral lumen, usually at a point of abrupt caliber change. MRU may identify distal ureteral calculi and manifest the "double-kink sign" – a column of urine in the distal ureter in association with ureteral constriction at the pelvic brim and vesicoureteral junction [35].

Biliary Disease

Hormones of pregnancy lead to hypersecretion of biliary cholesterol and gallbladder stasis, predisposing a patient to cholelithiasis and subsequent risk for acute cholecystitis, the second-most common surgical abdominal emergency affecting pregnant women [25, 28]. Ultrasonography is routinely used as a first-line evaluation of acute right upper quadrant pain and suspected hepatobiliary pathology. The presence of shadowing gallstones (95% sensitivity), gallbladder wall thickening (>3 mm), distention (>5 cm transverse diameter), pericholecystic fluid, and the presence of a sonographic Murphy sign may be used to diagnoses acute cholecystitis [28] (Fig. 4.5). Dilation of the biliary tree may suggest the presence of choledocholithiasis. However, direct detection of common bile duct stones may be possible in as few as 20% of cases, as bowel gas may obscure the distal duct and 10% of stones may not produce characteristic shadowing [20].

Findings of acute cholecystitis on MRI reflect those of US, with gallbladder wall thickening and edema (increased signal on T2-weighted images), pericholecystic fluid, and low signal filling defects within the lumen of the gallbladder reflecting gallstones [25, 40]. In addition, choledocholithiasis is well evaluated by MR

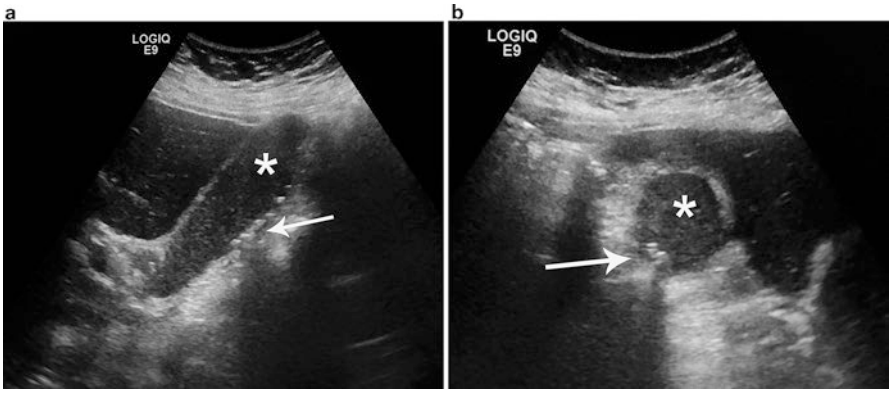

Fig. 4.5 US of acute cholecystitis: acute cholecystitis in a 26 y/o pregnant patient at 19 weeks' with right upper quadrant pain. Longitudinal (**a**) and transverse (**b**) images through the gallbladder demonstrating a distended gallbladder with echogenic intraluminal sludge (*asterisks*), small layering shadowing echogenic gallstones (*arrows*) and gallbladder wall thickening (5 mm). Gangrenous cholecystitis was found at time of surgery and confirmed at pathology

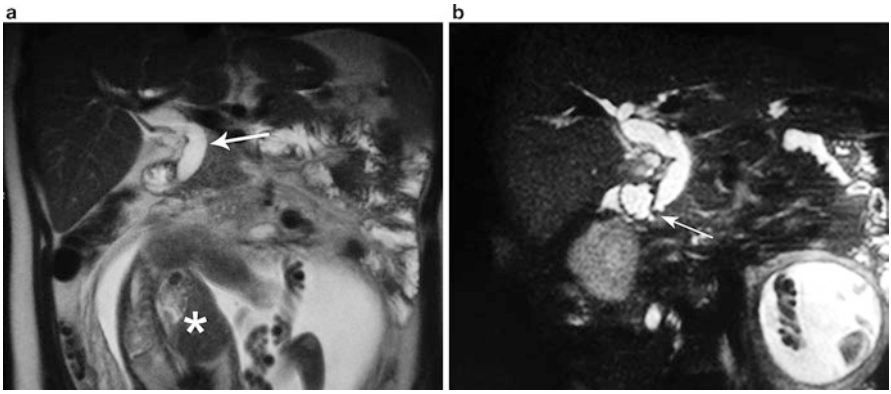

Fig. 4.6 MRI of choledocholithiasis: Choledocholithaisis in a 19 y/o pregnant patient at 25 weeks' with epigastric pain and elevated bilirubin. (**a**) Coronal T2 HASTE image demonstrates a dilated common bile duct (*arrow*), which measured up to 14 mm, and intrauterine pregnancy (*asterisk*). (**b**) Coronal oblique T2 HASTE fat-saturated image from MRCP demonstrates an intraductal-rounded T2 hypointense filling defect in the distal common bile duct measuring 4 mm compatible with choledocholith (*arrow*). Patient subsequently underwent ERCP with stone removal and stent placement

cholangiopancreatography (MRCP) [40]. The positive predictive value of MR is 100% for diagnosis of biliary obstruction. Thin-section (1 mm) overlapping MRCP images depict small-rounded hypointense filling defects in T2-hyperintense lumen of the biliary tree, indicating choledocholiths (Fig. 4.6). Common bile duct dilation is present when the distance between the outer walls of the common bile duct measures greater than 7 mm [41].

Although US and MRI are the preferred modalities for evaluation of the biliary system, CT with dose reduction techniques may be utilized when there are contraindications to MRI or when other means for rapid diagnosis are not available [40]. Despite being slightly less sensitive than MR for detecting small noncalcified stones, CT has similar performance to even noncontrast MR in detecting the presence of biliary ductal dilation and choledocholithiasis [42].

Pancreatitis

Pancreatitis is a rare cause of abdominal pain in pregnancy, occurring most frequently in the third trimester and usually as a result of gallstones [43]. Pancreatitis may affect 1 in every 3300 pregnancies [20, 28]. Ultrasonography is limited in the evaluation of the pancreas in the acute setting, as inflammation contributes to generalized ileus, causing bowel loops to interdigitate between the transducer and the pancreatic parenchyma, obscuring its evaluation though bowel gas shadowing [43]. However, US is frequently used as first-line imaging to evaluate for the presence of gallstones. When seen by US, the pancreas may appear enlarged and hypoechoic (edematous), with or without peripancreatic fluid, which may become organized into a collection [34].

As in nonpregnant patients, contrast-enhanced CT depicts changes of pancreatic parenchymal edema, peripancreatic inflammation and fluid, and associated complications such as pancreatic necrosis (parenchymal nonenhancement), peripancreatic fluid collections, ductal dilation, or vascular complications (pseudoaneurysm, venous thrombosis, or hemorrhage) [44]. In general, CT evaluation of pancreatitis requires multiphasic technique, which would subject the patient and fetus to high doses of radiation. Therefore, noncontrast MR is typically utilized in the evaluation of acute pancreatitis in pregnancy, discussed subsequently.

MR findings of acute pancreatitis include parenchymal edema and peripancreatic fluid with or without pancreatic ductal dilation. Complicated pancreatitis may result in peripancreatic fluid collections, which manifest as variable signal on T2-weighted images. As gadolinium-based contrast is typically contraindicated in pregnancy, evaluation for pancreatic necrosis or vascular complications may be limited but can manifest as fluid signal areas surrounding the pancreas on T2-weighted images in the former and lack of flow voids in the setting of splenic vein thrombosis [44]. Diffusion-weighted sequences: diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC), are highly sensitive for early pancreatic inflammation. Furthermore, the presence of hemorrhage may be suggested as heterogenous areas of T1-hyperintense signal within the pancreatic bed [34]. MRCP may be helpful in evaluation of the pancreatic and biliary ductal system, identifying obstructive lesions or variant anatomy [44].

Hepatic Disease

HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) occurs in up to 12% of pregnant patients with severe hypertension. Findings on ultrasound may be the first signs of the disease, occurring even before biochemical changes, such as hepatic edema (hypertrophy, periportal hypoechoic "halos," a "starry sky" appearance of the liver with echogenic portal triads admixed among the edematous parenchyma, capsular thickening, or scattered areas of increased echogenicity) [44]. The syndrome may result in hepatic hemorrhage, rupture, or infarction. US diagnosis of hemorrhage can be made by visualization of a heterogeneously echogenic, nonvascular, complex cystic mass with or without lacy internal echoes representing fibrin strands. Serial US examinations should document progressive involution of the hematoma and exclude an underlying mass. Both adenomas and hemangiomas can enlarge during pregnancy, with increased risk of hemorrhage [44]. Although these findings are nonspecific, other causes of hepatic hematoma must be excluded, such as hemorrhagic adenoma, trauma, or intrahepatic vascular abnormalities [20]. Hepatic infarcts manifest as peripheral, geographic, or wedge- shaped hypoechoic areas with diminished vascularity [40].

Pregnancy induces a hypercoagulable state, which predisposes patients to thrombosis [20]. Budd-Chiari syndrome, manifesting clinically as portal hypertension and liver failure, may result from thrombosis of hepatic venules, veins, or the inferior vena cava. Depending on the age of thrombus, venous thrombus may appear

hypo- or hyperechoic, with associated expansion of the affected vessel and lack of color signal on color Doppler imaging [45]. A thin fibrotic echogenic cord may be seen within a retracted vessel lumen with chronic occlusion, or as treatment resolves the clot. Color Doppler may also depict extrahepatic or intrahepatic collateral vessels, an indirect, though specific sign of Budd-Chiari syndrome. Hepatic congestion leads to portal hypertension, with dampened or reversal of flow within the portal veins with color and spectral Doppler. A secondary sign of portal hypertension is ascites, visualized on US as simple peritoneal free fluid [45].

Magnetic resonance findings in HELLP syndrome reflect those of sonography. The areas of increased echogenicity on US may demonstrate increased signal on T2-weighted images, indicating edema and early hepatic necrosis [25, 40]. MR appearance of hepatic hematomas varies on the acuity of the blood products but will appear heterogeneous on T1 and T2-weighted images, causing mass effect, with or without capsular rupture, manifest as focal irregularity of the capsule and adjacent sentinel clot [40].

Acute fatty liver of pregnancy (AFLP) most often manifests in the third trimester of nulliparous women with a diffusely hyperechoic hepatic parenchyma on US, a nonspecific qualitative finding [20, 40]. Acute fatty liver of pregnancy on MR appears as hepatomegaly with diffuse increased signal on T1-weighted in-phase images with signal dropout on opposed phase images (representing intracellular triglycerides), or signal dropout on fat-saturated images (revealing the presence of macroscopic hepatic fat) [25].

Budd-Chiari syndrome may manifest on MR as morphological changes in liver contour with subacute and chronic stages (particularly caudate lobe hypertrophy) but diffuse hepatomegaly with smooth contours in the acute stage [45]. Evaluation of hepatic venous patency may be suboptimal without contrast. However, a filling defect within the hepatic vein or inferior vena cava flow voids may suggest the presence of a thrombus. On contrast-enhanced examinations, variations in hepatic perfusion are a prominent feature in Budd-Chiari syndrome, a manifestation of intrahepatic and extrahepatic collateralization. MR may reveal the presence of multiple 1–4 cm regenerative nodules with iso- to hyperintense signal on T1 sequences and iso- to hypointense signal on T2-weighted images, with arterial enhancement and retention of contrast on the portal venous phase [40, 45]. However, given the contraindication of gadolinium in pregnancy, the imager may have to rely on noncontrast features.

Gastrointestinal Disease

Bowel obstruction is another leading cause of abdominal pain, during pregnancy, most often occurring in the second or third trimester [28]. Intestinal obstruction represents the third leading cause for surgical intervention for acute abdominal pain in pregnancy [44]. Most commonly, the obstruction is due to adhesions, which generally cannot be visualized on imaging. Following initial examination with abdominal radiography, CT is typically the next modality utilized in the evaluation of

suspected intestinal obstruction in the nonpregnant patient. However, this algorithm is often altered in pregnancy to avoid the use of ionizing radiation by utilizing US or MRI.

The use of sonography has been advocated as a first-line modality for the evaluation of suspected small bowel obstruction in pregnant patients, both because of the lack of ionizing radiation, and targeted evaluation of the bowel, when a gravid uterus in the third trimester may displace the bowel, making typical patterns of bowel obstruction on radiography less reliable [34, 44]. US findings include dilated (>3 cm), hyperperistaltic bowel loops with swirling of intraluminal contents involving long segments (>10 cm) of bowel [46]. Identification of these findings should prompt further evaluation with MRI or CT to identify the transition point and associated complications of obstruction [34].

Findings of small bowel obstruction on CT and MRI include the presence of dilated fluid-filled bowel loops measuring >2.5–3.0 cm in diameter, intraluminal air-fluid levels, "fecalization" of bowel contents from delayed small bowel transit, mesenteric fluid and haziness, and decompressed bowel distal to the site of obstruction indicated by "beaking" of the stenosed bowel segment [25, 34, 47, 48]. Closed-loop obstructions manifest with clustered small bowel loops tethered in one quadrant of the abdomen and twisting of mesenteric vessels. Bowel wall thickening, mesenteric edema, and hypoperfusion of bowel segments (seen on contrast-enhanced CT as hypoenhancing bowel walls) suggest strangulation [47, 48].

Other etiologies of intestinal obstruction in pregnancy may be secondary to underlying inflammation or fibrosis from active or chronic changes of inflammatory bowel disease (IBD), particularly Crohn's disease or less likely ulcerative colitis [44]. Although fluoroscopic examinations (namely small bowel follow through) have been traditionally used for evaluation of the small bowel, cross-sectional imaging with CT or MRI is typically preferred as it offers evaluation of extramural disease extent [44]. CT (and particularly CT enterography) findings include mural thickening and enhancement, luminal narrowing, mesenteric or mural inflammation, and fibrofatty proliferation of chronically affected segments [20]. Other complications of IBD are readily depicted on CT and include abscess, fistula, and sinus tract formation. Typically, however, pregnant patients with IBD are imaged with MRI [34].

MR and MR enterography findings mirror those of CT, with increased sensitivity of depicting early bowel wall inflammation in the setting of IBD as increased signal on T2-weighted images. Sensitivity and specificity of MR for detecting these features may be as high as 98% and 100%, respectively [20].

Vascular

Various vascular complications of pregnancy may occur. Pregnant patients are predisposed to ovarian venous thrombusthat is believed to be secondary to the relative hypercoagulable state of pregnancy and venous stasis from compression of the

gonadal vein at the pelvic brim by the gravid uterus. As a rare complication of pregnancy, affecting nearly 0.2% of pregnancies, mortality may exceed 60%. [34]. The retroperitoneal location of the ovarian vein often precludes complete visualization by US. The reported sensitivity of US for depicting ovarian venous thrombosis is just over 50% [34, 49].

MR venography (with time-of-flight sequencing) may offer the highest sensitivity and specificity (100%) for diagnosis of ovarian venous thrombosis, manifesting as an area of signal void within the vein. T1- and T2-weighted sequences may reveal intermediate to high signal of the intraluminal clot, depending on the acuity [25, 34, 49]. Therefore, noncontrast MR venography is recommended as the next-line evaluation for patients with inconclusive findings at US [49].

Contrast-enhanced CT with adequate bolus timing and opacification of the gonadal veins may depict the low-attenuation intraluminal filling defects within dilated retroperitoneal tubular structures, indicating thrombus [49].

Splenic artery aneurysms affect approximately 10% of the general population, exhibit a distinct association with pregnancy, and may be complicated by rupture in up to 25% of cases [34, 50]. Several risk factors exist for splenic artery aneurysms, including pregnancy itself. Splenic artery aneurysms may be diagnosed using gray scale and spectral Doppler US as hypo- or anechoic dilations of the native artery near the splenic hilum and a weak, turbulent pulsatile flow pattern. In the presence of mural thrombus or calcification, no flow may be seen.

CT may show a peripherally calcified mass in association with the splenic vessels, most frequently near the splenic hilum. Most measure less than 2.5 cm in size [34]. Aneurysm rupture may be noted as dense fluid in the region of the spleen. MR of splenic aneurysms may show a rounded dark flow void next to the splenic hilum in the presence of flow. Otherwise, thrombosed or calcified aneurysms would appear as iso- to hyperintense masses on T1- or T2-weighted images, near the native vessel [34].

Physiological adaptations to pregnancy include increased circulating blood volume and hormonal changes of the aortic wall, which may predispose to aortic dissection, particularly in the third trimester [51]. Underlying connective tissue disorders, such as in the Marfan syndrome, contribute to inherent weakness of the aortic media, making these patients particularly susceptible to aortic dissection with a fivefold increased risk (4.4%) [52]. Older patient age (>32 years) and ascending aortic lumen diameter > 4.2 cm are both associated with increased risk of dissection and rupture [52, 53]. Contrast-enhanced CT angiography is first employed in the setting of suspected acute aortic dissection, as it is rapid and the extent of the dissection and associated complications can be readily defined. CT findings include the presence of a displaced intimomedial flap which divides the true and false lumens [54]. Complications of branch vessel occlusion, thrombosis, or vessel rupture may also be detected. While not typically used in the acute setting, MRI may provide not only structural information of abdominal aortic aneurysms, but also dynamic and flow-related information [55].

Trauma

Rapid and accurate assessment of the maternal abdomen, placenta, and fetus for traumatic injury is imperative. FAST exams are rapid bedside procedures used by initial responders and physicians as a screening tool for the presence of pericardial, pleural, and peritoneal blood. Their sensitivity may be low for detecting small bleeds, but a positive exam allows for rapid triage of the patient for appropriate treatment algorithms. Placental abruption is the most common cause of fetal mortality in trauma followed by maternal visceral (splenic and liver) injury [20, 21, 23, 30, 56]. In many centers, the FAST examination is first performed to assess maternal wellbeing, and once stabilized, a fetal US is performed [23]. In a large review, Meisinger et al. concluded that FAST examinations (with extended examination of the kidneys, liver, spleen, placenta, amniotic fluid volume, and limited fetal evaluation including M-mode interrogation of fetal heart rate) in pregnant patients who sustained blunt abdominal trauma, were 85.7% sensitive and 99.7% specific, which is similar to that of abdominopelvic CT [24]. Richards et al. reported similar sensitivity (64%) and specificity (94.4%) which were highest in the first trimester [57]. The sensitivity of US tends to decrease with increasing gestational age, and osseous, retroperitoneal, and hollow viscus injury may be missed by US [3].

Hesitation over the perceived risk of radiation exposure should not delay the use of contrast-enhanced CT in the evaluation of the pregnant patient who sustains abdominal or pelvic trauma [1, 21, 23]. CT has important implications for clinical management, allowing for the rapid diagnosis of immediate life-threatening conditions and permitting appropriate patient triage [23]. Injury patterns in pregnant patients favor the abdomen and pelvis relative to other body regions, especially when compared with those of nonpregnant trauma patients, thought to be related to physiological and anatomical changes of pregnancy [23, 58]. Especially in the third trimester, the gravid uterus will displace the liver and spleen, making them prone to injury from overlying ribs [23, 58]. Solid organ injury is depicted as peripheral linear or wedge-shaped areas of hypoattenuation, indicating laceration or fracture. Physiological hydronephrosis of pregnancy may predispose the renal collecting systems to blunt or sheer injury, leading to calyceal rupture, and may be best visualized on delay scanning as spillage of contrast material from the collecting system [23]. Low-dose CT cystogram should be considered in the presence of pelvic fractures to exclude bladder injury, as the displaced urinary bladder is at the higher risk for injury in pregnancy. Pelvic and acetabular fractures are associated with high maternal and fetal mortality [23, 58] (Fig. 4.7). Placental injury is the most common pregnancy-related injury in the setting of blunt abdominal trauma, followed by uterine rupture and direct fetal injury [20, 23]. Placental abruption manifests as large confluent areas of hypoattenuation and hypoenhancement that may be retroplacental or extend through the entirety of the placental thickness [58, 59]. Hyperdense amniotic fluid may further suggest the diagnosis, indicating hemorrhage within the amniotic fluid [58]. However, the CT findings of placental abruption vary significantly and may be hard to detect, likely from lack of data available on the normal appearance of the placenta as well as pathology mimics (e.g., myometrial

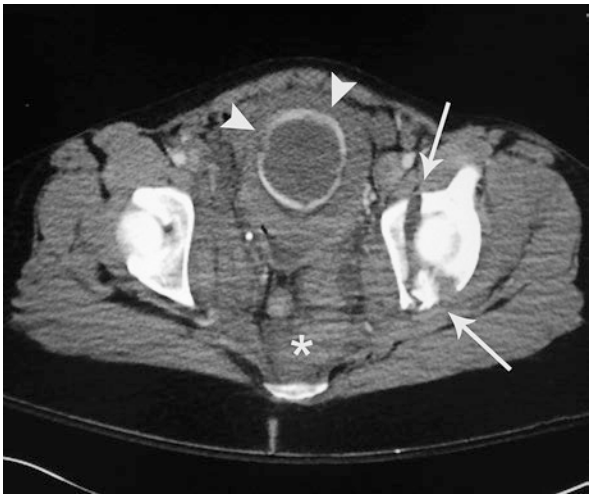

Fig. 4.7 CT of a pregnant trauma patient: 30 y/o pregnant patient at 30 weeks was an unrestrained driver in a high-speed MVC. Axial CT through the pelvis demonstrates a comminuted left acetabular fracture (*arrows*) and pelvic hematoma (*asterisk*). Partial visualization of fetal skull (*arrowheads*). Acute traumatic aortic injury of the thoracic aorta was identified in the chest (not shown). Intrauterine fetal demise was noted at time of arrival to the trauma bay. Upon delivery of the fetus, multiple fetal skull fractures were noted. The patient expired in the operating room

contraction) [59]. Uterine rupture manifests as decreased enhancement in the affected uterine wall extending though a variable thickness and rarely an empty uterus with a free-floating fetus within the maternal abdomen [58].

MR imaging is typically reserved for follow-up examinations after the patient has been clinically stabilized, as the length of the MR exam and difficulty in patient monitoring would place undue risk to the patient and fetus in the acute care setting [21, 23, 56].

Gynecological Causes of Abdominal Pain

Adnexal Masses

The increased utilization of routine obstetric ultrasound has resulted in the more common detection of adnexal masses during pregnancy. Etiologies are variable, ranging from the frequently encountered physiologic, hormonally influenced cyst to the rarely encountered malignant ovarian neoplasm. Most adnexal masses in pregnancy are asymptomatic and incidentally visualized on imaging. However, adnexal masses can be a source of acute pain in pregnancy, particularly in the first trimester [60, 61].

Ultrasound is the initial imaging modality of choice for the evaluation of pelvic pain in pregnancy and for characterization of pelvic masses [61, 62]. This characterization helps guide clinical management by determining those masses likely to

spontaneously regress with progression of pregnancy from those that place the patient at increased risk for future complications such as torsion or preterm labor or those that have features that raise concerns for malignancy [61].

Functional Cysts

The corpus luteum of pregnancy and other hormonally responsive cysts are the most commonly encountered adnexal masses of pregnancy. Although the majority of these physiological structures resolve by 14–16 weeks of gestation [60], they can be a source of pelvic pain. Symptoms typically are located on the ipsilateral side of the lesion and can be secondary to size (from compression of or by adjacent structures), internal hemorrhage, or rupture [61, 62]. In addition, as with any of the following adnexal masses, there is a predisposition for ovarian torsion leading to acute pelvic pain (particularly in lesions >5 cm), which will be discussed later [63].

Corpus Luteum

The physiological corpus luteum is responsible for the maintenance of early pregnancy until the development of the placenta and is a common cause of pain in the first trimester [60, 62]. Familiarity with the variable sonographic appearances of the corpus luteum is key; these cysts can be confused with an ectopic pregnancy or suspicious mass. The corpus luteum may appear as a simple cystic structure with variable wall thickness or as a complex cystic lesion [60]. When complex, the corpus luteum may appear as an isoechoic or hypoechoic solid-appearing structure due to wall thickening or internal hemorrhage [64]. The thickened wall is typically hypoechoic with pronounced peripheral vascularity noted on color or power Doppler producing a "ring of fire" appearance [60, 64]. This is not to be confused with the "ring of fire" seen in ectopic pregnancies (which often demonstrate hyperechoic walls), which will be discussed later. In the absence of hemorrhage, corpus lutea are centrally anechoic. In the presence of internal hemorrhage, internal debris is noted with the appearance dependent on the acuity and extent of bleeding and paralleling the internal appearance of other hemorrhagic cysts, discussed below [62]. In the setting of rupture, patients can present with acute onset pelvic pain with free fluid, either simple or containing internal echoes reflecting hemoperitoneum [62]. With corpus luteum rupture, the walls may appear partially collapsed.

Simple Cysts

Simple cysts are anechoic, rounded structures with a thin, smooth wall, and no internal septations or solid components. While most are commonly asymptomatic, when large (greater than 5 cm), simple cysts can produce symptoms due to compression and have a higher propensity to persist throughout pregnancy [61, 65]. Larger cysts should, therefore, be followed on serial ultrasounds. On MRI, simple cysts appear as round, circumscribed lesions with high signal on T2-weighted images and low to intermediate signal on T1-weighted images [25].

Hemorrhagic Cysts

Hemorrhagic cysts demonstrate a variable appearance depending on the duration and degree of internal blood products. However, classic patterns of internal hemorrhage include internal reticular echoes from fibrin strands that produce a lacy or fishnet appearance (not to be confused with thicker septations) or more solid appearing hypoechoic internal echoes, which can be diffuse or focal. Lack of internal blood flow as well as concave margins and angularity (seen with retracting clot) within these more solid appearing areas as well as increased through transmission help to distinguish internal hemorrhage from a true solid mass or solid mural nodularity [60, 64]. Evolution of the findings over serial ultrasounds also helps to confirm the diagnosis and exclude a more worrisome mass. Acutely, hemorrhagic cysts can be centrally hyperechoic relative to ovarian tissue or centrally heterogenous [60, 65]. On MRI, hemorrhagic cysts typically demonstrate high signal on T1-weighted images and variable signal on T2-weighted images [25].

Adnexal Masses Unique to Pregnancy

Hyperstimulated Ovaries and Ovarian Hyperstimulation Syndrome

Several entities involving the adnexa which are unique to pregnancy can be a source of pelvic pain and have a classic ultrasound appearance. Hyperstimulated ovaries can occasionally be seen in unassisted pregnancies but are more commonly observed in the setting of ovulation induction [60, 65]. Ultrasound shows enlarged bilateral ovaries with multiple predominantly peripherally located cysts of variable sizes (most commonly simple but can be complicated by hemorrhage) with thin intervening cyst walls appearing like echogenic intervening septa and echogenic ovarian stroma centrally producing a classic "spoke wheel" appearance [60, 66]. A potentially severe complication of ovarian induction which can be seen in early pregnancy is ovarian hyperstimulation syndrome (OHSS), which is associated with the above ovarian findings (often with massively enlarged ovaries > 12 cm in severe cases) in combination with fluid shift out of the intravascular space, visualized on US as ascites [66]. Pleural effusions can also be seen with more severe cases. The increased ovarian volumes significantly increase the risk of ovarian torsion, with an incidence of 7.5% in patients with OHSS [66]. These findings typically resolve over the course of pregnancy on serial ultrasounds. The appearance of hyperstimulated ovaries with apparent septations due to abutting thin cyst walls should not be confused with a multiseptate cystic ovarian neoplasm. Key distinguishing features include lack of solid components or mural nodules and visualization of central ovarian stroma [66].

MRI features of ovarian hyperstimulation parallel the ultrasound findings, with enlarged bilateral ovaries with multiple T1 hypointense and T2 hyperintense cysts seen in the characteristic peripheral distribution with ovarian stroma centrally. When cysts are complicated with hemorrhage, increased T1 signal and variable T2 signal are noted [66]. If ascites is present, it is most commonly simple, with T2 hyperintense, T1 hypointense-free fluid visualized.

Hyperreactio Luteinalis and Theca Lutein Cysts

In nonassisted reproduction, an abnormal, hypersensitivity of the ovary to circulating levels of hCG can lead to a similar but less pronounced appearance of hyperstimulated ovaries. This is referred to as hyperreactio luteinalis and can be seen in the setting of normal serum β-hCG levels or in elevated levels as seen with multiple gestations or fetal hydrops [60, 65]. This entity is more commonly observed in the 3rd trimester. A similar ultrasound appearance can also be seen with theca lutein cysts, which develop in the setting of gestational trophoblastic disease (molar pregnancies) in response to markedly elevated levels of serum β-hCG. Ultrasound will demonstrate enlarged ovaries with multiple prominent anechoic cysts [62, 65] (Fig. 4.8).

Endometriomas

Endometriomas are an infrequent cause of abdominal pain in pregnancy and account for approximately 4% of adnexal masses in pregnancy [67]. The classic ultrasound appearance of an endometrioma is that of a complex cyst with diffuse low-level or medium-level internal echoes (ground glass appearance) with no internal flow [64, 68] (Fig. 4.9). Depending on the stage of internal hemorrhage, a hemorrhagic cyst can sometimes demonstrate a similar appearance. Small echogenic foci in the cyst

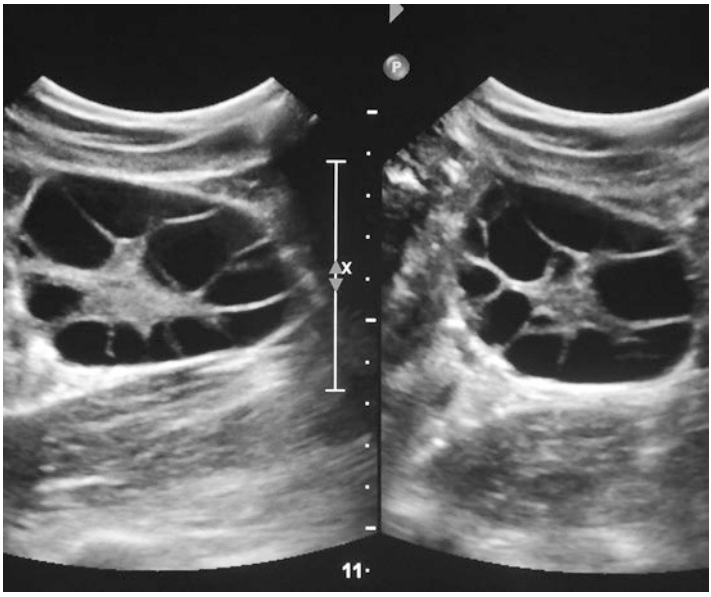

Fig. 4.8 US of theca lutein cysts: 33 y/o pregnant patient at 14 weeks' with partial molar pregnancy and β-hCG >200,000. Longitudinal and transverse gray scale images of the left ovary demonstrate ovarian enlargement with numerous anechoic cystic structures predominantly in the periphery with echogenic central ovarian stroma producing a "spoke wheel pattern". The ovary measured up to 7 cm

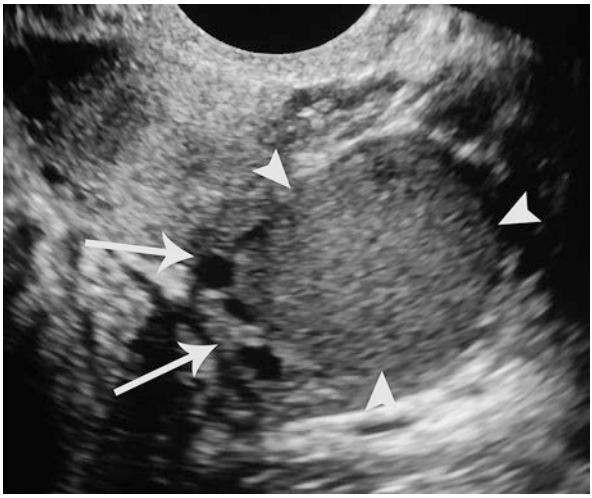

Fig. 4.9 US of an incidental endometrioma: 36 y/o pregnant patient at 5 weeks' presented with vaginal bleeding. Gray scale image of the left ovary demonstrates a hypoechoic cyst with homogenous low-level internal echoes classic of an endometrioma (*arrowheads*). See adjacent ovarian tissue with follicles (*arrows*)

walls thought to represent cholesterol crystals have also been described with endometriomas [64, 68].

On MRI, endometriomas classically demonstrate high signal on T1-weighted images and signal lower than simple fluid on T2-weighted images, which has been coined "T2 shading" [69]. Fat saturated T1-weighted sequences can help distinguish endometriomas (which will remain T1 hyperintense) from fat containing dermoid cysts (which will decrease in signal) [69].

Decidualization of an endometrioma during pregnancy is a recognized entity that can mimic ovarian neoplasm. In this process, mural nodules or papillary excrescences with vascularity develop in ectopic endometrial stroma in response to increased circulating progesterone, paralleling the response of the normal endometrium as it becomes the decidual lining of pregnancy. While these findings can appear worrisome on ultrasound and MRI and overlap with malignancy, a key feature described on MRI can help distinguish this entity. The nodules of a decidualized endometrioma have been described to demonstrate similar T2 signal hyperintensity to that of the decidualized endometrium [68–70].

Ovarian Neoplasms

Mature Cystic Teratoma

The most common benign ovarian neoplasm in pregnancy is the mature cystic teratoma or dermoid cyst [25]. Although often asymptomatic and diagnosed incidentally on a routine screening ultrasound, these, like other ovarian masses, predispose the ovary to torsion and can be a source of acute abdominal pain. Dermoid cysts have a complex appearance on ultrasound, but key characteristic findings help confirm the diagnosis. Hyperechoic areas with pronounced posterior shadowing result in a "tip of the iceberg sign"; a hyperechoic nodule in a background of complicated

cyst described as the Rokitansky nodule or "dermoid plug," and multiple hyperechoic lines and dots, so called "dermoid mesh" or "dot-dash" appearance (which represents floating hair in sebum) are classic features. Additional findings are calcifications (often due to bone or teeth) and fluid-fluid levels with hyperechoic floating fat and more hypoechoic dependent echoes [60, 64, 71]. Two or more of these features allow for the diagnosis of a dermoid cyst with a high degree of accuracy [60]. In indeterminate lesions, MRI can be utilized to evaluate for the presence of fat. The sebaceous components of dermoid cysts demonstrate high signal on T1-weighted images with signal dropout on fat-saturated sequences [71] (Fig. 4.10). Despite its specificity for detecting fat and calcification within dermoid cysts, which can confirm the diagnosis, CT is typically avoided in pregnancy due to the ionizing radiation.

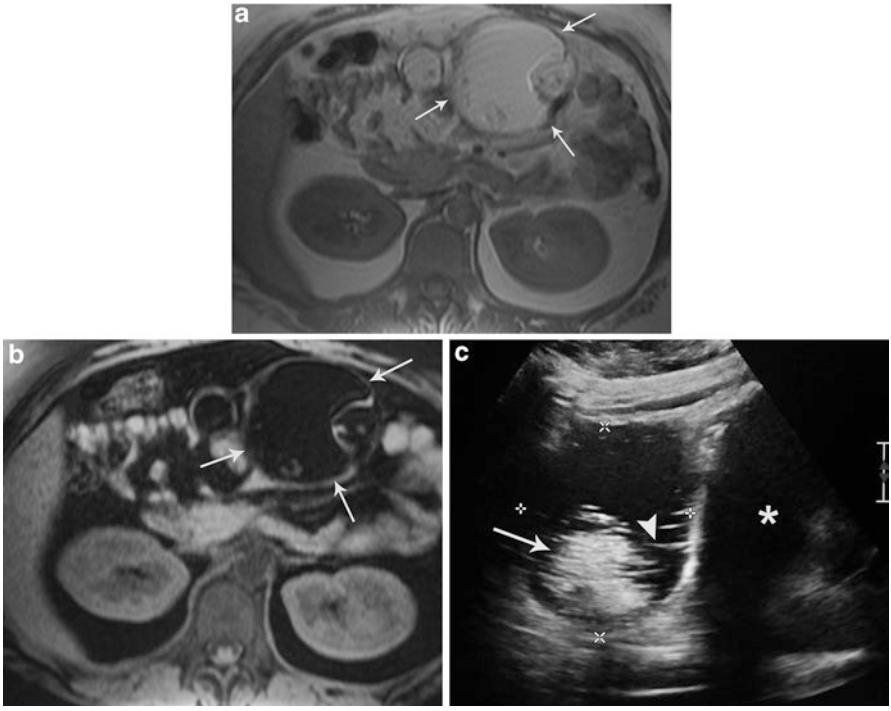

Fig. 4.10 MRI and US of a dermoid cyst. 35 y/o pregnant patient at 25 weeks' with an incidental dermoid cyst. (**a**) T1-weighted axial MRI of the upper abdomen superior to a gravid uterus demonstrates a rounded, lobulated predominantly T1 hyperintense mass (*arrows*). (**b**) Fat-saturated T1-weighted image at the same level demonstrates signal drop out (*dark signal*) within a majority of the mass (*arrows*), compatible with internal fat. (**c**) Gray scale US of the upper abdomen superior to the uterus containing IUP (*asterisk*) demonstrates a complex mass (between calipers) with multiple hyperechoic lines and dots suggestive of dermoid mesh (*arrowhead*) and rounded echogenic component suggestive of Rokitansky nodule (*arrow*) classic of a dermoid cyst. The ovary was displaced superiorly in the abdomen by the gravid uterus

Epithelial Neoplasms

Epithelial neoplasms include benign cystadenomas, tumors of low malignant potential, and malignant cystadenocarcinomas. As mentioned with other masses, these entities are often detected incidentally on routine imaging but increase the risk of torsion by acting as a lead point and can present in the acute setting. In addition, advanced ovarian malignancy may be symptomatic due to size or metastases. After teratomas, cystadenomas (serous and mucinous), are the next most common benign ovarian neoplasms of pregnancy [25, 67]. Serous cystadenomas are characteristically unilocular, simple appearing cystic structures with or without thin septations which persist or grow throughout pregnancy and are typically larger than functional cysts [60]. Mucinous cystadenomas can be indistinguishable on ultrasound from serous cystadenomas; however, more commonly contain multiple septations and low-level internal echoes [60].

An estimated 1% of adnexal masses detected during pregnancy are malignant [25]. Features that increase the suspicion for malignancy include solid components with vascular flow, papillary projections (> 3 mm), thick, irregular walls, and multiple thick septations (> 2–3 mm) with vascular flow [60, 64] (Fig. 4.11). Ascites is an indirect finding seen with malignancy, usually as the result of peritoneal metastasis [60, 64] but by itself is a nonspecific finding. MRI can be used as an adjunct in indeterminate masses on US, or for further staging. MRI features of malignant masses reflect the US features, including solid components, mural nodules, papillary excrescences, and thick septations. Because gadolinium is avoided in pregnancy, evaluation for internal enhancement is not possible. MRI also allows for additional imaging information, including evaluation for adenopathy, peritoneal or omental implants, ascites, and distant metastases [72].

Other Ovarian Neoplasms

Other ovarian neoplasms such as sex cord stromal tumors are rare, but if detected by ultrasound, can be further characterized with MRI [60].

Limited Role of CT

In general, CT is of limited benefit in the characterization of adnexal masses [64], particularly during pregnancy due to the risk of ionizing radiation. There is much overlap in the CT appearances of benign ovarian masses, and ultrasound and MRI are far superior at demonstrating the internal characteristics of the masses. Macroscopic fat and calcifications can be easily demonstrated on CT to reliably diagnose a dermoid cyst. However, when these features are absent, CT is of little benefit in distinguishing dermoid cysts from other lesions [64]. Although MRI is preferred in the setting of pregnancy, CT can be useful in the staging of malignancy and for evaluation for metastatic disease if MRI is inconclusive.

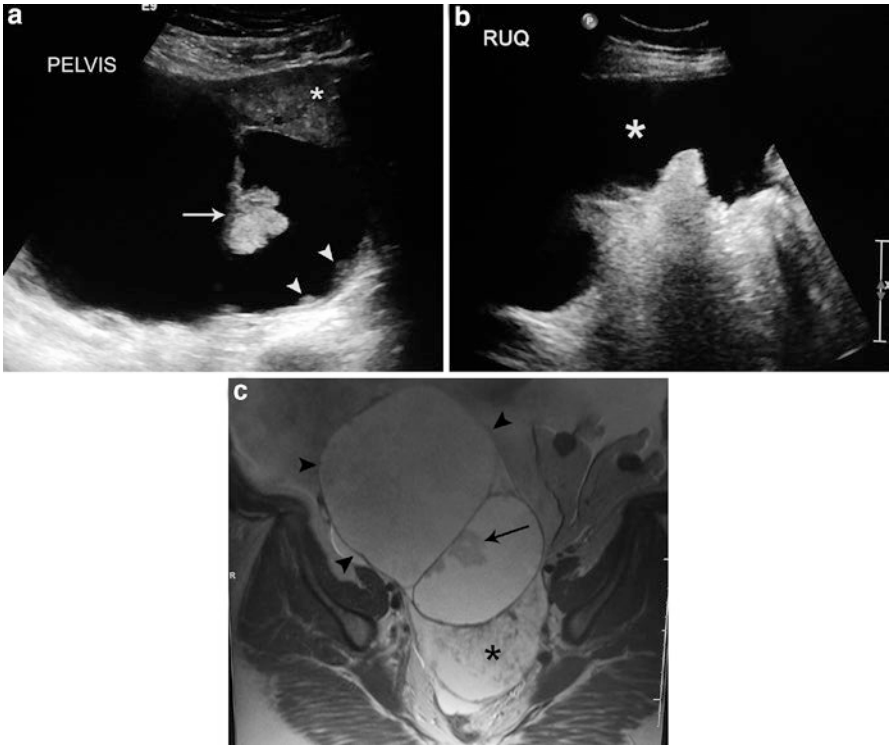

Fig. 4.11 US and MRI of ovarian cancer. 29 y/o pregnant patient presented at 7 weeks' with left-sided pelvic pain. (**a**) Gray scale image of the pelvis demonstrates a large complex cystic mass with large central solid nodule (*arrow*) along a septation, small mural nodules along the periphery (*arrowheads*) and solid component (*asterisk*). Internal blood flow was present in the solid components (not shown). (**b**) Gray scale image of the right upper quadrant shows moderate abdominal ascites (*asterisk*). (**c**) Coronal oblique T2-weighted MR mage of the pelvis demonstrates a large complex cystic mass (*arrowheads*) with solid central mural nodule along a septation (*arrow*) and heterogenous solid component inferiorly (*asterisk*). Ascites is also present. The patient underwent exploratory laparotomy with debulking surgery at 10 weeks due to increasing distension and shortness of air. Seven liters of ascites was found along with a 15 cm right ovarian mass with papillary frond like projections and diffuse carcinomatosis. Pathology revealed high-grade papillary serous carcinoma. The patient received chemotherapy during pregnancy and delivered a viable neonate at 39 weeks

Ovarian Torsion

Ovarian or adnexal torsion has an increased incidence in pregnancy, estimated at 1:1800 [67] and most commonly occurs during the mid to late 1st trimester [62]. The increased incidence is thought to be due to increased laxity of supporting ligamentous structures, the increased movement of the ovaries and adnexa during rapid enlargement of the uterus, and the increased incidence of masses during pregnancy which can serve as pathological lead points [60, 61, 73]. An estimated 7% of

ovarian masses in pregnancy are complicated by torsion [25, 61]. However, torsion can still occur in the absence of an underlying ovarian mass, in which case it more commonly occurs on the right [61].

Torsion results from a twisting of either the ovary (and/or fallopian tube) and its vascular pedicle in its suspensory ligament, first compromising low-pressure venous outflow, then later, the higher pressure arterial inflow. This leads to thrombosis, progressive ischemia, and eventual hemorrhagic infarction [73]. Ultrasound is the imaging modality of choice to evaluate suspected ovarian torsion. Characteristic gray scale findings include a unilaterally enlarged ovary, abnormally positioned ovary (often midline or on the contralateral side), multiple peripherally displaced follicles, and heterogenous, edematous central ovarian stroma [60, 73]. A coexisting dominant cyst or mass may be seen, which serves as the lead point, but is not a necessity. A specific sign, when seen, is the twisted vascular pedicle adjacent to the ovary resulting in a "whirlpool sign" which can be detected using a combination of gray scale and color Doppler [73].

Doppler findings in torsion are variable and depend on the degree or extent or duration of torsion. The absence of blood flow to an enlarged ovary on the ipsilateral side of pain is the most specific Doppler finding on ultrasound. However, a critical point to note is that the presence of blood flow (either arterial or venous) does *not* exclude the diagnosis of torsion, and the presence of ovarian blood flow in the setting of a classic clinical history and the aforementioned gray scale findings should not dissuade one from the diagnosis. The ovary has a dual blood supply, receiving arterial blood flow from ovarian and uterine branches, which can preserve arterial flow. Torsion can be incomplete or intermittent, which can also preserve blood flow [60, 65]. Free pelvic fluid with echoes suggesting hemoperitoneum may be observed as a secondary finding.

MRI features of ovarian torsion parallel those of US and are best visualized on T2 weighted as increased ovarian volume with increased T2 signal within central edematous ovarian stroma and multiple peripherally located T2 hyperintense follicles. With progressive torsion and internal hemorrhage, increased signal on T1-weighted images can be seen. A T1 hyperintense rim has been described as a finding associated with ovarian torsion relating to subacute hemorrhage [73]. A dominant mass acting as lead point may or may not be seen. Use of multiplanar reformatted images can increase the detection of a twisted vascular pedicle and associated thickened fallopian tube.

CT is typically not indicated for the diagnosis of torsion given the superiority of US and MRI; however, similar findings to those previously described can be seen on CT. The most common finding on CT is a unilaterally enlarged ovary, sometimes in an atypical location. A twisted vascular pedicle, peripherally located follicles, and areas of nonenhancement are better seen in the presence of IV contrast. However, like Doppler, the presence of ovarian enhancement does not exclude the diagnosis of torsion. Heterogenous increased attenuation can be seen in the setting of internal hemorrhage and an underlying mass may or may not be detected [73].

Massive Ovarian Edema

Massive ovarian edema is a rare condition that results from vascular congestion of the ovary, thought to be due to intermittent or partial ovarian torsion or compression of the vascular pedicle between the gravid uterus and adjacent stationary pelvic structures. This most commonly occurs in the 2nd and 3rd trimesters. Venous and lymphatic obstruction causes progressive accumulation of fluid within ovarian stroma resulting in a massively enlarged, edematous ovary with peripherally displaced follicles [74, 75]. This is usually unilateral. Imaging findings are often indistinguishable from torsion. Ultrasound demonstrates an enlarged ovary with peripherally located follicles with some internal blood flow [74]. MRI demonstrates asymmetric ovarian enlargement and a classic "teardrop" configuration, stromal T2 hyperintensity, peripheral T2 bright follicles, and variable T2 and T1 hyperintensity depending on the presence of hemorrhagic congestion [75].

Leiomyomas

Leiomyomas (also known as fibroids) are detected in 1–4% of pregnancies [65, 67] and are considered the most common solid masses in pregnancy [65]. Fibroids can be intramural, submucosal, and subserosal (in which case they may be pedunculated and mimic an ovarian mass). Fibroids can produce acute pain due to internal degeneration, hemorrhagic infarction, or torsion (if pedunculated).

Fibroids can have a variable sonographic appearance but often appear as round, heterogenous hypoechoic masses. Uterine contractions can mimic a fibroid but can be distinguished by the lack of persistence during the scan. During pregnancy, fibroids can enlarge, decrease in size, or remain stable [60, 61, 67]. When fibroids enlarge during pregnancy as a result of hormonal influence, they can outgrow their blood supply and undergo hemorrhagic infarction, so called "red degeneration [62]." Ultrasonographically, this is manifested as internal cystic spaces or heterogenous echogenicity within fibroids [61, 65] (Fig. 4.12). Pain elicited with the transducer directly over the degenerating fibroid can confirm this as the etiology of the patient's symptoms [61].

A torsioned, pedunculated fibroid can demonstrate a similar sonographic appearance and can also be "probed" by the transducer to confirm this is the cause of the patient's pain. A variable internal flow pattern can be noted with Doppler interrogation due to the twisted stalk [60], including the absence of flow. Detection of a connecting stalk of the fibroid to the uterus should be sought to exclude a solid adnexal mass. When not able to be visualized, MRI can be helpful to confidently distinguish a pedunculated fibroid from adnexal mass [65]. On MRI, fibroids with red degeneration demonstrate peripheral or diffuse increased T1 signal and a variable appearance on T2-weighted images, often with a low T2 signal rim [61].

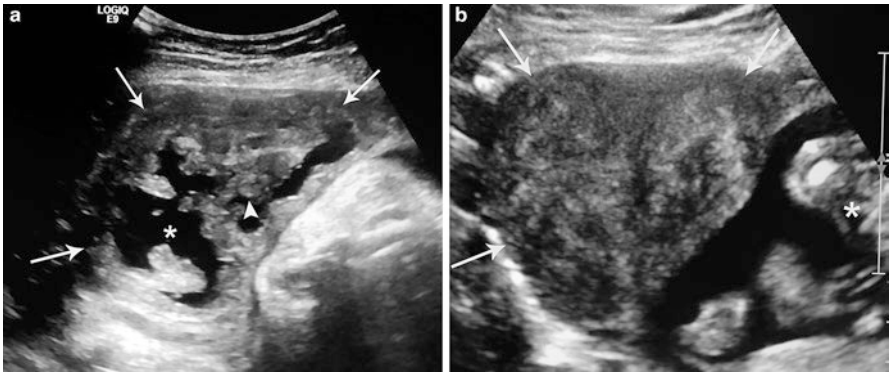

Fig. 4.12 US of cystic degeneration of a fibroid: 29 y/o pregnant patient at 35 weeks' presenting at follow-up US. (**a**) Gray scale image through the right lower uterus demonstrates a lobulated mass (*arrows*) compatible with fibroid with internal cystic (*asterisk*) and hypoechoic solid appearing areas (*arrowhead*) compatible with fibroid with cystic degeneration. (**b**) Gray scale image of the same area 3 months prior demonstrating the fibroid (*arrows*) was previously solid throughout with heterogenous echogenicity. Adjacent IUP (*asterisk*)

Pelvic Inflammatory Disease

Patients with pelvic inflammatory disease (PID) often present with fever and nonspecific abdominal or pelvic pain. Ultrasound is the diagnostic imaging modality of choice for the evaluation of suspected PID. Findings of early PID are difficult to detect on US but include the subtle findings of increased echogenicity of peritoneal fat surrounding the uterus and adnexa as well as indistinctness of the uterine serosal surface [76]. More advanced PID is more easily depicted on US. Inflamed fallopian tubes appear as dilated, fluid-filled, tubular structures with thickened, hyperemic walls, and thickened endosalpingeal folds (cogwheel sign). Often, the internal fluid is echogenic, owing to pyosalpinx. If inflammation extends beyond the fallopian tube, but a distinct ovary is still visualized separately, a tubo-ovarian complex is described. If the normal ovarian architecture is no longer visualized, then the term tubo-ovarian abscess (TOA) is used [60, 76]. TOAs can have a variable appearance but often appear as heterogeneous, complex adnexal masses with hypervascularity, unilocular or multilocular cystic spaces, and variable solid appearing areas [64].

In the nonpregnant patient, CT can be useful as an adjunct to US to document the extent of disease and involvement of any adjacent structures. However, MRI is preferred with pregnancy to avoid ionizing radiation. MRI findings in PID parallel the US findings, with dilated, tubular structures in the adnexa with thickened walls reflecting pyosalpinx. An ill-defined, heterogeneous adnexal mass with thick, irregular walls and variable signal fluid components suggest TOA. The signal of the fluid in TOA can be variable, ranging from low to intermediate to high signal on T1-weighted imaging and heterogenous or high on T2-weighted imaging [77]. Diffusion-weighted imaging (DWI) can improve the accuracy of MRI detection of

PID. On DWI, abscess cavities and pyosalpinx can demonstrate high signal and corresponding low apparent diffusion coefficient (ADC) values [78].

Obstetric Causes of Abdominal Pain

First Trimester Causes

Common causes of pregnancy-related abdominal and pelvic pain in the first trimester include early pregnancy failure and ectopic pregnancy. However, early viable pregnancies can also present with mild symptoms including crampy abdominal pain and can be concerning enough for a gravida to seek medical attention [62]. Recognition of the early signs of an intrauterine pregnancy is important to be able to distinguish a normal early intrauterine pregnancy (IUP) from abnormal findings.

Early Normal Pregnancy

Ultrasound is the diagnostic imaging modality of choice for pregnant patients who present with acute pelvic pain. Evidence of an IUP can be visualized as early as 4–4.5 weeks' on transvaginal (TV) US. The earliest ultrasound finding is the visualization of the gestational sac (GS), and an "intradecidual sac sign" helps distinguish the GS from potential mimickers. The intradecidual sac sign occurs with visualization of a small, discrete fluid collection with echogenic rim eccentrically positioned in the endometrium (renamed the decidua during pregnancy) [62, 79] (Fig. 4.13). This structure should not change in appearance during the scan and should be visualized in two planes to document precise location embedded within the endometrium. This should not be confused with a pseudogestational sac, which is anechoic or hypoechoic fluid most often representing blood products, located centrally within the endometrial cavity – a finding associated with approximately 10% of ectopic pregnancies [62, 79, 80]. This endometrial fluid of a pseudogestational sac can also be noted to move during real-time scanning. In addition, the intradecidual sac sign should be distinguished from decidual cysts – small, thin-walled simple appearing cysts in the endometrium, typically located at the endometrial–myometrial junction (Fig. 4.14). Decidual cysts are often multiple and occur in both ectopic pregnancies and early IUPs. The lack of an echogenic rim helps distinguish these from an early GS. However, at times, differentiation is not possible and short-term follow-up is advised.

Around 5 weeks' gestation, a "double decidual sac sign" is briefly seen as the GS is surrounded by the decidua capsularis and decidua parietalis with a small intervening crescentic focus of fluid sometimes visualized in the endometrial cavity [81]. A secondary yolk sac (YS) is visualized within the GS at approximately 5.5 weeks' and confirms the presence of an IUP, although viability cannot be assessed until an embryo is visualized at around 6 weeks' gestation [79]. Cardiac activity is observed shortly after formation of the embryo, also at approximately 6 weeks', and can be detected in embryos as small as 1–2 mm [81].

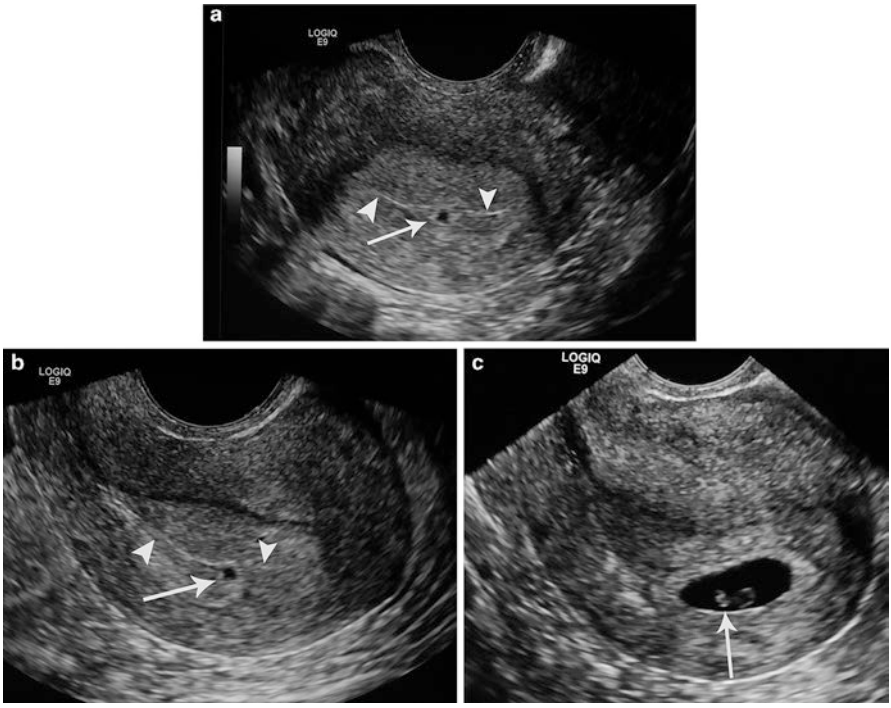

Fig. 4.13 US of intradecidual sac sign: US of a 25 y/o pregnant patient with cramping and pink discharge and β-hCG of 471. Transverse (**a**) and longitudinal (**b**) gray scale images through the uterus demonstrate a tiny sac-like structure with echogenic rim (*arrows*) eccentrically positioned in the endometrium compatible with the intradecidual sac sign. The adjacent echogenic linear interface of the endometrial walls is visualized (*arrowheads*). (**c**) Follow-up US performed 2 weeks later demonstrates a 6 week IUP with gestational sac, yolk sac, and embryo (*arrow*)

Early Pregnancy Failure

Approximately 12% of first trimester pregnancies result in spontaneous abortion [82]. Most commonly, patients present with pain and vaginal bleeding and are evaluated with ultrasound to determine the presence and viability of an IUP as well as features suggestive of active spontaneous abortion or early pregnancy failure. Recently, generous thresholds for absolute criteria for diagnosing nonviable pregnancy have been recommended and are being adopted to prevent any potentially dreadful surgical or medical action from being taken on a potentially viable early pregnancy [83]. The goal in the diagnosis of nonviable pregnancies is a specificity of as close to 100% as possible, to prevent any false positive results (or a pregnancy that is potentially viable deemed nonviable) [83]. The higher measurements are in part to account for interobserver variability in measurements and differing ultrasound equipment. Based on these guidelines, findings diagnostic of pregnancy failure include a crown-rump length (CRL) of an embryo ≥7 mm and no heartbeat, a mean sac diameter of the GS ≥ 25 mm and no embryo, as well as follow-up ultrasound demonstrating no embryo with heartbeat ≥2 weeks after a scan that showed

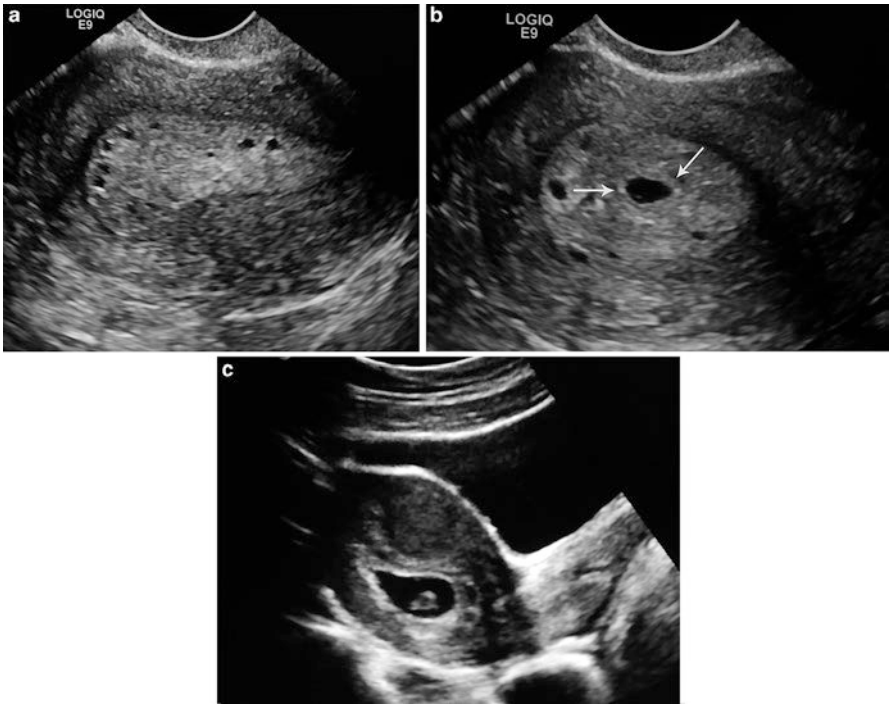

Fig. 4.14 US of decidual cysts and early gestational sac: 19 y/o pregnant patient with quantitative β-hCG of 2967 and abdominal pain. (**a**) Longitudinal gray scale image through the uterus demonstrates a thickened endometrium with numerous tiny thin-walled anechoic foci suggestive of decidual cysts predominantly in the periphery of the endometrium. (**b**) Transverse gray scale image through the uterus demonstrate a larger dominant cystic structure with echogenic rim (*arrows*) suspicious for early gestational sac with surrounding decidual reaction. No yolk sac or embryo was seen, expected given mean sac diameter of 5 mm. (**c**) Follow-up US 18 days later shows an early IUP. Decidual cysts can be seen with early intrauterine pregnancy, early pregnancy failure or ectopic pregnancy

a GS without a YS or ≥11 days after a scan that showed a GS with a YS. Additional features suspicious for but not diagnostic of early pregnancy failure include an enlarged YS (> 7 mm), small GS in relation to the embryo (< 5 mm difference between GS and CRL), and CRL < 7 mm with no heartbeat, among others [83]. These measurements are all based on a TV exam. Ultrasounds with findings suspicious for early pregnancy failure should have short-term ultrasound follow-up [81].

Ectopic Pregnancy

Ectopic pregnancy is estimated to occur in approximately 2% of all pregnancies [79]. However, the incidence is even higher with the use of assisted reproductive technology (ART), which is becoming increasingly utilized with greater than 1% of

all births now involving ART [66]. Risk factors for ectopic pregnancy include a history of previous pelvic inflammatory disease or sexually transmitted disease, previous personal history of ectopic pregnancy, previous tubal surgery, endometriosis, and ART, among others [61, 80]. Patients often present with pelvic pain and vaginal bleeding, and ultrasound is the first-line imaging modality to evaluate a suspected ectopic pregnancy. Timely diagnosis is crucial as ectopic pregnancy remains the leading cause of obstetric related death in the first trimester [80].

Serum β-hCG levels are helpful in the final interpretation of the ultrasound exam and for follow-up recommendations; however, ultrasound scanning should not be delayed in a patient suspected of having an ectopic pregnancy to await the results. A delay in scanning could be catastrophic in the setting of a ruptured ectopic pregnancy. An intrauterine GS is usually able to be visualized with a β-hCG of 1000–2000 or greater [82]. The β-hCG levels in ectopic pregnancies can be highly variable and are often lower (less than 1000) [83]. Therefore, a certain β-hCG level should never preclude an ultrasound exam in the setting of a positive pregnancy test and clinical suspicion of ectopic pregnancy [83]. On the other hand, it is also extremely important to not "overcall" the diagnosis of ectopic pregnancy based solely on discriminatory levels, as this would lead to a catastrophic early termination of a potentially viable but occult IUP. While higher β-hCG levels and an empty uterus increase the likelihood of an ectopic pregnancy, at a β-hCG level of >3000, there is still a 0.5% chance of a viable IUP [81].

Transabdominal ultrasound exam should be performed first for an initial evaluation of the uterus and adnexa and to evaluate for the presence of free fluid. Rarely, a transabdominally detected ectopic pregnancy may not be visualized on TV exam if obscured by leiomyomas or other pelvic masses [79]. In addition, if free fluid is detected in the pelvis, the upper abdomen (particularly Morrison's pouch between the liver and right kidney) should be evaluated to document the extent of free fluid. In the vast majority of cases, a TV scan will also be required for better visualization and characterization of the uterus and adnexa. In the presence of a large amount of free fluid suggestive of hemoperitoneum, the ultrasound exam should be expedited to facilitate rapid patient treatment.

Tubal Ectopic Pregnancy

Approximately 95% of ectopic pregnancies occur within the fallopian tube with the remaining rare sites accounting for less than 5% of ectopic pregnancies [84]. The most common ultrasound finding in tubal ectopic pregnancy is an adnexal mass separate from the ovary. The mass can be of variable sonographic appearance, ranging from a sac-like structure to an amorphous complex solid and cystic mass, commonly seen with rupture or surrounding tubal hemorrhage (Fig. 4.15). The "tubal ring sign" manifests as an a sac-like structure in the adnexa representing the GS with surrounding echogenic rim and often demonstrates a "ring of fire" pattern of pronounced peripheral vascularity on color or power Doppler [61, 79, 82] (Fig. 4.16). Specificity of ectopic pregnancy increases with the visualization of an internal YS or embryo. When an extrauterine live embryo is detected in the adnexa, diagnosis of an ectopic pregnancy is made with certainty. A thorough evaluation of the uterus for

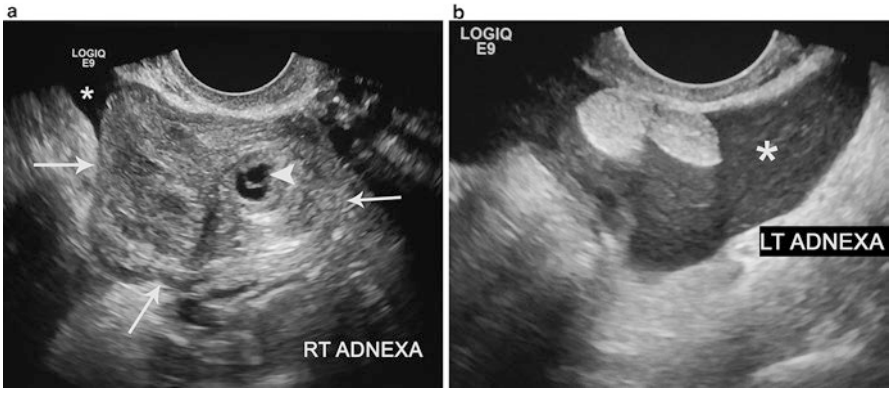

Fig. 4.15 US of tubal ectopic pregnancy: US of a 25 y/o pregnant patient with right-sided abdominal pain and quantitative β-hCG of 2757. (**a**) Gray scale image of the right adnexa demonstrates a large amorphous mass (*arrows*) with small central sac-like structure containing yolk sac (*arrowhead*). Tiny embyro with heartbeat was also present (not shown). Small amount of adjacent free fluid present (*asterisk*). (**b**) Gray scale image of the left adnexa demonstrates complex-free pelvic fluid (*asterisk*) compatible with hemoperitoneum. Surgery confirmed right tubal ectopic pregnancy with swollen tube and adherent clot adjacent to the tube

coexisting IUP should be performed to exclude the rare heterotopic pregnancy (discussed later) [61, 82] (Fig. 4.17). Intra-ovarian ectopics are rare. The mass must be demonstrated to be separate from the ovary, thus, increasing specificity. Gentle pressure applied on the TV probe can confirm an extra-ovarian location of the mass by demonstrating movement of the mass separate from the ovary [80]. The size of the mass should be documented as this has implications for management. The presence of complex-free fluid (suggesting hemoperitoneum) in the setting of a positive pregnancy test and no visualized IUP increases the likelihood of ectopic pregnancy, even when an adnexal mass is not visualized [80]. However, hemoperitoneum alone is nonspecific and can be seen with a ruptured hemorrhagic cyst.

Up to 12–35% of ectopic pregnancies may not manifest as an adnexal mass on ultrasound, and in these cases, the diagnosis cannot be excluded by imaging [66, 80]. In these situations, if the patient is hemodynamically stable, follow-up of serial β–hCG levels (to evaluate for appropriate or inappropriate doubling time) and short-term follow-up US are indicated until the location of pregnancy is confirmed. This scenario (in which no IUP is seen and the remaining pelvic ultrasound is normal) has been recently termed "pregnancy of unknown location" to emphasize that the differential considerations include both IUP and ectopic pregnancy [81].

The endometrium can have a variable appearance in the setting of ectopic pregnancy. A "pseudogestational sac" can be seen in up to 10% of ectopic pregnancies as anechoic or hypoechoic fluid centrally positioned in the endometrial cavity (as opposed to the eccentric location of a GS). A trilaminar appearance of the endometrium can also be visualized, which is typically seen in the late proliferative phase of the menstrual cycle as opposed to the usual hyperechoic appearance of

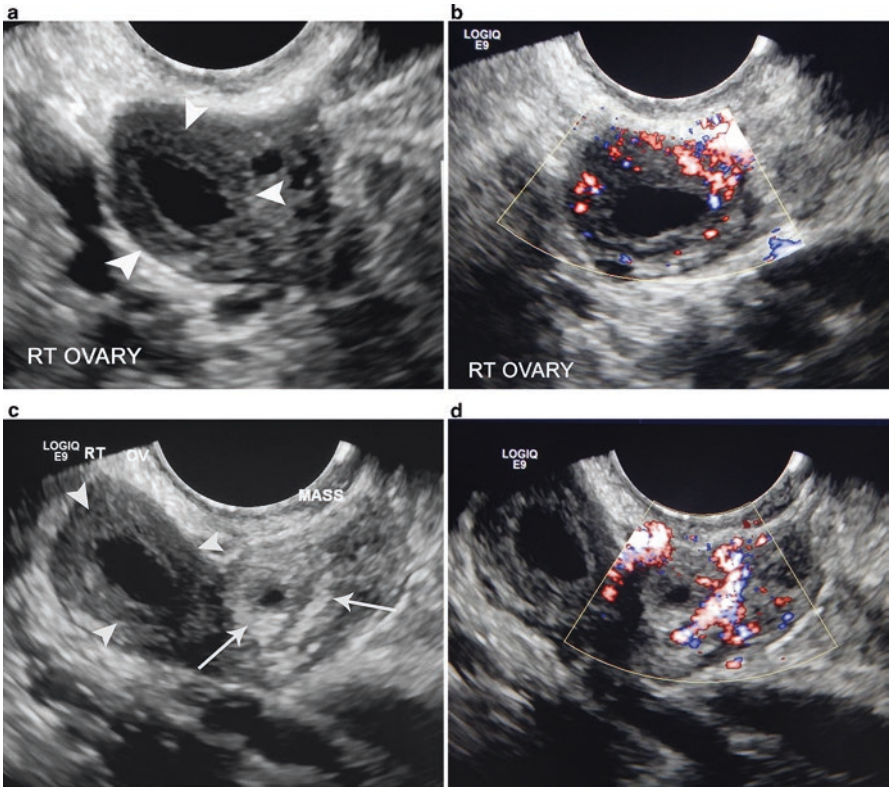

Fig. 4.16 US of a corpus luteum and tubal ectopic pregnancy: US of a 30 y/o pregnant patient with quantitative β-hCG of 266 with cramping and vaginal bleeding. (**a**) Gray scale image of the right ovary demonstrates a thick-walled cystic structure with hypoechoic wall (*arrows*) compatible with typical appearance of a corpus luteum. (**b**) Color Doppler demonstrates pronounced peripheral flow producing a so-called "ring of fire" pattern. (**c**) Gray scale image of the right adnexa demonstrates an echogenic thick walled cystic structure compatible with "tubal ring sign" (*arrows*) in the right adnexa adjacent to and separate from the right ovary. Contrast the echogenic wall of the tubal ectopic with the hypoechoic wall of the corpus luteum (*arrowheads*). (**d**) Color Doppler demonstrates significant peripheral vascularity in a "ring of fire" pattern

pregnancy. Decidual cysts or small, thin-walled cystic foci can also be seen. However, these can be present in both normal and ectopic pregnancies [80].

Less Frequent Sites of Ectopic Pregnancy

Less common sites of ectopic pregnancy account for <5% of ectopic pregnancies but can have very strong clinical implications, with increased maternal morbidity and mortality [80].

Interstitial Ectopic Pregnancy

Interstitial ectopic pregnancies, estimated at 2–4% of ectopic pregnancies, occur in the interstitial or intramyometrial portion of the fallopian tube. Due to the proximity

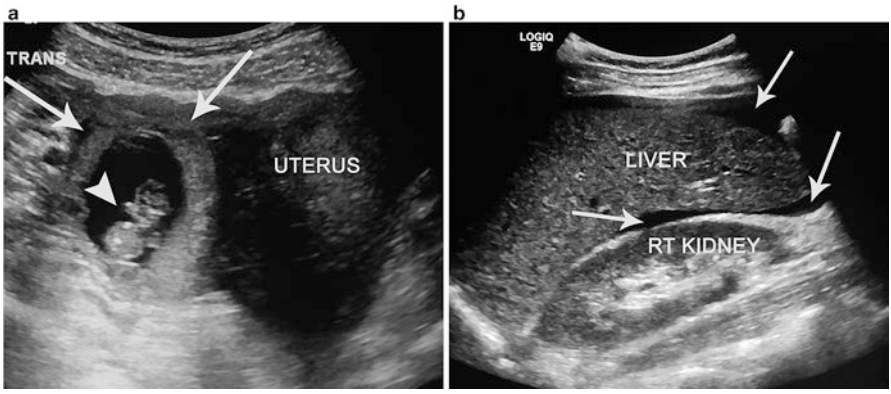

Fig. 4.17 US of living right adnexal ectopic pregnancy: 33 y/o pregnant patient presented at 9 weeks' for a routine dating ultrasound. (**a**) Gray scale transverse image through the superior uterus and right adnexa demonstrate an extrauterine right adnexal pregnancy (*arrows*) with embryo (*arrowhead*). Embryonic heart beat was present (not shown). (**b**) Gray scale image of Morrison's pouch in the RUQ demonstrates free fluid (*arrows*) compatible with large volume hemoperitoneum. 1500 ml hemoperitoneum was noted at time of surgery

of the implantation site to prominent vasculature, massive hemorrhage can occur with interstitial ectopic rupture leading to increased maternal mortality of up to 15 times that of tubal ectopics [84]. The term cornual ectopic pregnancy has been used interchangeably to describe this entity. However, cornual pregnancy more accurately describes pregnancy occurring in the horn of a bicornuate or unicornuate uterus. These gestations are located in the endometrial cavity, albeit in an ectopic location.

Ultrasound findings in interstitial ectopic pregnancy include a far high and lateral location of the GS within the uterine fundus surrounded by a thin rim of myometrium measuring <5 mm [79, 84] (Fig. 4.18). An "interstitial line sign" refers to visualization a thin echogenic line extending from the lateral endometrial cavity through the myometrium to the GS, which represents visualization of the interstitial portion of the fallopian tube. Bulging of the outer lateral fundal uterine contour can also be seen [84].

Cervical Ectopic Pregnancy

Cervical ectopic pregnancies account for less than 1% of ectopics. They are defined by implantation within the cervix below the internal OS. Gray scale ultrasound findings include a GS with or without embryo within the cervix. Doppler interrogation often demonstrates peritrophoblastic blood flow, but flow can be variable. Related to the expansion and enlargement of the cervix, the uterus may take on an hourglass or figure-of-eight configuration [66]. The main differential diagnosis is a spontaneous abortion in progress, in which case a sac can also be seen in the endocervical canal. However, the sac is often more irregular in a spontaneous abortion compared with the rounded sac of a cervical ectopic and peripheral flow is usually absent due

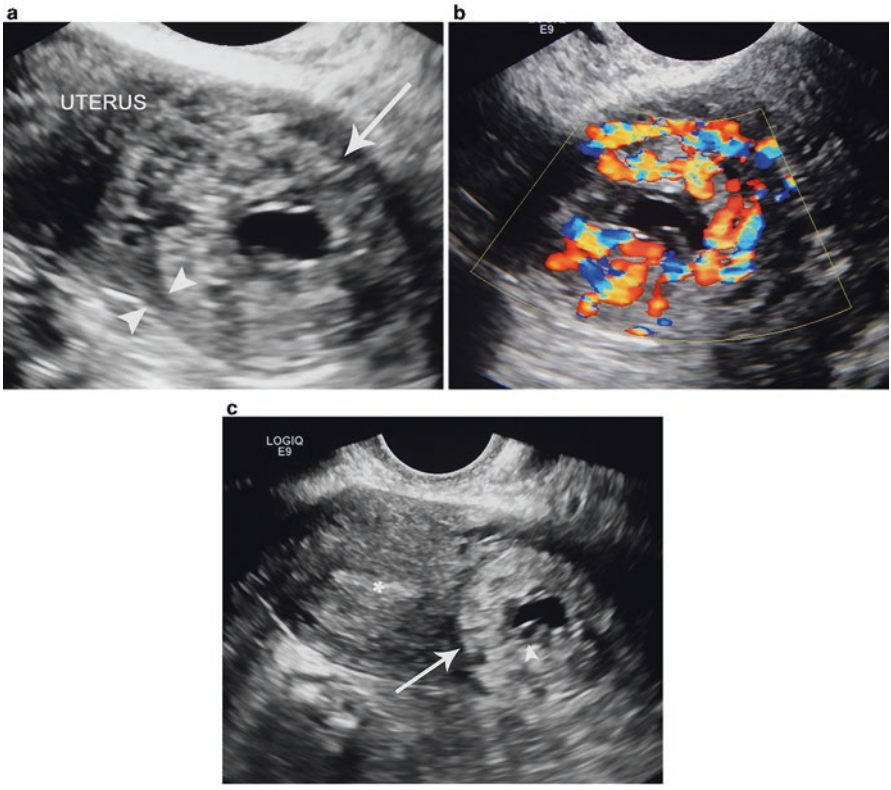

Fig. 4.18 US of interstitial ectopic pregnancy: US of a 38 y/o pregnant patient with lower pelvic pain and spotting with β-hCG of 16,060. (**a**) Gray scale image of the left superior uterus demonstrates a very high and laterally located sac-like structure with thick echogenic rim (*arrow*). Only a thin rim of surrounding myometrium surrounds the sac measuring 3 mm (*arrowheads*). (**b**) Image with Color Doppler demonstrates marked peripheral vascularity compatible with peritrophoblastic flow. (**c**) Additional transverse image through the superior uterus demonstrates the endometrium (*asterisk*) separate from the gestational sac (*arrow*) which contains a yolk sac (*arrowhead*). Embryo with heartbeat was also present (not shown). Interstitial ectopic pregnancy was confirmed at surgery. Resection of the ectopic and cornu of the uterus was performed

to detachment from the site of implantation [84]. Another potentially helpful distinguishing feature is the mobility of an abortion in progress which can occasionally be elicited with gentle pressure applied with the TV probe, distinguishing it from the nonmobile, fixed cervical ectopic. An open cervix with blood products in the endometrial cavity can also be seen with miscarriage [84]. If the diagnosis is unclear and the patient is hemodynamically stable, a short-term follow-up US in 2–3 days can help to differentiate the two entities. An abortion in progress would be expected to change position, though a cervical ectopic will remain fixed and demonstrate growth. Recognition of a cervical ectopic pregnancy and alerting the referring physician to the diagnosis are critical due to the increased risk of massive hemorrhage with dilatation and curettage [79, 84].

Caesarian Scar Ectopic Pregnancy

Caesarian-section (C-section) scar ectopics account for <1% of ectopics and are defined as implantation of the embryo into the scar of a prior C-section [66]. US shows a GS embedded in the anterior lower uterine segment myometrium at the site of the scar, which is best visualized on longitudinal views through the uterus. An echogenic rim and peritrophoblastic vascularity can also be observed. Scar ectopic pregnancies pose a high risk for uterine rupture and massive hemorrhage. Thus, detection is critical [66].

Ovarian Ectopic Pregnancy

Ovarian ectopic pregnancies are extremely rare. Ultrasound findings include an echogenic, thick walled cystic structure with or without internal YS or embryo inseparable from ovarian parenchyma [62]. A "ring of fire" pattern of vascularity is commonly seen. However, distinguishing an intraovarian ectopic pregnancy from a corpus luteum (which also characteristically demonstrates a "ring of fire") can be challenging. In general, the wall of a corpus luteum is typically lower echogenicity than that of an ectopic. In addition, the vast majority of thick-walled cysts with peripheral flow will be corpus lutea because intraovarian ectopic pregnancies are so uncommon. If the diagnosis is unclear and the patient is clinically stable, short-term follow-up US and repeat β-hCG levels are advised [84].

Abdominal Ectopic Pregnancy

Abdominal ectopic pregnancies are exceedingly rare. On ultrasound, the pregnancy is visualized separate from the uterus and not associated with the ovaries or adnexa. Abdominal ectopics most commonly implant in the broad ligament. However, implantation may occur anywhere along the peritoneal surface or abdominal viscera [62]. MRI can provide useful management implications by identifying sites of placental implantation [85].

Heterotopic Pregnancy

Heterotopic pregnancy is defined by the coexistence of an IUP and ectopic pregnancy and is exceedingly rare in unassisted, spontaneous conceptions (estimated between 1:21,000 and 30,000) [84, 85]. However, the incidence is much higher (1–3%) in the setting of ART [61, 66, 84, 85]. When an IUP is documented by ultrasound, a thorough evaluation of the adnexa and entire pelvis must be conducted to avoid a "satisfaction of search" and exclude this life-threatening entity. Particularly if hemoperitoneum is visualized in the setting of an IUP, a careful search for a concomitant ectopic pregnancy should be performed (Fig. 4.19).

Role of MRI in the Diagnosis of Ectopic Pregnancy

Although most ectopic pregnancies are diagnosed by ultrasound, MRI can be a useful adjunct in certain situations and has the potential to diagnose clinically unsuspected ectopic pregnancies with the increased utilization of MRI in the evaluation of abdominal pain in the pregnant patient. MRI is particularly useful for further characterization of the uncommon types of ectopic pregnancy previously discussed,

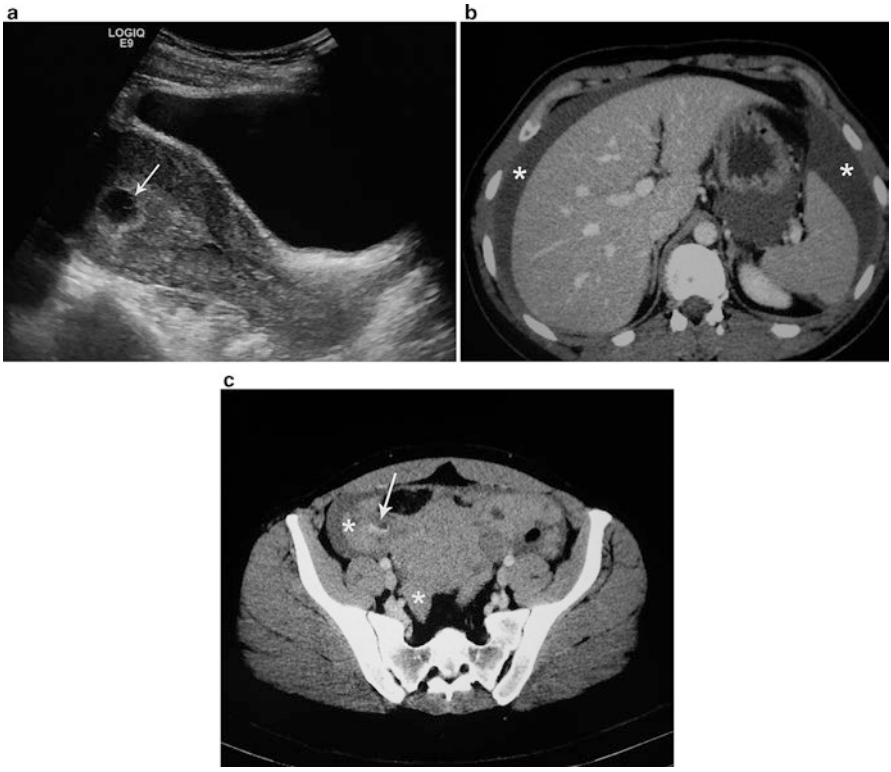

Fig. 4.19 US and CT in heterotopic pregnancy: (**a**) Gray scale image of a 34 y/o pregnant patient with mild low back pain and abdominal pain demonstrates an early IUP with gestational sac and yolk sac (*arrow*) at 6 weeks' (embryo with heartbeat was also present, not shown). No free fluid was seen, and bilateral ovaries were normal in appearance (not shown). The patient returned the following day with severe pain, syncope, and hypotension. (**b**) Axial contrast-enhanced CT through the upper abdomen demonstrates complex-free fluid compatible with hemoperitoneum (*asterisks*). (**c**) Axial CT through the pelvis demonstrates an ill-defined focus of hyperattenuation in the right adnexa suggestive of active bleeding (*arrow*) and areas of intermediate attenuation clotted blood (*asterisks*). Ruptured right tubal ectopic pregnancy with active bleeding was found at surgery. The patient went on to deliver the intrauterine pregnancy at 40 weeks

such as interstitial, scar, cervical, ovarian, and intraabdominal, due to the larger field of view and high soft tissue contrast with this modality. A key feature will be the absence of an IUP in the vast majority of cases, keeping in mind the rare heterotopic pregnancy will be an exception.

As in ultrasound, hemoperitoneum raises suspicion for ectopic pregnancy in the absence of a documented IUP and is most often visualized on MRI as iso- to hyperintense-free fluid on T1-weighted images. The T2 signal of the fluid is often variable or heterogeneous [85]. Tubal ectopic pregnancy on MRI may manifest as a thick-walled, cystic structure with increased signal on T2-weighted images and variable amounts of acute hemorrhage, depicted on MRI as intermediate or

hyperintense signal on T1-weighted images. At times, a heterogeneous predominantly high T2 signal mass-like adnexal structure will be seen without a discrete GS. Hematosalpinx, visualized as a dilated tubular structure with high signal intensity fluid on T1-weighted images, is highly concerning for ectopic pregnancy in the absence of an IUP, even when a discrete adnexal mass is not visualized [85].

On MRI, interstitial ectopic pregnancies appear as heterogeneous, predominantly high T2 signal masses in the lateral uterine fundus which are contiguous with the myometrium. A location lateral to an intact junctional zone can help distinguish these from eccentrically positioned IUPs [85]. In the setting of scar ectopics, MRI can be useful to evaluate for adjacent organ invasion (i.e., urinary bladder). As mentioned previously, MRI can help delineate placental implantation sites in the setting of an abdominal pregnancy [85].

Placental Abruption

Placental abruption is a rare complication of pregnancy, occurring in less than 1% of all pregnancies but associated with significantly increased fetal mortality and increased risk of preterm labor [86, 87]. Classically, patients present with vaginal bleeding and abdominal pain. Sonography is the initial modality of choice to evaluate for this diagnosis, although sensitivity for its detection is low with US, with a reported sensitivity of only 25% [86]. The detection of hemorrhage deep to the placenta or deep to the chorion suggests the diagnosis of placental abruption on ultrasound (Fig. 4.20). Hemorrhagic collections can have a variable sonographic appearance depending on acuity, ranging from iso- to hyperechoic in acute to subacute hematomas to hypoechoic in subacute to chronic hematomas [61]. In the acute setting, abruption commonly manifests as an apparently thickened placenta, with the hemorrhage deep to the placenta isoechoic to and difficult to delineate from the placenta (Fig. 4.21). Comparison with the appearance of the placenta on previous ultrasounds can help confirm this finding as a true abnormality. Cases not detectable by US are felt likely due to hemorrhage from the placental separation passing through the cervix and not forming a discrete hematoma deep to the chorion or placenta [61, 86]. When present, sonographic findings of placental abruption have a high positive predictive value and portend a worse clinical prognosis [61, 86]. MRI can be used as a problem-solving tool, yet should not delay clinical management. On MRI, hematoma will demonstrate increased signal on T1-weighted images compared with the lower signal intensity placenta [61].

Uterine Rupture

Uterine rupture is a rare, life-threatening complication of pregnancy associated with high fetal and maternal morbidity and is considered a true surgical emergency. The diagnosis is often suspected clinically, and thus, imaging is not routinely performed. Risk factors for uterine rupture include previous uterine surgery (including cesarean

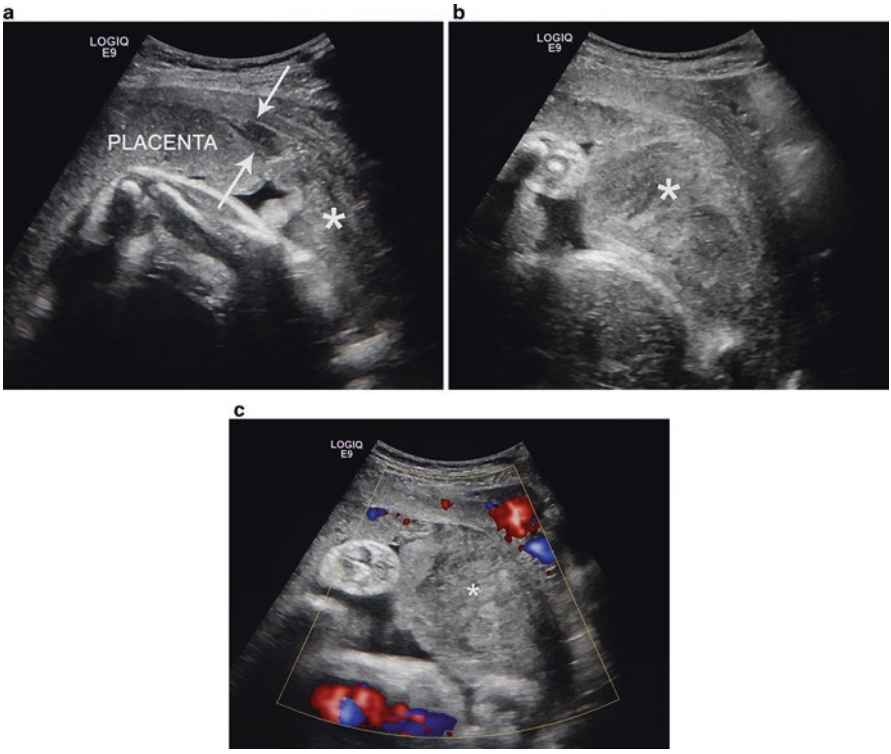

Fig. 4.20 US of marginal placental abruption: US of a 35 y/o pregnant patient at 34 weeks' with irregular contractions and decreased fetal movement. (**a**, **b**) Transverse gray scale images through uterus demonstrate a large, heterogenous mixed isoechoic and hypoechoic collection with small retroplacental component (*arrows*) and larger subchorionic component (*asterisks*) without internal flow with Doppler (**c**) compatible with placental abruption. Patient underwent emergent C-section with delivery of a viable neonate

section or myomectomy), trauma, abnormal placentation (placenta percreta), and ectopic pregnancy (particularly interstitial and scar ectopics) [61, 84, 88]. Complete uterine rupture involves disruption of all layers of the uterus surrounding the fetus with incomplete rupture only involving the myometrium [89]. Rupture can occur during or shortly after delivery, or well before delivery in the setting of ectopic pregnancies [61, 90]. Imaging will demonstrate disruption of the uterine wall with possible herniation of the GS contents and fetus beyond the uterus. Hemoperitoneum is usually present. Contrast-enhanced CT will show a full thickness defect within the uterine wall, which is typically low density compared with adjacent normally enhancing myometrium [23, 88]. Hemoperitoneum will invariably be present as intermediate to high density-free fluid, and one should carefully search for active extravasation. In severe cases, the fetus will be seen extruding into the abdomen [23].

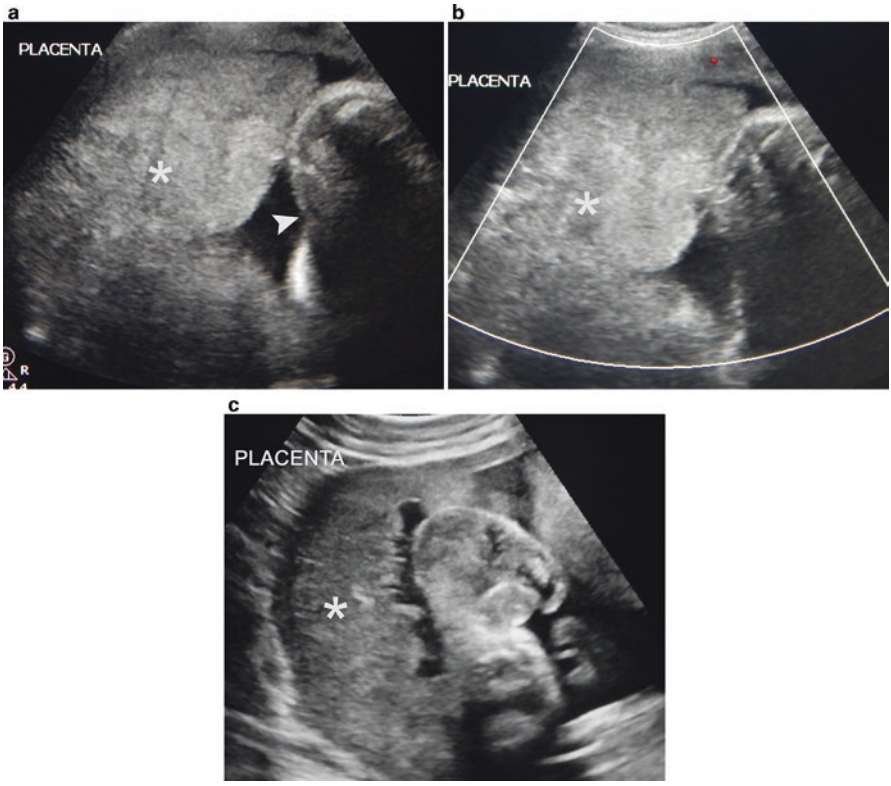

Fig. 4.21 US of retroplacental placental abruption: US of a 40 y/o pregnant patient at 38 weeks' with decreased fetal movement. (**a**) Gray scale image of the uterine fundus demonstrates an apparent markedly thickened placenta (*asterisk*) and IUP (*arrowhead*). (**b**) Image with color Doppler demonstrates no internal flow. (**c**) This represented a significant change from previous US of the placenta (*asterisk*) performed 2 weeks prior. Findings are compatible with massive retroplacental abruption with the hemorrhage isoechoic to and unable to be delineated from the placenta. Intrauterine fetal demise was noted at the time of the scan (not shown). 800 ml of blood clot was noted at delivery

Conclusion

Imaging the pregnant patient with acute abdominal and pelvic complaints presents a unique challenge to the clinician and radiologist. Patients should be adequately informed about the imaging procedures proposed for their care, particularly the risks of radiation exposure, contrast administration, as well as the potential benefits of the information obtained. Accurate and timely imaging is requisite as clinical and laboratory examinations may be nonspecific or misleading. Imaging serves a vital role in directing treatment algorithms, avoiding underdiagnoses, diagnostic delay, or unnecessary interventions. When possible, imaging algorithms should be directed toward the use of imaging modalities that avoid ionizing radiation, reserving CT for

specific clinical scenarios. As in all instances of medical imaging including ionizing and nonionizing procedures, the principle standard of "as low as reasonably achievable (ALARA)" should be routinely applied.

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Laboratory Studies

5

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The acute abdomen in pregnancy is a diagnostic challenge due to the presences of the gravid uterus obscuring meaningful clinical evaluation and changes in most of the laboratory parameters during pregnancy. For example, leukocytosis is a normal occurrence in pregnancy, and C-reactive protein values are already elevated throughout all semesters. Many clotting factors including fibrinogen, factors VII, VIII, IX, and XII continue to rise throughout the pregnancy and reach their peak at term [1].

One should not rely heavily on laboratory testing to make a diagnosis of an acute abdomen. However, with an adequate knowledge of the physiological and biochemical variations that occur during pregnancy, the clinician can use these studies to aid and/or confirm already established diagnoses or help narrow down a differential diagnosis. A list of commonly used laboratory tests and their variations during pregnancy are listed at the end of this chapter.

The acute abdomen in pregnancy may result in etiologies that are pregnancy related and/or unrelated. Diagnosis of some of the conditions may not require laboratory studies. The following are the important etiological considerations for an acute abdomen in pregnancy and laboratory tests that help confirm the diagnoses.

Pregnancy-Related Conditions

- Extrauterine pregnancy including simultaneous intrauterine and tubal/abdominal pregnancy
- Premature separation of placenta (Placental Abruption)
- Chorioamnionitis
- HELLP syndrome

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Causes Unrelated to Pregnancy

- Appendicitis
- Cholecystitis
- Bowel obstruction
- Acute Pancreatitis
- Nephrolithiasis

The Following Nonabdominal Conditions May Present as Acute Abdomen

- Myocardial infarction
- Pulmonary embolism
- Pneumonia
- Sickle cell crisis
- Porphyria

Useful Laboratory Tests for Pregnancy-Related Conditions

Extrauterine Pregnancy

A positive urine pregnancy test without evidence of intrauterine pregnancy should immediately raise the suspicion of extrauterine gestation.

Premature Separation of Placenta Causing Abruption

Disseminated intravascular coagulation (DIC) and massive hemorrhage are the most serious complications of abruption.

Helpful Laboratory Tests

- Complete blood count with platelet count
- D-dimer assay
- prothrombin time (PT)
- partial thromboplastin time (PTT)
- Fibrinogen levels

Thrombocytopenia, prolonged PT and PTT, elevated D-dimer levels, and low fibrinogen levels support the diagnosis of disseminated intravascular coagulation. Of these, the D-dimer assay is the most sensitive laboratory test (95% sensitivity). A scoring system has been developed by the International Society of Thrombosis and Hemostasis for the diagnosis of DIC [2].

Chorioamnionitis

Chorioamnionitis can present as an acute abdomen and when severe, carries a significant maternal and neonatal risk of morbidity. The following laboratory tests are useful in establishing the diagnosis.

- CBC: Elevated white cell count with bandemia is often seen in chorioamnionitis.
- Amniotic fluid: Amniotic fluid culture has a limited use in the diagnosis of acute chorioamnionitis due to the long turnaround time (usually 2–3 days). Amniotic fluid culture will isolate the causative pathogen; however, clinical usefulness of this exercise is limited [3].
- Placental histology: Histological examination of the placenta can detect clinical as well as subclinical chorioamnionitis. However, one should not wait for placental histology to diagnose acute chorioamnionitis. This should only be the confirmatory finding of the clinical diagnosis after the fetus is delivered.

HELLP Syndrome (Hemolysis, Elevated Liver Enzymes and low Platelet Count)

The three most important laboratory diagnostic criteria are as follows:

- Elevated liver enzymes: Marked elevation of serum transaminase levels up to 4000 U/L has been reported, but moderate elevation is common.
- Evidence of hemolysis: Low hemoglobin, the presence of schistocytes, fragmented red cells, and nucleated red cells in the peripheral smear are strong evidence of hemolysis.
- Low platelet count: Any pregnant women with a significant drop in the platelet count during the antenatal period should be suspected as having a potential risk of developing HELLP syndrome.

Based on the platelet count, HELLP syndrome can be divided into three subclasses.

- Class I – Platelet count >50,000 per mm^3
- Class II – Platelet count 50,000–100,000 per mm^3
- Class III – Platelet count 100,000–150,000 per mm^3

Women with the diagnosis of Class I HELLP carry a higher morbidity and mortality.

Coagulation tests are normal in patients with HELLP syndrome unless complicated by disseminated intravascular coagulation (DIC). Low fibrinogen (less than 300 mg/dL) is a strong indicator that the patient also has DIC.

Common Conditions Unrelated to Pregnancy that Can Present as Acute Abdomen

Appendicitis

This is the most common cause for nonobstetrical surgical intervention in pregnancy [1, 4]. The laboratory test that can support the diagnosis is leukocytosis with bandemia. Note that leukocytosis is common in normal pregnancy, and acute appendicitis may not always show leukocytosis. However, in the proper clinical setting, leukocytosis with bandemia favors acute appendicitis. The serum procalcitonin level is not a useful test for uncomplicated appendicitis, but elevated procalcitonin levels are of diagnostic use in appendiceal perforation with abscess formation and/or peritonitis.

Small Bowel Obstruction

Small bowel obstruction can produce symptoms that are nonspecific such as nausea and vomiting; symptoms that are commonly associated with pregnancy. Delay in diagnosis can be devastating to the fetus and the mother.

Blood gas analysis will yield abnormal results including base excess and elevated serum lactate levels. However, the specificity of these tests is low [5]. Furthermore, blood gas analysis may be normal in the early stages of intestinal obstruction [2, 6].

Cholecystitis

Laboratory tests are not commonly used in the diagnosis of acute cholecystitis although an elevated white blood cell count with bandemia is often present. Elevated liver enzyme levels and direct bilirubin levels have been observed in acute cholecystitis. The clinical challenge is to rule out HELLP syndrome in this setting.

Acute Pancreatitis

Elevations of pancreatic amylase and lipase are the most important laboratory findings that help make the correct diagnosis of acute pancreatitis. Moderate elevation of the white blood cell count is also commonly observed in acute pancreatitis. Elevation of the serum procalcitonin level is useful in the diagnosis of pancreatitis and peritonitis. This disease is very serious, in general, and particularly in gravid women.

Nephrolithiasis

Urinalysis may reveal red blood cells (75–95%), but this is not diagnostic of renal calculi. If there is a clinical suspicion of urinary tract infection, urine culture should be performed. There are other studies that will support this diagnosis in pregnancy, such as a variety of imaging options.

Myocardial Infarction

Serial cardiac troponin tests should be performed in suspected myocardial infarction. It is important to be familiarized with the laboratory method of the clinician's institution, and the reference ranges for accurate interpretation of troponin levels. Consultation with the cardiology team is helpful for their expert opinion in difficult and ambiguous cases.

Sickle Cell Crisis

Although rare, sickle cell crisis, particularly in a patient with undiagnosed sickle cell disease, may present with acute abdominal symptoms. The sickling test, CBC, and hemoglobin electrophoresis assist the clinician at arriving at the correct diagnosis.

Porphyria

Acute intermittent porphyria, the most common inherited form of porphyria should be considered in the differential diagnosis of the acute abdomen. Patient may present with acute abdominal symptoms, vomiting, and leukocytosis. The diagnostic laboratory findings include increased urinary porphobilinogen and acute and transient elevation of alkaline phosphatase and bilirubin.

Complete Blood Count with Peripheral Smear Recommended for Initial Evaluation of the Gravid Female Presenting with an Acute Abdomen

Red Blood Cells

Red cell morphology can be useful in the diagnosis and management of diseases causing microangiopathic hemolytic anemia (MAHA), thrombotic thrombocytopenic purpura (TTP) and HELLP syndrome. Many fragmented cells, schistocytes, and nucleated red cells are present in the peripheral blood as a result of hemolysis.

Table 5.1 Laboratory reference values in pregnancy [7]

	Nonpregnant adult	First trimester	Second trimester	Third trimester
Hematology				
Hemoglobin (g/dL)	12–15.8	11.6–13.9	9.7–14.8	9.5–15.0
Hematocrit (%)	35.4–44.4	31.0–41.0	30.0–39.0	28.0–40.0
Mean corpuscular hemoglobin (pg/cell)	27–32	30–32	30–33	29–32
Mean corpuscular volume (m3)	79–93	81–96	82–97	81–99
Platelets (×10 6/L)	165–415	174–391	155–409	146–429
WBC (×10 3/mm 3)	3.5–9.1	5.7–13.6	5.6–14.8	5.9–16.9
Neutrophils (×10 3/mm 3)	1.4–4.6	3.6–10.1	3.8–12.3	1.0–3.6
Coagulation				
PT (sec)	12.7–15.4	9.7–13.5	9.5–13.4	9.6–12.9
PTT (sec)	26.3–39.4	24.3–38.9	24.2–38.1	24.7–35.0
D-dimer (mug/mL)	0.22–0.74	0.05–0.95	0.32–1.29	0.13–1.7
Blood chemical constituents				
Alanine transaminase (U/L)	7–41	3–30	2–33	2–25
Aspartate transaminase (U/L)	12–38	3–23	3–33	4–32
Alkaline phosphatase (U/L)	33–96	17–88	25–126	38–229
Amylase (U/L)	20–96	24–83	16–73	15–81
Lipase (U/L)	3–43	21–76	26–100	41–112
LDH (U/L)	115–221	78–433	80–447	82–524
Bilirubin total (mg/dL)	0.3–1.3	0.1–0.4	0.1–0.8	0.1–1.1
Bilirubin unconjugated (mg/dL)	0.2–0.9	0.1–0.5	0.1–0.4	0.1–0.5
Bilirubin conjugated (mg/dL)	0.1–0.4	0–0.1	0–0.1	0–0.1
C-reactive protein (mg/dL)	0.2–3.0	Not reported	0.4–20.3	0.4–8.1

Data from: Abbassi-Ghanavati et al. [7]

WBC

Increased white cell count with neutrophilia is seen in infections including appendicitis, cholecystitis, and urinary tract infections and pyelonephritis. A Neutrophil series often shows a left shift with band forms in the peripheral blood. Note that a normal white blood cell count does not exclude any of the aforementioned conditions. Clinical history, positive physical examination signs, and radiographic evidence should lead to the correct diagnosis rather than relying on laboratory results. More severe life-threatening conditions including sepsis, peritonitis, and acute pancreatitis can present with high white count and neutrophilia.

Platelet Count

Low platelet counts are often associated with severe sepsis leading in to disseminated intravascular coagulation as well as a feature of TTP andHELLP syndrome.

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Obstetrical Etiologies of Abdominal Pain

6

Peter Bogach Greenspan

First-Trimester Spontaneous Abortion

Spontaneous pregnancy loss in the first 12 weeks of gestation is ubiquitous. The spontaneous or induced termination of pregnancy before fetal viability is the definition of abortion. The term miscarriage and abortion are used interchangeably. Many individuals prefer miscarriage for spontaneous fetal loss. The widespread use of sonography and human chorionic gonadotropin (hCG) measurements that identify extremely early pregnancies has resulted in new terminologies that include early pregnancy loss, wastage, or failure.

Abortion that occurs naturally is of clinical importance since spontaneous abortion can produce abdominal and pelvic pain, thus presenting a challenge to the clinician who is evaluating a pregnant woman who presents with pain.

Spontaneous abortion includes subclassifications such as threatened, inevitable, incomplete, complete, and missed abortion. When any of these variations in pregnancy loss result in infection, then the term septic abortion is applicable.

Spontaneous abortions occurring within the first 12 weeks of gestation account for >80% of pregnancy losses. It appears that embryonic or fetal death almost always precedes the spontaneous expulsion of the products of conception. Hemorrhage into the decidua basalis occurs as a result of this death. The adjacent tissue necrosis stimulates uterine contractions and expulsion of the products of conception. Inspection of the gestational sac demonstrates that it is fluid-filled and may or may not contain an embryo or fetus [1] (Fig. 6.1).

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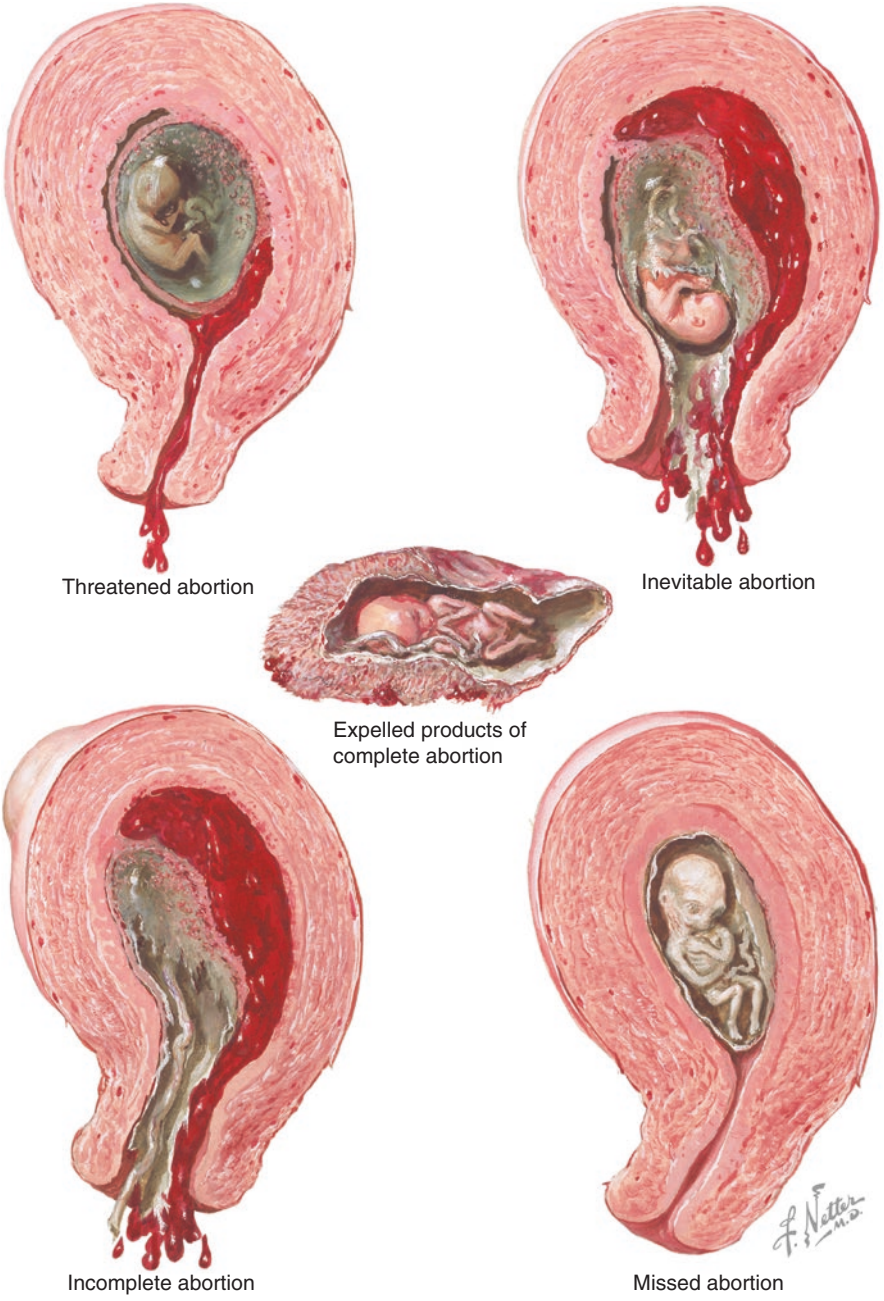


Fig. 6.1 Spontaneous abortion (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Diagnosis

The spontaneous loss of an intrauterine pregnancy (IUP) prior to 20 weeks of gestation is diagnostic of abortion. This is accompanied by low or falling levels of Human Chorionic Gonadotropin (hCG), bleeding and/or midline cramping pain, open cervical os, and the complete or partial expulsion of the products of conception.

Nearly 20% of clinically diagnosed pregnancies terminate in spontaneous abortion.

Greater than 60% of spontaneous abortions result from chromosomal defects.

Another 15% of losses are associated with maternal trauma, infection, dietary deficiency, diabetes mellitus, hypothyroidism, the lupus anticoagulant-anticardiolipin-antiphospholipid antibody syndrome, and anatomic malformations.

Evidence suggests that psychic stimuli such as severe fright, grief, anger, or anxiety can induce pregnancy loss. However, there is no evidence that electromagnetic fields are associated with an increased risk of abortion.

Women with the diagnosis of incompetent cervix should be distinguished from more typical early abortion, premature labor, or rupture of the membranes [1, 2].

Symptoms and Signs

Incompetent cervix typically presents as "silent" cervical dilation (without contractions) between weeks 16 and 28 of gestation. An antecedent history is valuable in such patients. A "threatened abortion" is any bleeding in the first half of pregnancy. There may or may not be cramping noted and evaluation with imaging, etc., demonstrates that the pregnancy is intact. There is no cervical dilation noted in cases of threatened abortion [1] (Fig. 6.2).

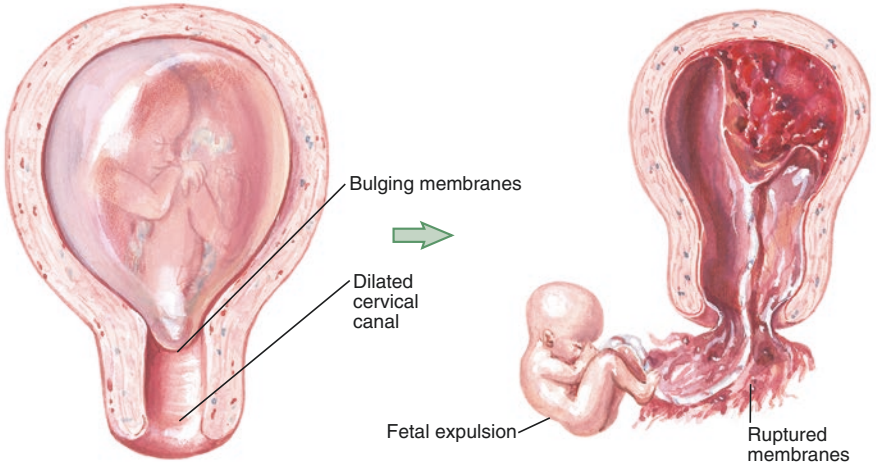
Inevitable abortion implies that the process has begun towards eventual pregnancy loss. The cervix in this case is dilated and the fetal membranes can have undergone rupture. There has been no passage of the products of conception but if visible at the cervical os, then abortion would be inevitable [1].

Complete abortion is defined as the passage of intact products of conception usually accompanied by the alleviation of cramping and pain, with or without persistent spotting and bleeding. The patient's cervical os can already have closed upon visual inspection [1].

Incomplete abortion describes the passage of partial products of conception while a portion thus remains in the uterus. The patient can have mild cramps and can experience bleeding which is persistent and at times presents as hemorrhage.

Missed abortion is a term used to describe a pregnancy that has ceased to develop, but the products of conception have not been expelled. This diagnosis is usually made sonographically. The gravida can note brownish vaginal discharge but generally there is no active bleeding. Often, both the subjective and objective signs and symptoms of pregnancy disappear, often rather abruptly [1].

The pregnant patient who is experiencing abdominal and pelvic pain in the first half of pregnancy must be considered for the evaluation of a pregnancy loss.



Surgical management of cervical insufficiency (cerclage)

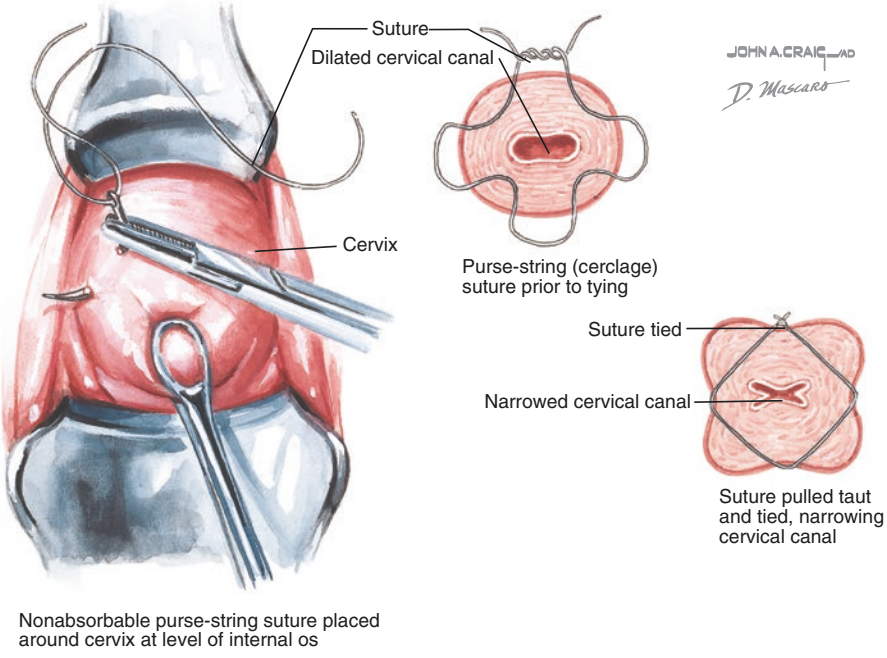


Fig. 6.2 (**a**) Cervical insufficiency. (**b**) Cerclage for surgical management of cervical insufficiency (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Other diagnoses that should be closely considered include ectopic pregnancy, hydatidiform mole, anovulatory bleeding in a nonpregnant women, cervical neoplasm, and other uterine pathologies.

The diagnosis of spontaneous abortion is rarely challenging or confusing, especially when accurate laboratory studies and imaging are readily available.

Simple measurement of the serum hCG will demonstrate declining levels. If there is considerable blood loss, a complete blood count should be obtained immediately. It is critical to ascertain the Rh type and Rho (D) Ig should be administered if the maternal blood type is Rh negative. Failure to do so can result in Rh isoimmunization. Any passed tissue should be assessed by a pathologist, as this can provide clues to other processes such as choriocarcinoma or hydatidiform mole. Transvaginal sonography (TVS) can identify a gestational sac 5–6 weeks from the first day of the last menstrual period, a fetal pole by 6 weeks, and fetal cardiac activity at 6–7 weeks. A small, irregular sac without a fetal pole is usually diagnostic of an abnormal pregnancy [1, 2].

Management

Antibiotics should not be routinely administered unless there is evidence of infection. The use of Misoprostol, 200–800 μg orally or vaginally once, combined with an antiprogesterone (i.e., mifepristone, 600 mg orally once) has afforded a nonsurgical option in the treatment of early pregnancy loss; however, if there is excessive bleeding, a surgical procedure can be required.

Incomplete or inevitable abortions are treated with prompt removal of any remaining products of conception to stop bleeding and prevent infection.

Threatened abortion is managed with conservative observation. Whether bed rest reduces the incidence of pregnancy loss has never been substantiated in any studies to date. The recommendation of abstinence from coitus and douching is also unsubstantiated but seems to make sense.

When the pregnancy loss is inevitable or in cases of missed abortion, medically induced first-trimester treatment with prostaglandins (i.e., misoprostol given vaginally or orally in a dose of 200–800 μg) combined with an antiprogesterone (i.e., mifepristone 600 mg orally) has been shown to be safe, effective, less invasive, and more private than surgical intervention. However, if this approach is unsuccessful or if bleeding is excessive, then a surgical procedure (dilation and curettage, suction curettage) can still be needed [1, 2].

Midtrimester Abortion

Midtrimester fetal loss ranges from 12 weeks until the fetus weighs ≥500 g or gestational age reaches 20 weeks. A gestational age of 22–23 weeks is more accurate. The etiology of midtrimester pregnancy loss can be more readily explained if a careful evaluation is undertaken.

Incidence and Etiology

By the end of the first trimester, spontaneous abortion becomes much less common and continues to decline as the pregnancy progresses. Spontaneous loss in the second trimester is estimated at 1.5–3%. After 16 weeks, the incidence is about 1% [3, 4]. Bleeding in the first trimester increases the incidence of second-trimester loss by a factor of two [5, 6]. Unlike first-trimester abortions that commonly are caused by chromosomal aneuploidies, midtrimester fetal losses are the result of a multitude of causes. The accurate estimate of the incidences of these various causes has no supportive data.

Race, ethnicity, prior poor obstetrical outcomes, and extremes of maternal age are risk factors for second-trimester abortion. There is speculation that first-trimester bleeding has been cited as a potent risk factor [5]. Edlow et al. found that 27% of women with such a loss in the index pregnancy had a recurrent second-trimester loss in their next pregnancy. Furthermore, one-third of these women had a subsequent preterm birth [7].

The clinical presentation of second-trimester abortion is much like first-trimester loss. The gravida can present with pain and cramping in the lower abdomen, in the midline. Multigravid women who have experienced labor may report that their symptoms are very similar to labor contractions. Membrane rupture and/or vaginal bleeding are significant, ominous signs. When evaluated for their symptoms, cervical dilatation can be advanced and delivery of a nonviable fetus can be inevitable.

Other diagnoses need consideration if the patient is having pain, but does not seem to be contracting or is not bleeding. The differential diagnosis should include torsion of an adnexa, degeneration of uterine leiomyomata, urinary tract infection or calculi, and any number of gastrointestinal disorders including bowel obstruction. Concealed placental abruption should also be considered.

Ectopic Pregnancy

Normally, the blastocyst implants in the endometrial lining of the uterine cavity following fertilization and fallopian tube transit. Implantation anywhere other than that is considered an ectopic location. Ectopic pregnancies comprise 1–2% of all first-trimester pregnancies in the United States. Nonetheless, this disproportionally accounts for 6% of all pregnancy-related deaths [8, 9]. Furthermore, subsequent successful pregnancy likelihood is reduced after an ectopic pregnancy.

Urine and serum human chorionic gonadotropin (hCG) assays and transvaginal sonography have facilitated early diagnosis and treatment. Consequently, maternal survival and conservation of reproductive capability has improved (Fig. 6.3).

Approximately 95% of ectopic pregnancies occur in the fallopian tube giving rise to fimbrial, ampullary, isthmic, or interstitial tubal pregnancies [10, 11]. The ampulla is the most frequent site, followed by the isthmus. Five percent of nonfallopian tube ectopic pregnancies implant in the ovary, peritoneal cavity, cervix, or prior cesarean scar. Rarely, a twin pregnancy occurs with one conceptus in the

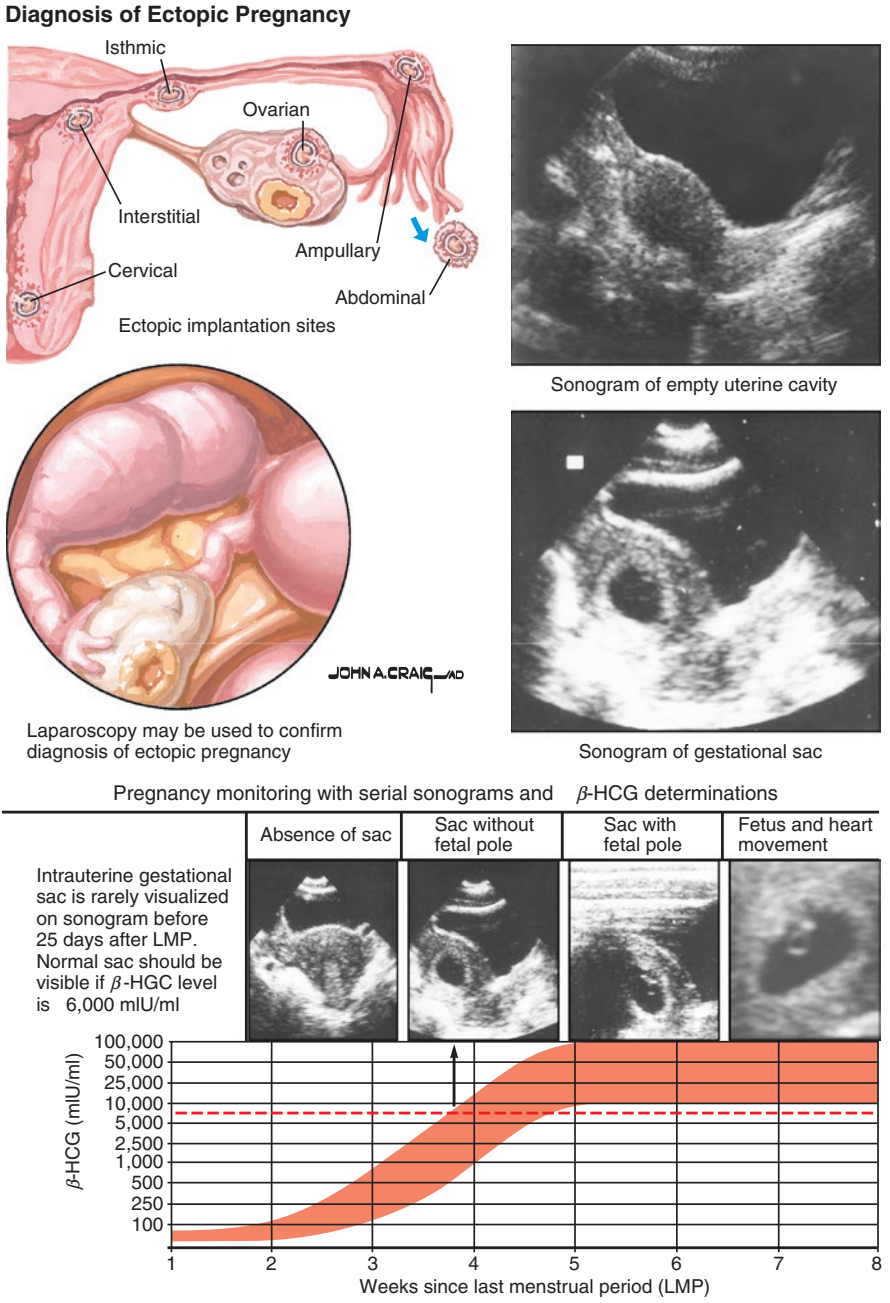


Fig. 6.3 Ectopic pregnancy (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

uterus and the other one implanted ectopically. This "heterotopic" pregnancy rate is approximately 1 per 30,000 pregnancies. Conversely, the development of assisted reproductive technologies (ARTs) has increased their incidence to 1 in 7000 overall, and following ovulation induction, it can be as high as 0.5–1% [12]. Twin tubal pregnancy with both embryos in the same tube or with one in each tube has been reported [13, 14]. The admiration of immunoglobulin G (IgG) anti-D immunoglobulin should be given to D-negative (Rh negative) women with ectopic pregnancies (Fig. 6.4).

Risks

The underlying cause of many tubal ectopic pregnancies is abnormal fallopian tube anatomy. Previous surgeries for prior tubal pregnancy, fertility restoration, or for sterilization render the highest risk of tubal implantation. After one previous ectopic pregnancy, the chance of another approximates 10% [15, 16]. History of sexually transmitted disease or other tubal infection, which can alter normal tubal anatomy, is a common risk factor. One episode of salpingitis can result in a subsequent ectopic pregnancy in up to 9% of women [17]. Peritubal adhesions consequent of salpingitis, appendicitis, or endometriosis can further increase the risk of tubal pregnancy. Salpingitis isthmica nodosa, a condition in which epithelium-lined diverticula protrude into a hypertrophied muscularis layer of the uterus, additionally poses an increased risk [18]. Congenital fallopian tube anomalies, especially those secondary to in utero diethylstilbestrol exposure (extremely rare today), can result in anomalous tubes and higher ectopic rates [19].

A number of ectopic pregnancies spontaneously fail and are therefore spontaneously reabsorbed. Sensitive hCG assays permit this to be documented more regularly (Fig. 6.5).

Clinical Manifestations

In modern practice, ectopic pregnancies rarely rupture. This is due to earlier patient presentation and more precise diagnostic technology. Early on, symptoms and signs of ectopic pregnancy are typically subtle or even absent. The gravida has no suspicion of tubal pregnancy and assumes that she has a normal early pregnancy or is experiencing a miscarriage.

A "classic" presentation is typified by the triad of delayed menstruation, pain, and vaginal bleeding or spotting. When rupture ensues, there is usually severe lower abdominal and pelvic pain that is commonly described as sharp, stabbing, or tearing. Tenderness is elicited during abdominal palpation. Bimanual pelvic examination causes exquisite pain. Cervical motion tenderness is often present. The posterior vaginal fornix can bulge from blood in the rectouterine cul-de-sac, or a tender, boggy mass can be felt to one side of the uterus. The uterus can be displaced to one side by an ectopic mass. The uterus can also be somewhat enlarged due to hormonal

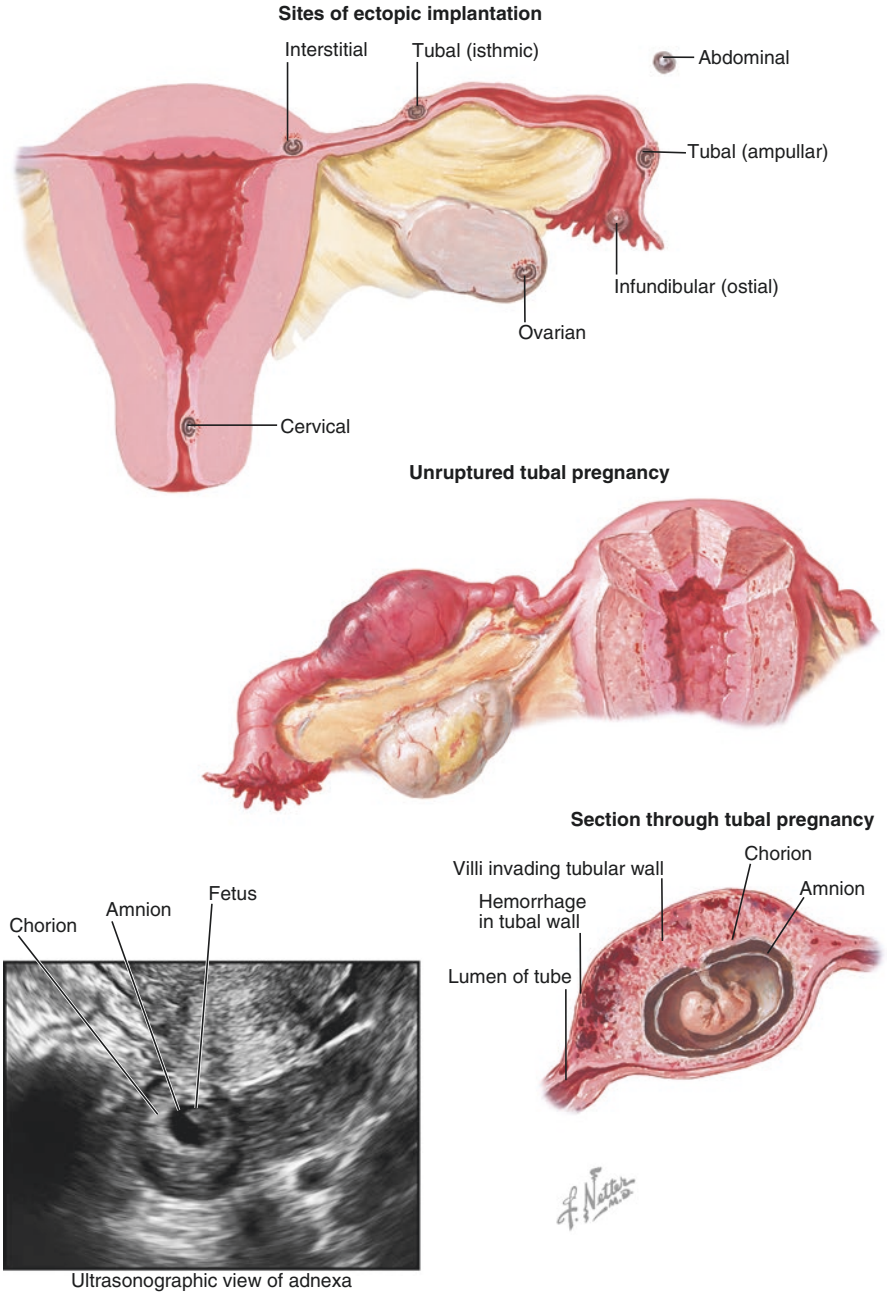


Fig. 6.4 Ectopic pregnancy (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

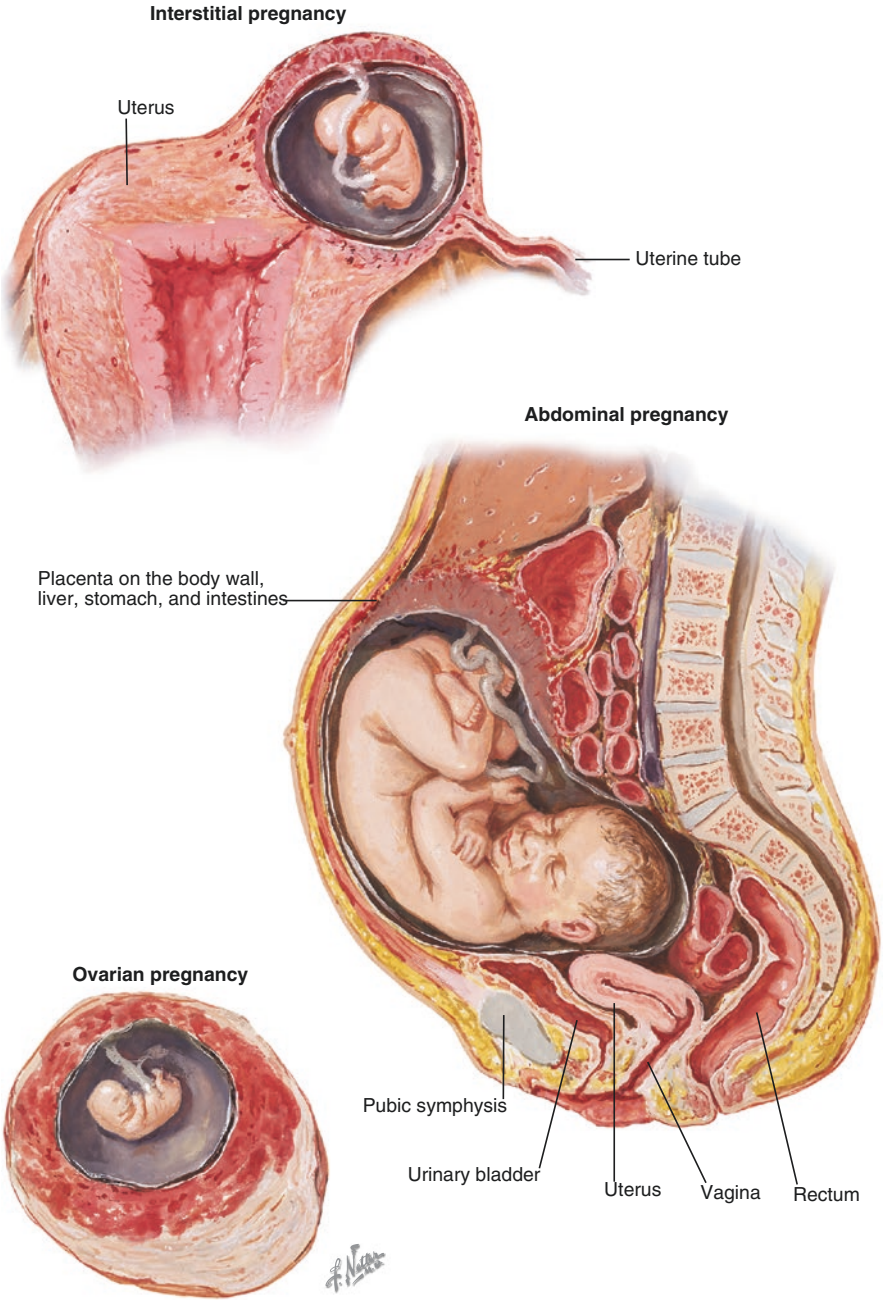


Fig. 6.5 Ectopic pregnancy (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

stimulation. Shoulder or neck pain, a result of diaphragmatic irritation, is observed in about half of patients with significant hemoperitoneum.

Vaginal spotting or bleeding is reported by 60–80% of women with tubal pregnancy. Occasionally, there is profuse vaginal bleeding which is suggestive of an incomplete abortion. Furthermore, ectopic pregnancy can lead to profound intraabdominal hemorrhage. Moderate bleeding can induce no change in vital signs, a slight rise in blood pressure, or a vasovagal response with bradycardia and hypotension. Birkhahn and colleagues observed that in 25 gravidas with ruptured ectopic pregnancy, the majority at presentation had a heart rate <100 beats per minute and a systolic blood pressure >100 mm Hg [20]. Blood pressure will fall and pulse will rise only if bleeding persists and hypovolemia becomes significant. Vertigo or syncope can develop.

Hemoglobin or hematocrit readings can at first show only a slight reduction even with significant hemoperitoneum. Therefore, following an acute hemorrhage, a decrease in hemoglobin or hematocrit level over several hours is a more valuable index of blood loss than is the initial level. In roughly half of women with a ruptured ectopic pregnancy, a leukocytosis of up to 30,000/μL can be found.

Endometrium that is hormonally prepared for pregnancy is called decidua, and the degree to which the endometrium is converted with ectopic pregnancy is variable. Consequently, along with bleeding, women with ectopic tubal pregnancy can pass a decidual cast. This is the sloughed endometrium that takes the form of the endometrial cavity (Fig. 6.6). Significantly, decidual sloughing can occur with uterine abortion. This tissue should be evaluated and then submitted to pathology for evidence of a conceptus. If there is no clear gestational sac or if no chorionic villi are identified histologically, then consideration of ectopic pregnancy must be entertained by the clinician.

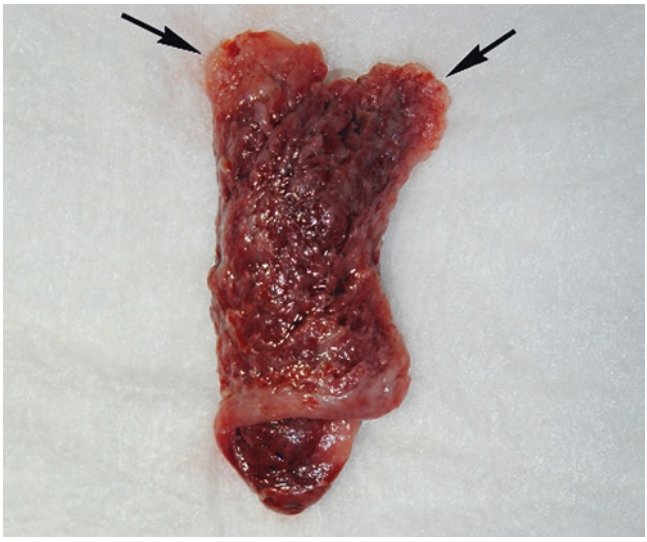


Fig. 6.6 Decidual cast (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

Abdominal pain in the pregnant patient creates an extensive differential diagnosis. Uterine conditions such as miscarriage, infection, degenerating or enlarging leiomyomata, molar pregnancy, or round-ligament pain are all under consideration. Adnexal pathology includes ectopic pregnancy; hemorrhagic, ruptured, or torsioned ovarian masses; salpingitis; or tuboovarian abscess. Furthermore, appendicitis, cystitis, renal stone, or gastroenteritis are nongynecologic sources of lower abdominal pain in early pregnancy.

Several algorithms have been proposed to diagnose ectopic pregnancy. The majority includes these crucial components: physical findings, transvaginal sonography (TVS), and serum hCG level measurement (the initial and the consequent pattern of rise or decline) and diagnostic surgery. Surgical options include uterine curettage, laparoscopy, and, occasionally, laparotomy. Women with presumed or obvious rupture should undergo urgent surgical intervention. When evaluating a suspected unruptured ectopic pregnancy, care must be taken to avoid the interruption of a normal pregnancy. However, strategies that reduce the potential for normal pregnancy interruption can postpone the diagnosis of an ectopic pregnancy.

Beta Human Chorionic Gonadotropin

The diagnosis of ectopic gestation requires a rapid and accurate determination of pregnancy. Available serum and urine pregnancy tests utilizing enzyme-linked immunosorbent assays (ELISAs) for hCG are sensitive to levels of 10–20 mIU/mL and are positive in >99% of ectopic pregnancies [21]. Ectopic pregnancies with negative hCG levels are rare.

Patients who present with bleeding or pain as well as a positive pregnancy test result should undergo initial transvaginal sonography (TVS) to identify the location of the gestation. Diagnosis is ascertained if a yolk sac, embryo, or fetus is identified within the uterus or the adnexa. However, often a TVS is nondiagnostic, and tubal pregnancy remains possible. When neither intrauterine nor extrauterine pregnancy is identified, the term "pregnancy of unknown location" (PUL) is applied until additional clinical findings allow determination of pregnancy location.

Levels Above the Discriminatory Zone

Several investigators have elucidated discriminatory hCG levels above which nonvisualization of an intrauterine pregnancy (IUP) indicates that the pregnancy is either nonviable or is ectopic. Barnhart et al. found that an empty uterus with a serum hCG concentration ≥1500 mIU/mL was 100% accurate in ruling out a live uterine pregnancy [22]. There are several institutions that set their discriminatory threshold higher at ≥2000 mIU/mL. Moreover, Connolly and colleagues stated that there is evidence to suggest an even higher threshold. They posited that with a viable uterine pregnancy, a gestational sac was seen 99% of the time with a discriminatory level of 3510 mIU/mL [23].

When initial hCG level surpasses the set discriminatory level and there is no evidence for a uterine pregnancy observed with TVS, then the diagnosis is attributed

to a failed uterine pregnancy, completed abortion, or an ectopic pregnancy. However, early multifetal gestation should be considered. If in a stable patient that a PUL that could still have a normal pregnancy, it is judicious to continue expectant management with serial hCG level assessment to prevent aborting an early normal pregnancy. The serial hCG levels will drop rapidly when the patient history or extruded tissue suggests a completed abortion. Curettage will differentiate an ectopic from a nonviable uterine pregnancy. Barnhart and colleagues do not recommend diagnostic curettage as it results in unnecessary surgical therapy [24]. This can be countered by concern for methotrexate toxicity if it is administered inappropriately to patients with a presumed ectopic pregnancy.

Levels Below the Discriminatory Zone

When the initial hCG level falls below the set discriminatory value, the location of the pregnancy may not be technically discernible with TVS. With cases of PUL, serial hCG level assays are repeated to identify patterns that specify either a growing or failing uterine pregnancy. Results that rise or fall outside these expected ranges increase the concern for ectopic pregnancy. Therefore, women with a suspected ectopic pregnancy, but whose initial hCG level is below the discriminatory threshold, are reevaluated at 2 days intervals. First, with early normally progressing uterine pregnancies, Kadar and Romero noted that the mean doubling time for serum hCG levels was approximately 48 h [25]. The lowest normal value for this increase was 66%. Barnhart et al. reported a rise of 53% within 48-h with a 24-h minimum rise of 24% [26]. Seeber and associates proposed a more conservative 35% 48-h rise [27]. Silva and colleagues advise that one-third of women with an ectopic pregnancy experience a 53% rise at 48 h. Furthermore, they reported that no single pattern characterizes ectopic pregnancy and that approximately 50% of ectopic pregnancies are found to have decreasing hCG levels, whereas the other half will have increasing levels [28].

Failing intrauterine pregnancies also show patterns of hCG level decline as well. Decline rates ranging between 21% and 35% are typical.

In pregnancies without these expected rises or falls in hCG levels, distinction between a nonliving intrauterine and an ectopic pregnancy can be aided by repeat hCG level evaluation [29]. Uterine curettage can be performed as well. Barnhart and coworkers concluded that endometrial biopsy was less sensitive than curettage [30]. Prior to curettage, a repeat TVS examination can reveal new informative findings.

Serum Progesterone

Serum progesterone determinations can clarify the diagnosis in a few patients [31, 32]. A value of 25 ng/mL or higher eliminates the likelihood of ectopic pregnancy with 92.5% sensitivity [33, 34]. Values <5 ng/mL are found in only 0.3% of normal pregnancies [35]. Therefore, values <5 ng/mL indicate either a nonviable uterine pregnancy or an ectopic pregnancy. Ectopic pregnancies typically demonstrate progesterone levels ranging between 10 and 25 ng/mL; therefore, the clinical utility of

progesterone is limited [36]. One exception is that pregnancy conceived via ART can be associated with higher than usual progesterone levels [37].

Transvaginal Sonography

Endometrial Findings

Patients with an ectopic pregnancy require TVS to find evidence of a uterine pregnancy or an ectopic gestation. An intrauterine gestational sac is typically observable between 4½ and 5 weeks. The yolk sac appears between 5 and 6 weeks, and a fetal pole with cardiac activity is first detected at 5½ to 6 weeks. These structures are visualized slightly later with transabdominal sonography.

In patients with an ectopic pregnancy, a trilaminar endometrial pattern can be diagnostic (Fig. 6.7). However, its specificity is 94%, but with a sensitivity of only 38% [38]. In addition, Moschos and Twickler found that in women with PUL at presentation, no normal pregnancies had a stripe thickness <8 mm [39].

Collections of anechoic fluid, often observed normally with an early intrauterine gestational sac, can possibly be seen with ectopic pregnancy. Two features observed include pseudogestational sac and decidual cyst. A pseudosac is a fluid collection between the endometrial layers and conforms to the cavity shape. Finding a pseudosac increases the risk of ectopic pregnancy [40, 41]. Secondly, a decidual cyst is an anechoic area within the endometrium but distant from the canal and often at the endometrial-myometrial border. Ackerman et al. proposed that this finding signifies early decidual breakdown and leads to decidual cast formation [42].

These findings are dissimilar to the intradecidual sign seen with intrauterine pregnancy, that being an early gestational sac and is eccentrically located within one of the endometrial stripe layers [43]. The American College of Obstetricians and

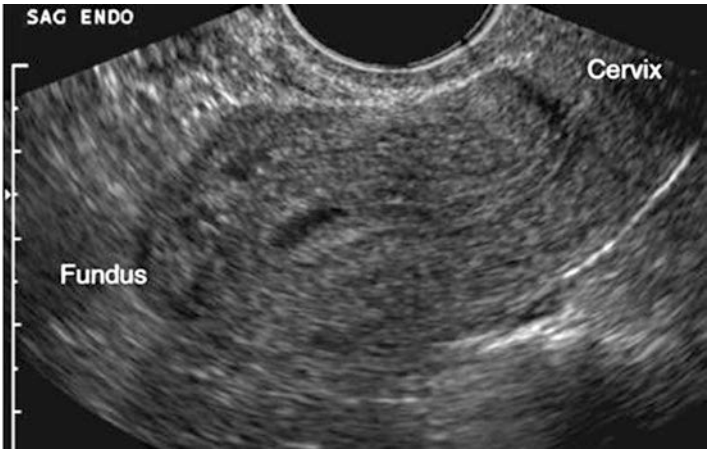


Fig. 6.7 Trilaminar sonographic pattern associated with ectopic gestation (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

Gynecologists recommends restraint in diagnosing a uterine pregnancy when a definite yolk sac or embryo is absent [44].

Adnexal Findings

The sonographic evidence of ectopic pregnancy depends on visualization of an adnexal mass separate from the ovary. An ectopic pregnancy is clearly confirmed if fallopian tubes and ovaries are seen and an extrauterine yolk sac, embryo, or fetus is identified. There are cases in which a hyperechoic halo or tubal ring surrounding an anechoic sac can be imaged. Alternatively, an inhomogeneous complex adnexal mass is usually the result of hemorrhage inside the ectopic sac or by an ectopic gestation that has ruptured into the tube. Generally, roughly 60% of ectopic pregnancies are seen as an inhomogeneous mass next to the ovary; 20% appear as a hyperechoic ring; and 13% have an obvious gestational sac with a fetal pole [45]. It is important to note that not all adnexal masses are ectopic pregnancies, and correlation of sonographic findings with other clinical information is essential in making an accurate diagnosis.

There is a color Doppler image referred to as "the ring of fire" which represents placental blood flow within the periphery of the complex adnexal mass. Though this can assist in the diagnosis, this finding also appears with a corpus luteum of pregnancy; therefore, differentiation can be challenging.

Hemoperitoneum

Evaluation for hemoperitoneum can add valuable clinical information in women suspected of having an ectopic pregnancy. Usually, this is detected with sonography. However, this can also be diagnosed by culdocentesis, a valuable diagnostic test that is utilized less and less today.

The sonographic fluid noted in cases of hemoperitoneum is anechoic or hypoechoic. Blood accumulates initially in the dependent retrouterine cul-de-sac, and then surrounds the uterus as it fills the pelvis (Fig. 6.8). Fifty milliliters can be imaged in the cul-de-sac using TVS, and transabdominal imaging improves the assessment of the extent of hemoperitoneum. Significant intraabdominal hemorrhage results in blood tracking up the pericolic gutters to fill Morison's pouch near the liver. Free fluid in this pouch is usually not apparent until accumulated blood reaches 400–700 mL [46–48]. Peritoneal fluid in conjunction with an adnexal mass is highly predictive of ectopic pregnancy [49]. A small amount of peritoneal fluid is physiologically normal.

Culdocentesis is a simple technique. It was used frequently in the past to diagnose hemoperitoneum. The cervix is grasped with a tenaculum and pulled outward and upward toward the symphysis. A syringe with a long 18-gauge needle is used to penetrate the posterior vaginal fornix into the retrouterine cul-de-sac. If fluid such as blood or pus is present, it can be aspirated. Failure to obtain fluid, however, is interpreted as an unsatisfactory entry into the cul-de-sac and does not rule out ectopic pregnancy. When fluid is obtained and contains fragments of old clots or frank

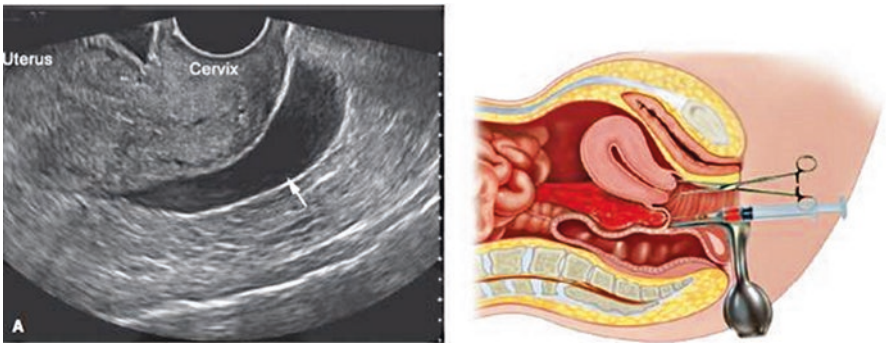


Fig. 6.8 (**a**) Sonographic evidence of hemoperitoneum. (**b**) Culdocentesis (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

nonclotting blood, this finding is compatible with the diagnosis of hemoperitoneum. Conversely, if the blood sample clots, it might have been drawn directly from an adjacent blood vessel or from a briskly bleeding ectopic pregnancy. A number of studies have challenged its usefulness, and culdocentesis has been largely replaced by TVS [50, 51]. This author appreciates the advances in imaging in the diagnosis of ectopic gestation, however, continues to train residents in the technique of culdocentesis so that if one encounters a patient with a suspected ectopic pregnancy and reliable imaging is unavailable, a simple diagnostic test can help to establish the diagnosis.

Pelviscopy

Minimally invasive, endoscopic procedures afford direct visualization of the fallopian tubes and pelvis. Pelviscopy affords a reliable diagnosis in the vast majority of cases of suspected ectopic pregnancy. Furthermore, pelviscopy is therapeutic in many instances, since the ectopic pregnancy can be managed with this technique.

Interstitial Pregnancy

Diagnosis

Interstitial pregnancies are lodged in the proximal tubal segment that lies within the muscular uterine wall. Sometimes, they are inaccurately called cornual pregnancies; however, cornual pregnancies describe a conception that develops in the rudimentary horn of a uterus with a müllerian anomaly. Risk factors are similar to others mentioned for tubal ectopic pregnancy; however, previous ipsilateral salpingectomy is a specific risk factor for interstitial pregnancy [51]. Interstitial pregnancies tend to rupture later than more distal tubal ectopic pregnancies, between 8 and 16 weeks of

amenorrhea. This is consequent to greater distensibility of the myometrium covering the interstitial fallopian tube segment. Ruptures of interstitial gestations are associated with an increased risk of mortality; as high as 2.5% because of the proximity of these pregnancies to the uterine and ovarian arteries, thus producing severe hemorrhage [52].

Interstitial pregnancy can be detected early in many cases utilizing TVS and serum hCG assays, but diagnosis can still be challenging. At times, these pregnancies appear sonographically comparable to an eccentrically implanted intrauterine pregnancy, more so in a uterus with a müllerian anomaly. Differentiation includes an empty uterus, a gestational sac seen separate from the endometrium and >1 cm away from the most lateral edge of the uterine cavity, and a thin, <5-mm myometrial mantle surrounding the sac [53]. Furthermore, an echogenic line, referred to as the "interstitial line sign," extending from the gestational sac to the endometrial cavity most likely represents the interstitial portion of the fallopian tube and is highly sensitive and specific [54]. Occasionally, three-dimensional sonography, magnetic resonance imaging (MRI), or diagnostic pelviscopy can also provide clarification [55, 56]. Pelviscopically, an enlarged protuberance lying outside the round ligament coexistent with normal distal fallopian tubes and ovaries is observed (Fig. 6.9).

Management

Surgical management with cornual resection or cornuostomy can be undertaken via laparotomy or pelviscopy, depending on patient hemodynamic stability and surgeon expertise [57, 58]. Whatever approach is chosen, intraoperative intramyometrial vasopressin injection can decrease surgical blood loss. Postoperative hCG levels should be obtained to exclude remnant trophoblast. Cornual resection excises the gestational sac and surrounding cornual myometrium by means of a wedge resection, whereas cornuostomy involves incision of the cornua and suction or

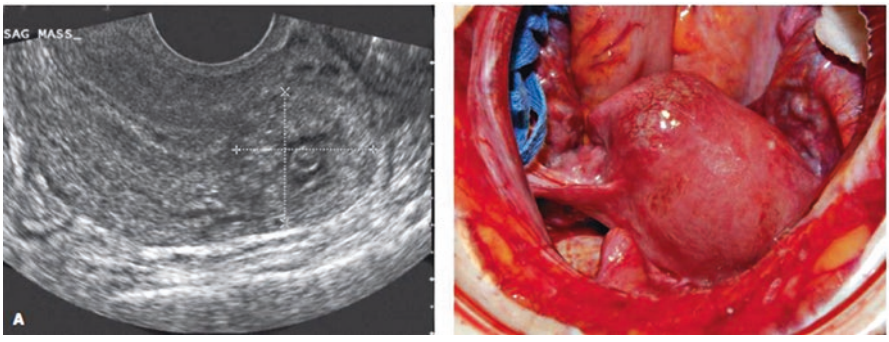


Fig. 6.9 (**a**) Sonographic evidence of interstitial pregnancy. (**b**) Operative view of interstitial pregnancy (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

instrument extraction of the pregnancy. The availability of computer-assisted pelviscopy in the hands of this author has considerably improved this operation.

Conservative medical management can be considered if the diagnosis is made early on [59]. Consensus regarding methotrexate route or regimen is lacking because of the low incidence of this ectopic gestation. Jermy and associates reported a 94% success with systemic methotrexate using a dose of 50 mg/m^2 BSA [60]. This, however, was a small series. Others have described direct methotrexate injection into the gestational sac [61]. Importantly, because these patients usually have higher initial serum hCG levels at diagnosis, a longer period of surveillance is usually needed.

It is not clear what risk of uterine rupture with subsequent pregnancies is following either medical or conservative surgical management. Therefore, close observation of these patients during subsequent pregnancy, as well as the strong consideration of elective cesarean delivery, is reasonable.

Different than interstitial pregnancy, the term angular pregnancy describes intrauterine implantation in one of the lateral angles of the uterus and medial to the uterotubal junction and round ligament. This is relevant since angular pregnancies sometimes can be carried to term attendant with an increased risk of abnormal placentation and its consequences [62].

Abdominal Pregnancy (Fig. 6.5)

Diagnosis

Abdominal pregnancy, technically, is an implantation in the peritoneal cavity exclusive of tubal, ovarian, or intraligamentous implantations. These pregnancies are rare with an incidence of 1 in 10,000 to 25,000 live births [63, 64]. A zygote can traverse the tube and implant primarily in the peritoneal cavity; however, the majority of abdominal pregnancies are assumed to follow early tubal rupture or abortion with reimplantation. In the rare instance of advanced extrauterine pregnancy, it is common that the placenta is still at least partially attached to the uterus or adnexa.

Diagnosis is challenging. There can be no or minimal symptoms. Laboratory tests are usually normal; however, maternal serum α-fetoprotein (MSAFP) levels can be elevated. Clinically, palpation can indicate an abnormal fetal position or the cervix can be displaced [65]. Imaging of an abdominal pregnancy might not be recognized, and the diagnosis is often overlooked [66]. Oligohydramnios is common but may or may not have significance. Other observations include a fetus seen separate from the uterus or eccentrically positioned within the pelvis; lack of myometrium between the fetus and the maternal anterior abdominal wall or bladder; and extrauterine placental tissue [67]. MR imaging can provide additional anatomical information and can be used to confirm the diagnosis and provide maximal details regarding placental implantation [68, 69].

Ovarian Pregnancy (Fig. 6.5)

Ectopic gestations implanted in the ovary are rare. Diagnosis is confirmed if four clinical criteria are met. These were outlined by Spiegelberg: (1) the ipsilateral tube is intact and distinct from the ovary; (2) the ectopic pregnancy occupies the ovary; (3) the ectopic pregnancy is connected by the uteroovarian ligament to the uterus; and (4) ovarian tissue can be demonstrated histologically amid the placental tissue [70]. Risk factors are like those for tubal pregnancies, but Assisted Reproductive Technology or IUD failure appears to be disproportionately associated with this rarity [71]. Presenting complaints and findings are identical to tubal ectopic pregnancy. The ovary can accommodate the expanding pregnancy more easily than the fallopian tube, but rupture early on is the usual consequence.

The availability of TVS has resulted in increased diagnosis of unruptured ovarian pregnancies. Sonographically, an internal anechoic area is surrounded by a wide echogenic ring, surrounded by ovarian cortex [72]. In their review of 49 cases, Choi et al. observed that the diagnosis cannot be made until surgery since the majority of cases are presumed to be tubal ectopic pregnancy [73]. Additionally, at surgery, an early ovarian pregnancy can be thought to be a hemorrhagic corpus luteum cyst or a bleeding corpus luteum.

Evidence-based management accrues mainly from case reports [74, 75]. The classical management of ovarian pregnancies has been surgical. Smaller lesions can be managed by ovarian wedge resection or cystectomy; however, larger lesions require oophorectomy. Systemic or locally injected methotrexate has been used successfully to treat small unruptured ovarian pregnancies [76]. Conservative surgery or medical management mandates hCG levels be monitored to exclude remnant trophoblast.

Cesarean Scar Pregnancy

Cesarean scar pregnancy (CSP) occurs when implantation of the gestation is within the myometrium of a prior cesarean delivery scar. Its incidence approaches 1 in 2000 normal pregnancies and has increased in recent years commensurate with the increased cesarean delivery rate [77, 78]. The pathogenesis of cesarean scar pregnancy has been equated to that of placenta accreta and carries similar risk of serious hemorrhage [79]. Whether the incidence increases with multiple cesarean deliveries or if it is affected by either one- or two-layer uterine incision closure is not known.

Pain and bleeding are common; thus, patients with CSP often present early on. As much as 40% of women are asymptomatic and are diagnosed during routine sonographic examination [78]. Rarely, early rupture can lead to an abdominal pregnancy [80].

The differentiation between a cervicoisthmic intrauterine pregnancy and CSP can be difficult; several investigators have described sonographic findings [81, 82]. Godin et al. report that there are four sonographic criteria that should be met for the diagnosis (Fig. 6.10) [83]. TVS is the usual first imaging tool; however, Magnetic

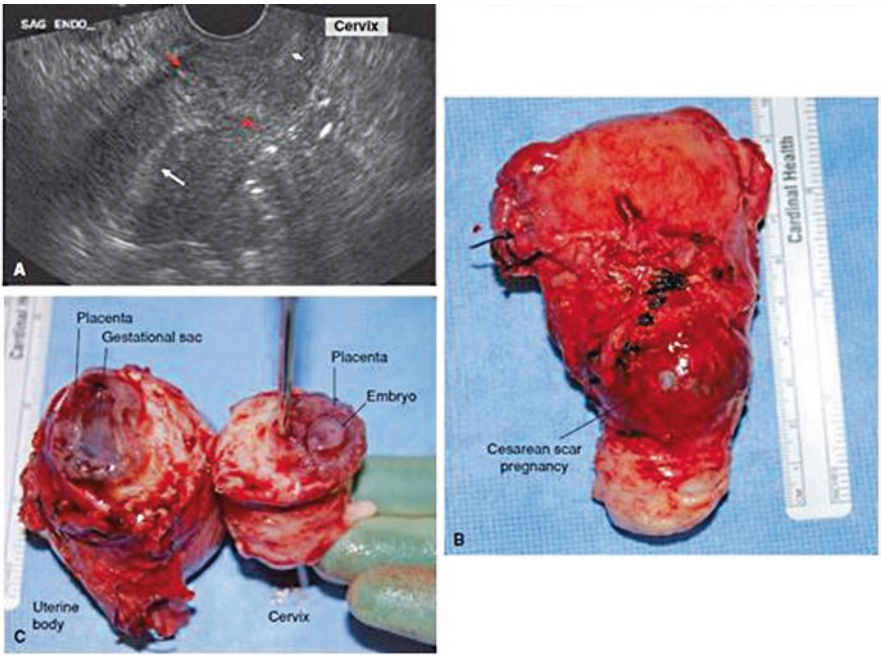


Fig. 6.10 (**a**) Sonographic evidence of uterine scar pregnancy. (**b**, **c**) Hysterectomy specimen with uterine scar pregnancy (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

Resonance imaging is helpful when sonography is equivocal or inconclusive before intervention [84].

There are currently no treatment standards for CSP. Several options are proposed. Hysterectomy is a reasonable initial choice in those desiring sterilization. At times, it is necessary to control heavy bleeding. If fertility preservation is desired, then options include systemic or locally injected methotrexate, either alone or combined with conservative surgery [85–87]. Surgical intervention includes visually guided suction curettage or transvaginal aspiration, hysteroscopic removal, or isthmic excision. These are completed solely or usually with adjunctive methotrexate [79, 88–92]. Preoperative uterine artery) embolization has been utilized to minimize hemorrhage risk [93, 94].

Uterine Rupture (Figs. 6.11 and 6.12)

Classification

Uterine rupture is usually classified as either (1) complete when all layers of the uterine wall are separated or (2) incomplete when the uterine muscle is separated but the visceral peritoneum is intact. Uterine dehiscence is another term for

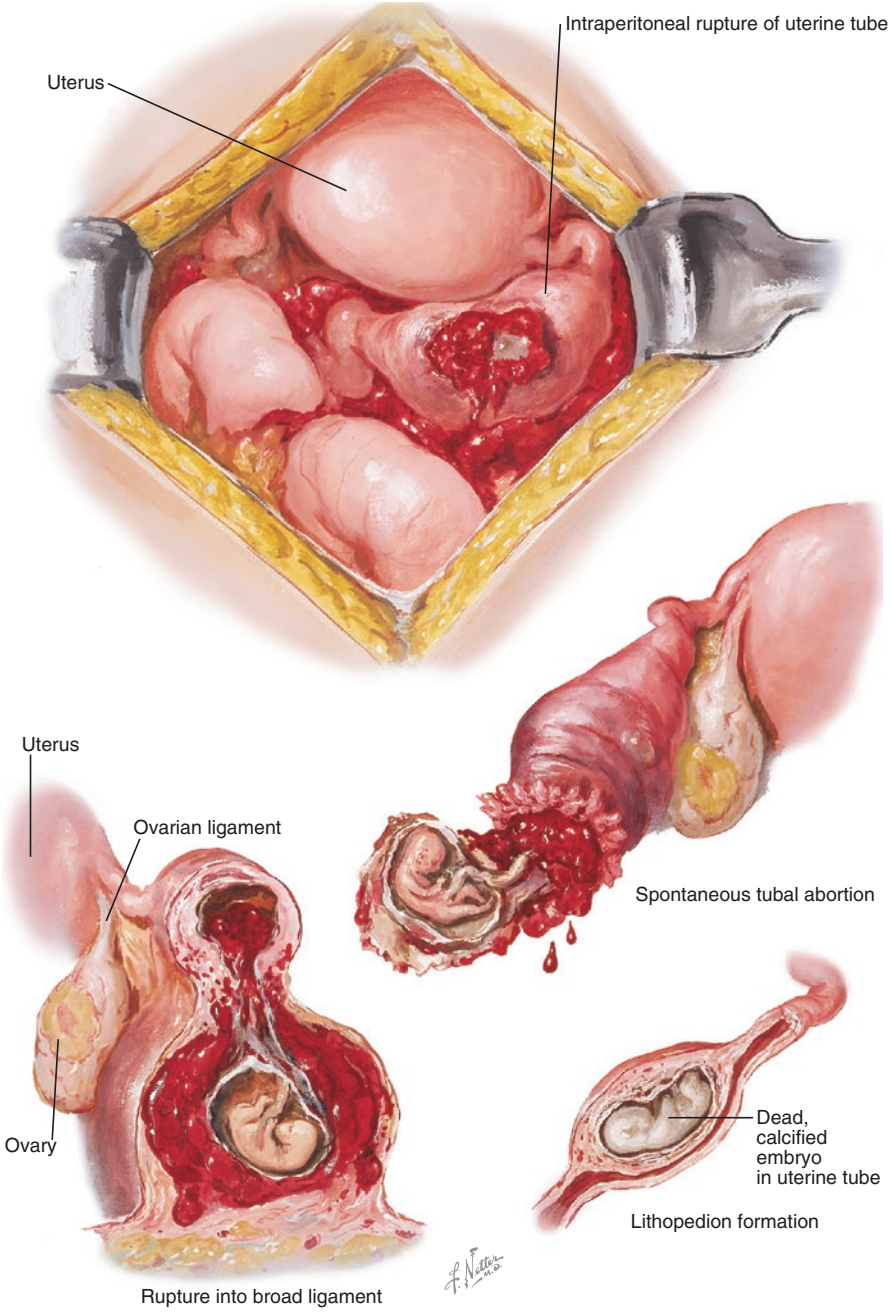


Fig. 6.11 Ectopic pregnancy 2 (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

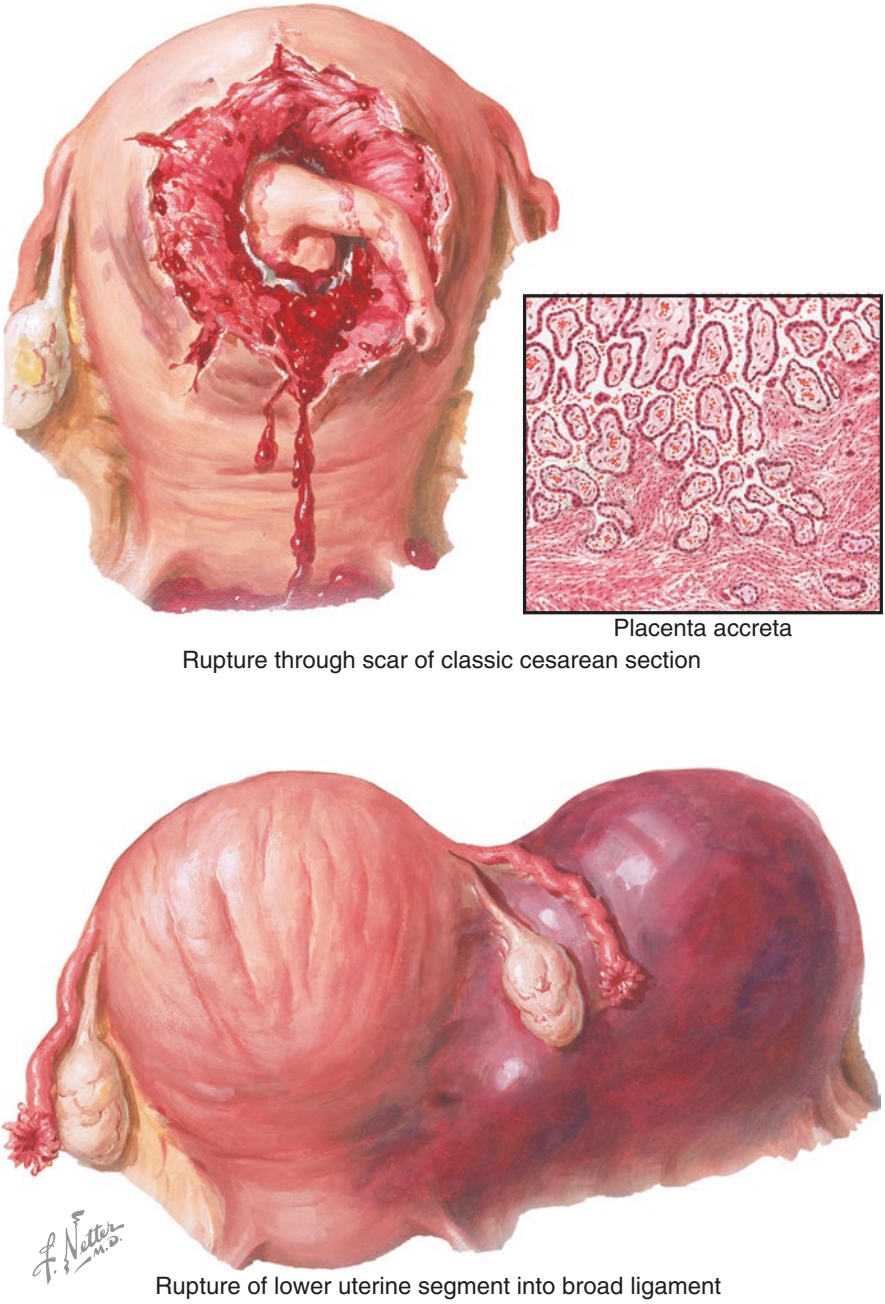


Fig. 6.12 Uterine rupture (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

incomplete rupture. Morbidity and mortality rates are considerably higher when rupture is complete. Prior cesarean delivery is the greatest risk factor for either form of rupture. Kieser and Baskett reported that 92% occurred in women with a prior cesarean birth [95]. Holmgren et al. described 42 cases of rupture in gravidas with a prior hysterotomy. Thirty-six patients were laboring at the time of rupture [96].

Diagnosis

Progress of labor in gravidas attempting Trial of Labor After Cesarean (TOLAC) is similar to regular labor, and there is no specific pattern that signals uterine rupture [97, 98]. Prior to the onset of hypovolemic shock, symptoms and signs in women with uterine rupture can appear unusual unless the possibility of rupture is kept in mind. Hemoperitoneum, for instance, as a result of ruptured uterus could cause diaphragmatic irritation with pain referred to the chest steering the clinician toward a diagnosis of pulmonary or amnionic fluid embolism instead of uterine rupture. The most consistent sign of uterine rupture is a Category II or III fetal heart rate pattern with variable heart rate decelerations that can progress into late decelerations and bradycardia (Fig. 6.13) [99].

Of 36 cases of uterine rupture during a trial of labor reported by Holmgren et al., there were fetal signs in 24, maternal in eight, and both in three [96]. Most patients do not experience cessation of contractions at the time of uterine rupture; therefore, the use of intrauterine pressure catheters has not been shown to be effective in the diagnosis [100].

The appearance of uterine rupture is identical to that of placental abruption in some patients. The majority, however, shows remarkably little appreciable pain or tenderness. Furthermore, since most gravidas in labor are managed for discomfort

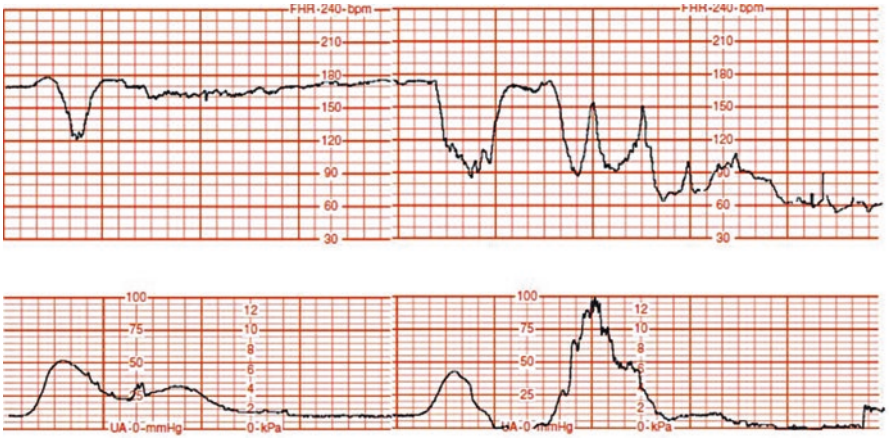


Fig. 6.13 Category III fetal heart rate pattern associated with uterine rupture (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

with either narcotics or epidural analgesia, pain and tenderness might not be obvious. Rupture is usually evident because of fetal intolerance signs and intermittently because of maternal hypovolemia due to concealed hemorrhage.

Loss of station can be apparent by pelvic examination if the fetal presenting part has entered the pelvis with labor. When the fetus is partially or totally extruded through the uterine rupture site, abdominal palpation or vaginal examination can help to identify the presenting part, which will have vacated the pelvic inlet. Firm contractions can be felt alongside the fetus.

Uterine Incarceration

Uterine incarceration refers to a pregnant uterus that is entrapped in the pelvis between the pubic symphysis and sacral promontory. It has been reported to occur in 1 in 3000 to 10,000 pregnancies [101].

Uterine retroversion occurs in up to 20% of pregnant women [102]. Uterine enlargement in the first trimester produces a rise of the fundus from the hollow of the sacrum to an anterior ventral position. This spontaneously corrects the retroversion. However, rarely, the fundus becomes wedged below the sacral promontory, which displaces the bladder and cervix upward and anterior, and in turn, can produce urethral obstruction [103].

Risk factors that contribute to uterine incarceration include adhesions from prior surgery, pelvic inflammatory disease, endometriosis, uterine leiomyomata, uterine anomalies, and a deep sacral concavity with pronounced sacral promontory. Laxity of the pelvic support architecture can also be involved in this process [104, 105]. In some patients, there are no risk factors at all [106, 107].

Gravidas usually present at 14–16 weeks of gestation with symptoms, associated with pressure on the anatomic structures adjacent to the enlarging uterus. The most common symptoms are pain and progressive difficulty with voiding. The pain can be abdominal, suprapubic, or in the lumbosacral spine; or can be limited to pelvic discomfort or a feeling of pelvic fullness. Urinary complaints include frequency, dysuria, sensation of incomplete bladder emptying, dribbling small volumes due to overflow incontinence, and, often, urinary retention. Gastrointestinal symptoms include rectal pressure, tenesmus, and worsening constipation due to compression of the rectum [104, 105]. Vaginal bleeding has also been described. Symptoms can be intermittent, resolving for a period of time and then returning weeks later.

The principal sign on physical examination is severe anterior displacement of the cervix behind the pubic symphysis. The examiner may not be able to visualize the cervix with a speculum or palpate the external os on pelvic examination [102]. Furthermore, the vagina is angulated anteriorly and a large, boggy, smooth, nontender mass (the incarcerated uterus) fills the cul-de-sac.

The bladder is displaced superiorly and elongated from compression by the cervix and uterus. The fundus is located in the hollow of the sacrum; as a result, a fundal placenta can be mistaken for a placenta previa. The fetus can be seen posteriorly against the sacrum deep in the pelvis.

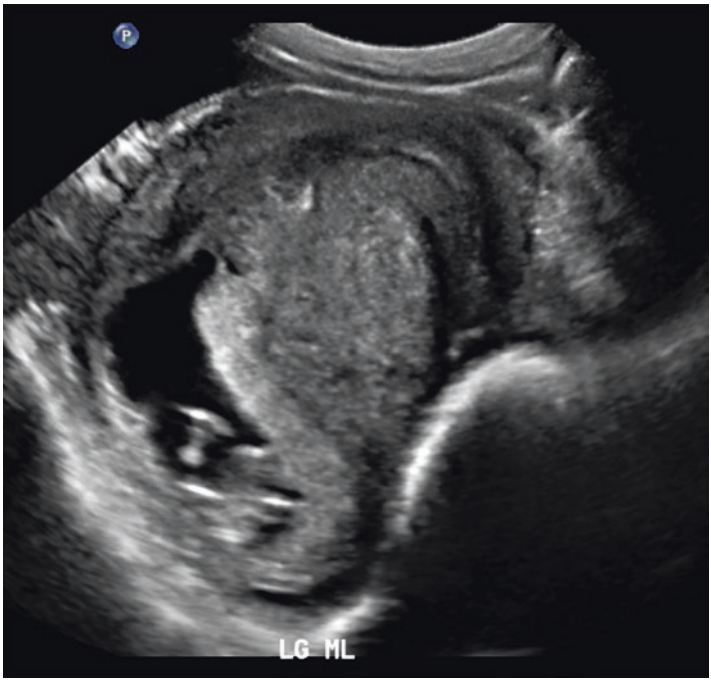


Fig. 6.14 Uterine incarceration (Personal Image of Peter B. Greenspan, DO, FACOG, FACS)

Sonographic imaging can demonstrate a cervix which might be obscured or appear thin and elongated, pulled anterior to the uterus [102]. Difficulty in identifying the cervix should raise suspicion for uterine incarceration [108] (Fig. 6.14).

The incarcerated uterus can produce complications such as an obstructed urethra. This can produce urinary retention to the point of hydronephrosis, urinary infection, and rupture of the bladder [105].

Malposition of the uterus can possibly compromise uterine arterial blood flow, which increases the risk of decidual bleeding, spontaneous abortion, oligohydramnios, fetal growth restriction, and fetal demise [109]. Second-trimester pregnancy loss has been reported to be as high as 33% [103, 104]. Van Winter et al. report an increased risk of premature rupture of membranes and preterm delivery [109].

Other complications described in case reports include uterine wall necrosis, uterine rupture, development of a cervicovaginal fistula, and rectal gangrene [105]. Compression of pelvic veins can promote thrombosis, resulting in postpartum pulmonary embolism in the absence of thrombosis in the deep veins of the lower limbs [106]. Labor is inevitably complicated by dystocia.

Incarceration can be confused with other physical findings such as pelvic masses, extrauterine pregnancy, adnexal torsion, leiomyomata, and uterine anomalies including uterus didelphys or rudimentary uterine horn [110].

Intervention is essential for the successful management of an incarcerated uterus. It is recommended to repeat a bimanual exam on any patient with a retroverted

uterus noted in the first trimester, at 16 weeks of gestation. If retroversion persists, reduction in the retroverted fundus may be indicated [111].

Passive reduction requires maneuvers on the patients' part in the knee-chest position, for 10 min at least 3 times a day. This works well in patients who are asymptomatic.

The use of manual reduction can be attempted without sedation or anesthesia, but those modalities may need to be implemented for success [112].

A ring forceps can be applied to the cervix and gently pulled toward the introitus to provide countertraction, while the fundus is being pushed cephalad. Use of sonographic guidance during manipulation of the uterus can be helpful [113].

In rare instances, colonoscopy, pelviscopy, or laparotomy has been employed to reduce uterine incarceration.

Recurrence is associated with persistence of predisposing factors mentioned above [104, 114].

Placental Abruption

Placental abruption, or abruptio placenta, is the premature separation of a normally implanted placenta from the uterus. Usually, abnormal maternal vessels in the decidua basalis rupture and cause the separation. Rarely, the separation can be caused by a disruption of the fetal-placental vessels [115]. The damaged vessels cause bleeding, resulting in a decidual hematoma that can lead to placental separation, destruction of placental tissue, and a loss of maternal-fetal surface area for nutrient and gas exchange.

Abruption is frequently associated with both acute and chronic processes. Thrombin, which is released in response to decidual hemorrhage or hypoxia, appears to play an active role in the pathogenesis of placental abruption [116]. Thrombin acts as a direct uterotonic, which augments the action of matrix metalloproteinases, and upregulates apoptosis genes, thus increasing the expression of inflammatory cytokines [116, 117]. These thrombin-mediated events initiate a cyclic pathway of vascular disruption, hemorrhage, inflammation, contractions, and rupture of membranes [115].

Incidence

Placental abruption occurs once in 100 births; however, a range of 1 in 75 to 1 in 226 deliveries has been reported [115, 118]. The range in incidence possibly reflects variable criteria for the diagnosis in addition to an increased recognition recently of milder forms of abruption. About one-third of all antepartum bleeding can be attributed to placental abruption [118]. The peak incidence of placental abruption occurs between 24 and 26 weeks of gestation [115]. The incidence has risen in the United States because of the increased rates of gestational diabetes mellitus, preterm labor, and umbilical cord abnormalities [119].

Clinical Manifestations

Various factors determine the clinical manifestations of placental abruption. These include the temporal nature of the abruption (acute versus chronic), the clinical presentation (overt versus concealed), and the severity [115]. An acute, frank abruption usually presents with sudden-onset vaginal bleeding, severe abdominal pain, and uterine contractions. Worsening of the placental separation results in uterine tenderness, tachysystole, non-reassuring fetal heart rate patterns, and fetal death can occur [120]. There is a poor correlation between the amount of vaginal bleeding and the extent of placental separation and its potential for fetal compromise. Concealed abruption is reported in 10–20% of cases [121]. With severe abruptions, >50% of the placental surface area separates [115]. In these clinical settings, maternal compromise in the form of consumptive coagulopathy can result from the triggering of the clotting cascade by hemorrhage and extensive thrombin deposition [120, 122].

The presentation of chronic abruption can be insidious and is commonly associated with ischemic placental disease [123]. Typically, these gravidas present with intermittent, light vaginal bleeding and evidence of chronic placental inflammation and dysfunction, such as oligohydramnios, fetal growth restriction, preterm labor, premature preterm rupture of membranes, and preeclampsia [124] (Fig. 6.15).

Risk Factors

Although the exact etiology of placental abruption is unclear, a variety of risk factors have been identified.

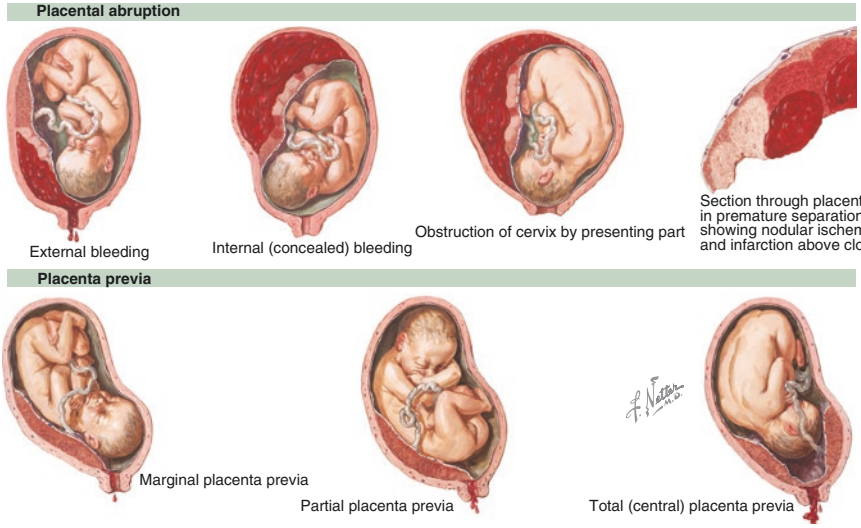


Fig. 6.15 Placental abruption, placenta previa (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

- Increasing parity and/or maternal age
- Cigarette smoking
- Cocaine abuse
- Trauma
- Maternal hypertension
- Preterm premature rupture of membranes
- Rapid uterine decompression associated with multiple gestation and polyhydramnios
- Inherited or acquired thrombophilia
- Uterine malformations or fibroids
- Placental abnormalities or ischemia
- Prior abruption

Diagnosis

Placental abruption is usually a clinical diagnosis that is supported by imaging, laboratory, and pathologic studies. Any gravida with findings of vaginal bleeding, preterm labor, abdominal pain, or trauma should prompt an investigation of placental abruption [115].

Imaging

Detection rates of abruption by sonography in the past were abysmal; however, recent advances in imaging have improved considerably. Hemorrhage in early gestation is usually hyperechoic or isoechoic. Resolving hematomas are hypoechoic within 1 week and sonolucent within 2 weeks of the abruption. Acute hemorrhage can be misinterpreted as a thickened placenta or fibroid.

Sonography is able to identify three predominant locations for placental abruption. These include subchorionic (between the placenta and the membranes), retroplacental (between the placenta and the myometrium), and preplacental (between the placenta and the amniotic fluid).

Figure 6.13 illustrates the classification of hematomas in and around the placenta. Figure 6.14 demonstrates a sonographic representation of a subchorionic abruption.

The location and extent of the placental abruption identified on ultrasound examination are clinically significant (Fig. 6.16). The worse prognosis for fetal survival is associated with retroplacental hematomas more so than subchorionic hemorrhage. Hemorrhage size is also predictive of fetal survival. Large retroplacental hemorrhages (>60 mL) are associated with a 50% or greater fetal mortality, while similarly sized subchorionic hemorrhages are associated with a 10% mortality risk [125].

Magnetic resonance imaging (MRI) is useful in diagnosing placental abruption when sonography is equivocal.

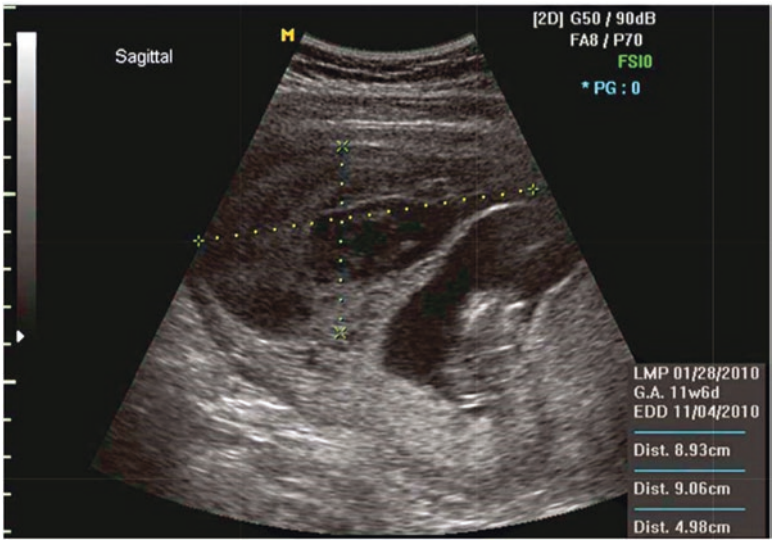


Fig. 6.16 Subchorionic hemorrhage (© McGraw-Hill Inc. All rights reserved. Williams' Textbook of Obstetrics, 24th ed. Used with permission)

Laboratory Findings

Few laboratory studies assist in the diagnosis of placental abruption. Hypofibrinogenemia and evidence of consumptive coagulopathy are indicative of a severe abruption; however, clinical correlation is necessary.

Abnormal serum markers early in pregnancy, such as an unexplained elevated maternal serum α-fetoprotein (MSAFP) and hCG, have been associated with an increased risk of subsequent placental abruption [115, 126].

Placenta Previa

Placenta previa is defined as the presence of placental tissue over or adjacent to the cervical os. While placental abruption is associated with a cause for abdominal pain in pregnancy, placenta previa is mentioned only in contradistinction to abruption, because bleeding from placenta previa is classically painless (see Fig. 6.13).

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Gynecologic Etiologies of Abdominal Pain in Pregnancy

7

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Adnexal Masses in Pregnancy

Introduction

The routine use of ultrasound in pregnancy, especially early pregnancy, has led to more incidental diagnoses of adnexal masses in women who were otherwise asymptomatic. The incidence of adnexal masses in pregnancy is 0.5–3.2% of live births, and 3.6–6.8% of patients with persistent masses are malignant [1]. Ovarian torsion is a gynecologic surgical emergency known to be increased in pregnancy. Of torsion cases, 10–22% occurred in pregnancy in some series [2, 3]. The exact incidence is unknown, but is estimated to be approximately 1 in 1800 [4].

Presentation

Most pregnant patients with adnexal masses are asymptomatic, with the diagnosis being incidentally discovered during antenatal ultrasound or at the time of cesarean delivery. The majority of symptomatic patients will present with nonspecific complaints such as abdominal or pelvic pain, constipation, abdominal distension, or loss of appetite, all of which are often attributed to pregnancy, thus unlikely to trigger a diagnostic evaluation.

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A small number of patients will present with acute abdominal pain, most commonly due to ovarian torsion or rupture of a mass. Most ovarian torsions occur in the later part of the first to early second trimester [5].

Causes

The most common benign adnexal masses diagnosed in pregnancy are usually functional simple cysts, being either follicular or corpus luteum cysts. Fibroids, mature teratomas (teratomata), and cystadenomas (cystadenomata), serous and mucinous, are other common benign cysts associated with pregnancy. Most pregnancy-associated ovarian malignancies are either malignant germ cell tumors, sex cord-stromal tumors, or epithelial tumors of low malignant potential (borderline tumors). Differential diagnoses should also include nongynecologic causes such as gastrointestinal (e.g., diverticular abscess, appendiceal abscess or mucocele or colorectal cancer) and urologic causes (e.g., pelvic kidney, or ureterocele).

Diagnosis

Diagnosis of an adnexal mass is generally made with ultrasound, which will usually provide sufficient information to guide management. Most cystic masses will resolve throughout the course of the pregnancy. Sonographic features of adnexal masses that predict persistence include size greater than 5 cm and "complex" morphology [6]. Adding color Doppler to ultrasound will increase specificity and sensitivity of the diagnosis. If additional imaging is required, magnetic resonance imaging (MRI) is the modality of choice (see Figs. 7.1 and 7.2).

Due to the quantitative increase in many tumor markers in normal pregnancy, such as human chorionic gonadotropin hormone, CA-125, and alpha-fetoprotein, these markers are not considered reliable for diagnosis or followed up in pregnancy unless significant elevations are found. Also, one must be aware that certain conditions in pregnancy may render the finding of even significant elevations not useful, such as in cases of fetal aneuploidy, open neural tube defects, or preeclampsia [7]. One tumor marker, human epididymis protein 4 (HE-4), appears to be unaffected by pregnancy [8]. It is currently used for treatment follow-up rather than screening of ovarian cancer. However, note that the baseline normal reference values are changed in pregnancy [9].

The diagnosis of ovarian torsion is made clinically and aided with Doppler ultrasound. Sonographic detection rates vary in different studies from 46% to 74% [10, 11]. A high index of suspicion is necessary for diagnosis of ovarian torsion in pregnant women as well as in nonpregnant women. Torsion should be suspected in all patients with an acute onset of severe pelvic or abdominal pain, which may be accompanied by fever or nausea, especially in the setting of an adnexal mass in the first or second trimester (see Fig. 7.3).

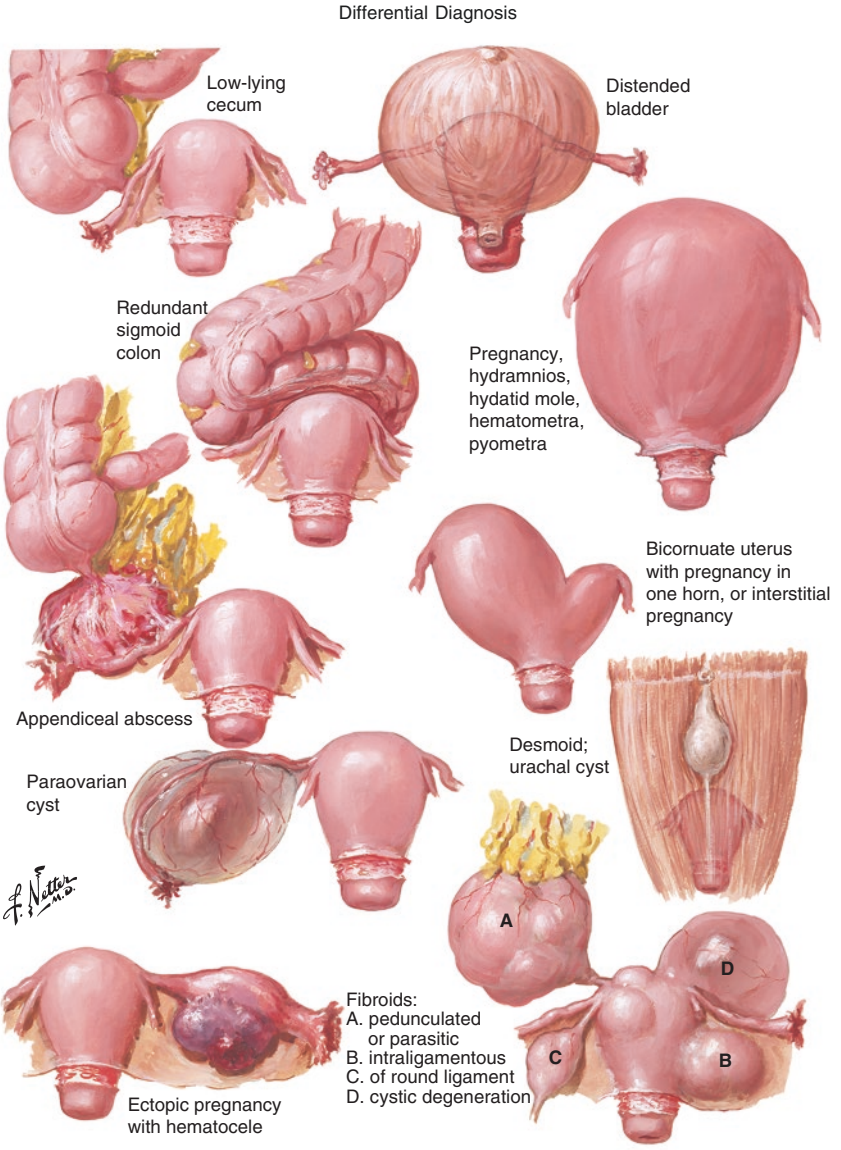

Fig. 7.1 Pelvic masses that may present in pregnancy (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Management

The definitive management of adnexal masses is surgery. However, because of the low likelihood of malignancy and acute complications associated with surgery during pregnancy, the risks of surgery frequently outweigh the benefits. Therefore,

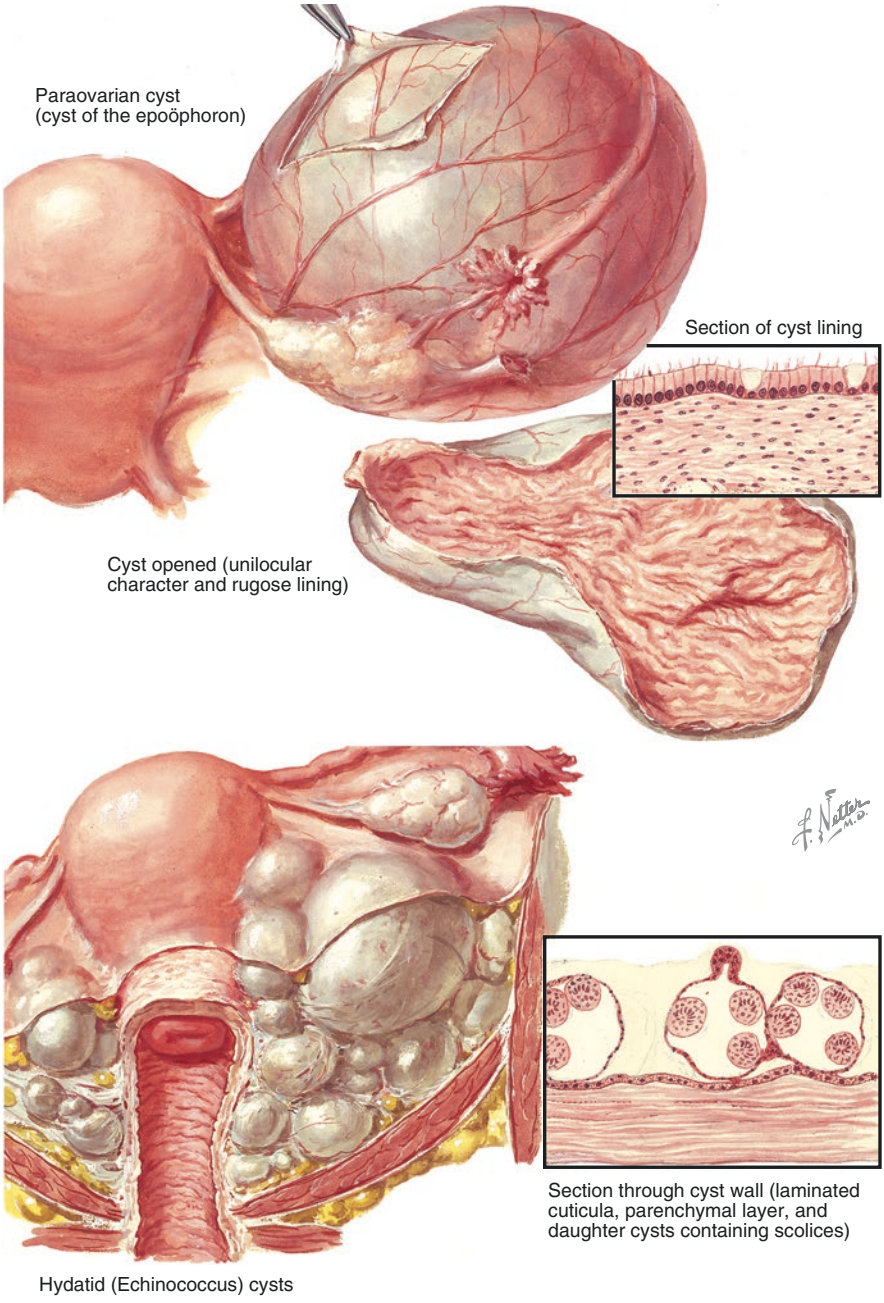

Fig. 7.2 Para-ovarian cysts are often identified during routine obstetrical sonographic evaluations (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

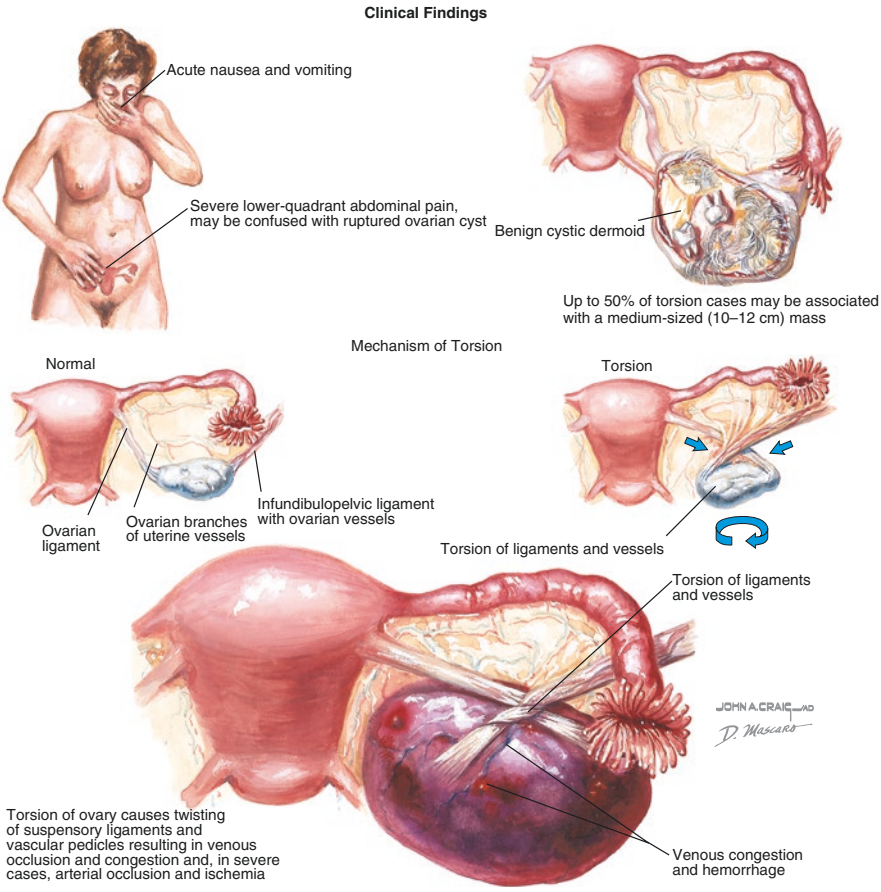

Fig. 7.3 Ovarian torsion (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

most adnexal masses in pregnancy can be managed expectantly and observed through the postpartum period. With the appropriate patient selection, adverse outcomes are not increased with conservative management [12]. Treatment should be tailored to the nature, symptoms, and clinical suspicion of the mass. Should there be a need for surgical excision, a minimally invasive approach in the early second trimester (around 14–16 weeks' gestation) will minimize the risks of preterm labor or loss of the pregnancy.

Indications for surgery include suspicion for ovarian torsion or malignancy as suggested by history, physical examination, or sonographic features. Laparoscopic versus laparotomy approach should be individualized depending on size of mass, gestational age, suspected malignancy, and expertise of the surgeon. More extensive surgery may be indicated for ovarian malignancies. The extent of the surgery must be tailored to the clinical situation such as gestational age, desire for retention of the

pregnancy, future fertility, histologic cell type, and extent of the disease. Some settings may be managed via minimally invasive surgery, while others might require a vertical skin incision, surgical staging, and cytoreduction [13].

The management of ovarian torsion is similar as that in nonpregnant patients, consisting of laparoscopic detorsion with or without ovarian cystectomy or oophorectomy. During the third trimester, the size of the gravid uterus may preclude a minimally invasive approach.

Ovarian cyst rupture is usually a self-limited event. However, significant hemoperitoneum leading to hemodynamic instability requires surgical exploration and source control of the bleeding.

Obstetrical Considerations

Generally, a vaginal delivery is not contraindicated unless the mass is fixed in the pelvis resulting in pelvic outlet obstruction. Cesarean delivery should be reserved for appropriate obstetrical indications. If a conservative approach is chosen, follow-up is appropriate 6–12 weeks after delivery, which coincides with return to pre-pregnancy physiology and resolution of most functional masses.

Uterine Fibroids in Pregnancy

Introduction

Uterine fibroids, or leiomyomata, are benign smooth muscle tumors of the uterus (see Figs. 7.4, 7.5, and 7.6). The prevalence of fibroids in pregnancy has been sited to be anywhere between 1.6% and 10% [14–16]. Fibroids are mainly asymptomatic and usually discovered during routine fetal ultrasound. Most fibroids will remain stable in size throughout pregnancy, while about 25% will increase and 10% will decrease in size. Enlargement occurs most commonly in the first trimester, with an average increase of approximately 12% [17, 18].

Presentation

Most fibroids are asymptomatic. Gravid patients may present with pelvic pain, pressure, or vaginal bleeding. Acute abdominal pain can occur in rare situations, namely, carneous degeneration, torsion, or prolapse through the cervix.

Degeneration occurs as a result of rapid growth of the fibroid subsequently outgrowing its blood supply, leading to ischemia and prostaglandin release, producing significant pain [19]. Other signs and symptoms may include low-grade fever, tenderness to palpation, or peritoneal signs. Torsion presents the same way, and should be suspected in the setting of a pedunculated or subserosal fibroid.

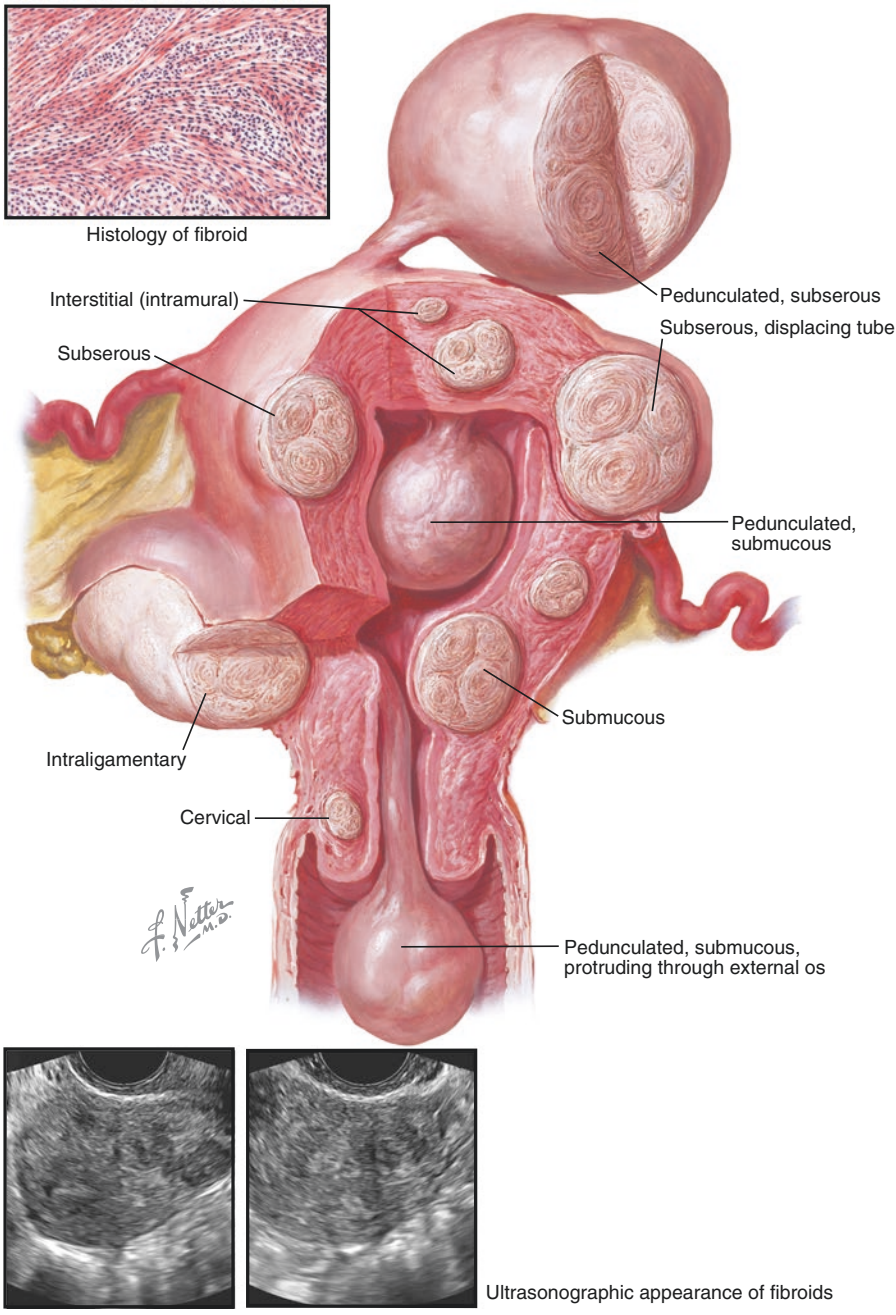

Fig. 7.4 Types of uterine leiomyomata (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

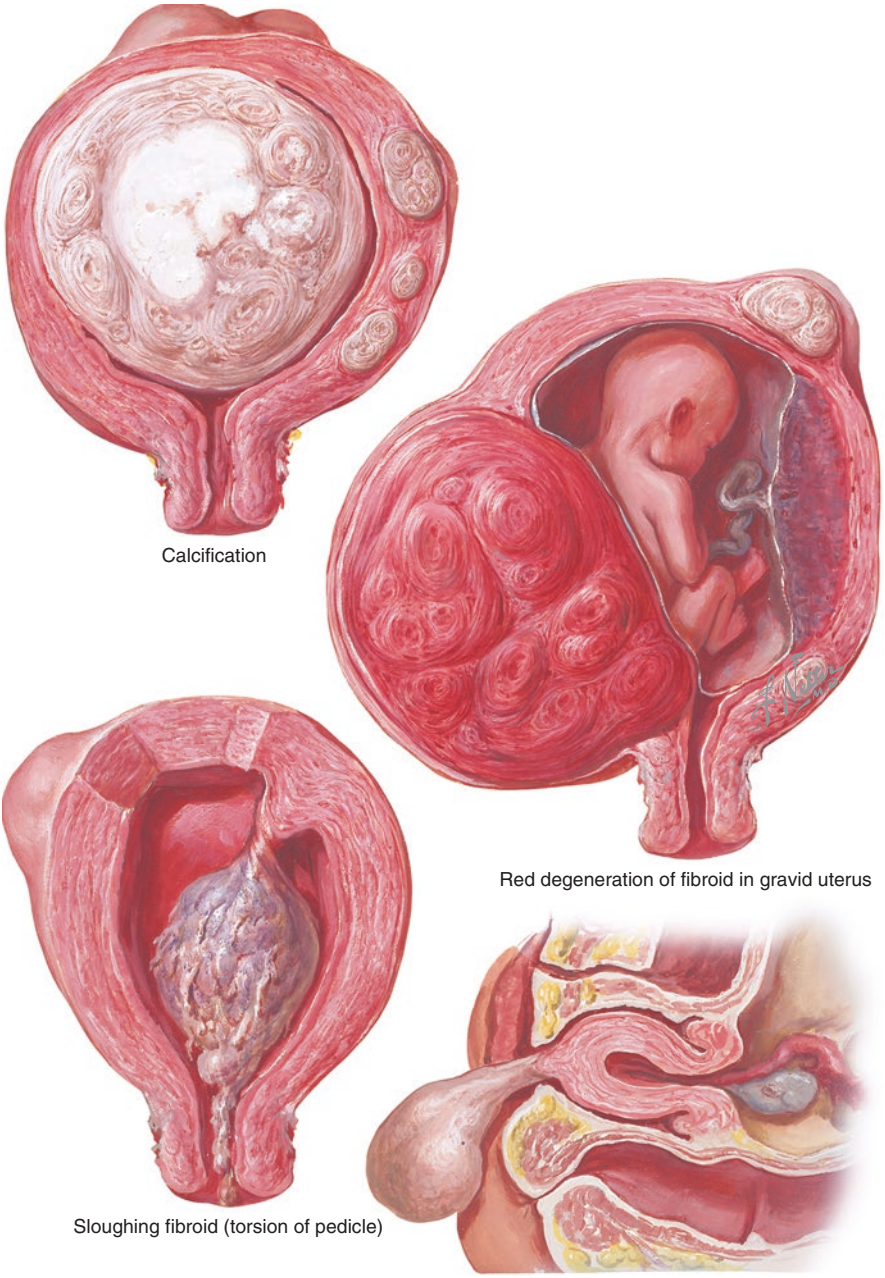

Fig. 7.5 Consequences of uterine leiomyomata (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

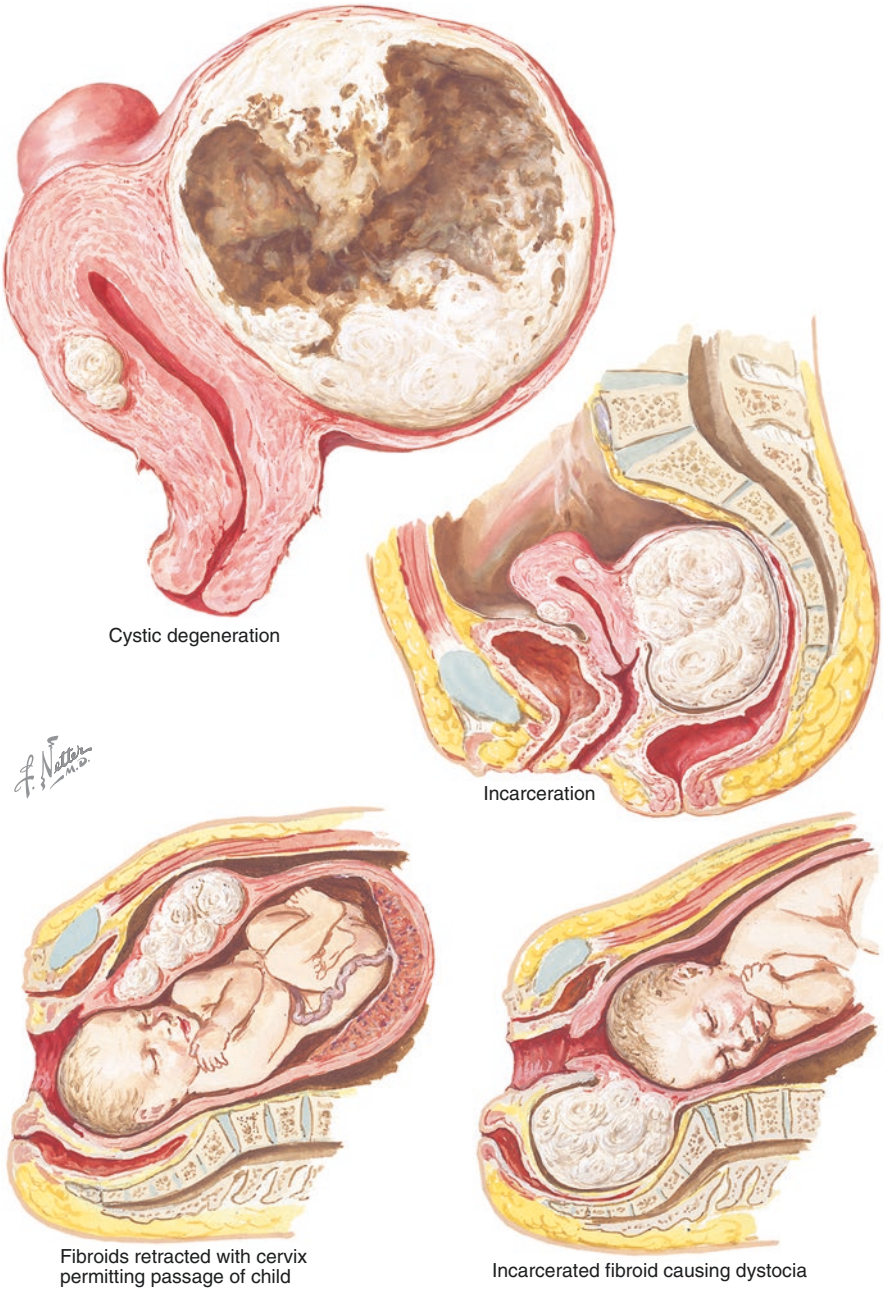

Fig. 7.6 Uterine leiomyomata complicating pregnancy (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Studies regarding the increased predisposition to placental abruption are inconsistent. Regardless, abruption may cause significant pain and should be ruled out [20].

Diagnosis

Ultrasound is usually sufficient to establish the presence of fibroids. Important characteristics to note are anatomic location, size, number, and blood supply. Torsion can be identified in pedunculated fibroids using Doppler sonography of the stalk, although this is not always possible [21]. Pelvic magnetic resonance imaging (MRI) without contrast can also aid in diagnosis if it is unclear. Note that gadolinium has been shown to be teratogenic in animal studies, thus it is considered contraindicated in pregnancy unless absolutely necessary [22].

Although we recommend ultrasound or MRI for detecting fibroids, there is no imaging modality that is perfectly sensitive or specific for detecting complications of fibroids such as degeneration or torsion, and diagnosis therefore must rely on a thorough history and physical examination. In rare select cases, a diagnostic laparoscopy or laparotomy may be necessary.

Management

Pain from degeneration of fibroids can be managed conservatively with oral analgesics, such as acetaminophen, a short course of nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen or indomethacin prior to 32 weeks, or opioid analgesia. Adverse fetal effects of NSAIDs when given after 32 weeks' gestation include premature closure of the ductus arteriosus, neonatal pulmonary hypertension, oligohydramnios, and fetal or neonatal platelet dysfunction and are best avoided [23]. Prior to 32 weeks' gestation, we suggest indomethacin dosing of 25 mg every 6 h for 48 h. Repeat courses can be administered as needed. Admission may be required for parenteral pain control.

Excision of a fibroid prolapsed into the vagina should only be performed in case of significant symptoms such as severe pain or bleeding, as intervention can lead to significant hemorrhage, rupture of membranes, and even fetal loss [24, 25]. In these cases, careful preoperative planning is crucial. Imaging to delineate the origin of fibroid, adequate anesthesia, and a blood type and cross-match should be available.

Torsion of a pedunculated fibroid is exceedingly rare. In a symptomatic patient, management of torsion is surgical. A laparoscopic approach is preferable if feasible, and it can be both diagnostic and therapeutic. In these cases, we recommend a myomectomy be carried out as detorsion is not usually sufficient [26].

Obstetrical Implications

Obstetrical complications of fibroids include spontaneous abortion, preterm delivery, fetal growth restriction, fetal malpresentation, and abnormal placentation (placenta previa or placental abruption) [20, 27–29]. In addition to counseling and routine prenatal care, there are no specific recommendations regarding follow-up of these patients. We recommend preemptive serial fetal growth ultrasounds in case of substantial fibroids that interfere with fundal height measurements. Neonatal outcomes are excellent overall. Poor outcomes are mainly related to prematurity.

Patients with fibroids are at increased risk for pre-labor cesarean delivery. Common reasons for cesarean delivery include fetal malpresentation, abnormal placentation, and presence of fibroid in the lower uterine segment. However, even after adjusting for the aforementioned factors, these patients still had a higher rate of cesarean delivery [30]. Gravid women with fibroids of any size may undergo a vaginal delivery, and cesarean delivery should be reserved for appropriate obstetrical indications. Patients should also be reassured that their likelihood of a successful vaginal delivery does not differ from that of the general population.

Endometriosis (see Fig. 7.7)

The state of pregnancy will often improve or eliminate endometriosis lesions as well as their associated symptoms. This is attributed to the altered hormonal environment of pregnancy that results in decidualization of the endometriotic lesions [31]. The decidualized lesions, however, may still be biologically active and produce symptoms and complications. There are reports in the literature that describe intestinal perforation [32] hemoperitoneum [33–35], uroperitoneum [36, 37], acute appendicitis [38, 39], and ruptured or infected ovarian endometrioma [40].

Endometriosis-induced complications that occur in pregnancy, albeit rare, may be associated with the expanding uterus putting traction on adhesions, increased friability of inflamed tissues, and alteration of vessel walls by decidualized lesions [40].

The rarity of these complications in pregnancy does not warrant additional monitoring or interventions in gravid women with an endometriosis history.

A retrospective populations-based study of more than 82,000 singleton pregnancies demonstrates a negative impact on pregnancy outcome in women with endometriosis. These adverse effects include an increased risk of preterm birth, preeclampsia, and abdominal delivery when compared to gravidas without endometriosis [41]. Other studies have shown that endometriosis is associated with an increased risk of spontaneous abortion, ectopic pregnancy, placenta previa, unexplained antepartum hemorrhage, postpartum hemorrhage, and preterm delivery when compared with unaffected women [42].

Other studies, however, report decreased or no change in risk of hypertensive disorders of pregnancy in gravidas with endometriosis [43, 44]. There is no known mechanism attributed to these problems and, again, closer scrutiny of pregnant women with endometriosis is not warranted [40].

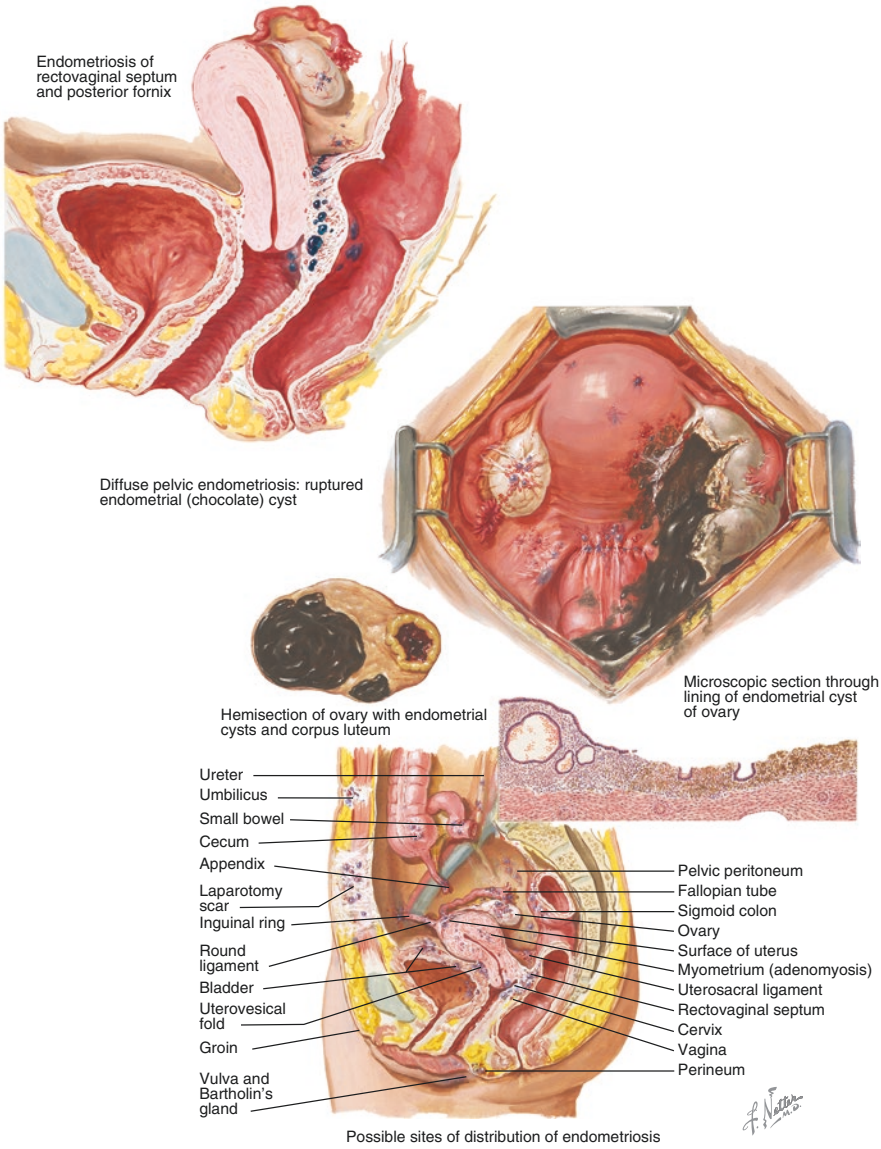

Fig. 7.7 Endometriosis (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Ovarian Malignancy in Pregnancy

The incidence of ovarian malignancy during pregnancy is generally lower than that of the general population, mainly because pregnancy occurs in a younger population [1]. Currently, the most common ovarian malignancy in pregnancy is germ cell tumors, and up to 30% of all ovarian malignancies are dysgerminomas.

Presentation for ovarian malignancy is generally similar to that of all adnexal masses with some exceptions. Sex cord-stromal tumors, although rare in pregnancy, can lead to evidence of hormonal excess (hyperestrogenism or virilization). Advanced stage ovarian malignancy may lead to small bowel obstruction.

When ovarian malignancy is suspected, the patient should be immediately referred to a gynecologic oncologist. Ovarian cancer, like most gynecologic malignancies, is surgically staged. During pregnancy, if discovered in the first trimester, the best time for surgery is after 8-10 weeks, when placental function is established and the corpus luteum has involuted, should there be a need for an oophorectomy. Surgical staging during pregnancy usually entails a unilateral salpingo-oophorectomy, omentectomy, peritoneal biopsies, lymphadenectomy, and peritoneal washings. More comprehensive staging will include the aforementioned in addition to a total abdominal hysterectomy and bilateral salpingo-oophorectomy. If the contralateral ovary appears normal, there is no need for ovarian biopsies or resection on that side. If discovered in the third trimester, more complete staging can be completed at the time of cesarean or after delivery. Decisions regarding timing and choice of surgery as well as need for adjuvant or neoadjuvant chemotherapy are made in consultation with a gynecologic oncologist. Note that pregnancy is not a contraindication to most chemotherapeutic agents, especially after the first trimester.

Prognosis mainly depends on the stage of the disease at the time of diagnosis and histologic tumor type, and is similar to that in nonpregnant patients.

Timing of delivery should be individualized. Things to consider are the stage and type of cancer, timing in pregnancy, and patient wishes regarding treatment and continuation of pregnancy especially before viability.

Cervical Intraepithelial Neoplasia and Cervical Cancer

Introduction

Although cervical cancer is the leading cause of gynecologic malignancy worldwide, it is rather uncommon in the developed world due to the Papanicolaou (Pap) smear. Cervical dysplasia, otherwise known as cervical intraepithelial neoplasia (CIN), is a pre-cancerous lesion that is not infrequently diagnosed, especially in pregnancy when women tend to have the most consistent medical care.

Presentation

CIN is usually asymptomatic, but may present with abnormal vaginal or postcoital bleeding. Cervical malignancy is a rare cause of pain. However, advanced disease with local invasion can lead to pelvic or lower back pain or pressure.

Diagnosis

Diagnosis is first suspected with a Pap smear and confirmed by directed colposcopic biopsies.

For cervical dysplasia found on Pap smear, we recommend following the American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines. This generally leads to observation without therapy, which is appropriate for pregnant women with cervical dysplasia if invasive cervical cancer has been excluded by colposcopy with or without biopsies. Of note, endocervical curettage is contraindicated in pregnancy, although the evidence that it adversely affects pregnancy is poor [45].

Cervical cancer is the only gynecologic cancer that is clinically staged. Staging in the nonpregnant woman includes physical examination and imaging, which consists of chest and skeletal radiographs, intravenous pyelogram, and barium enema. Other imaging studies may not be used for staging purposes. However, there are limited recommendations for staging in the pregnant woman, and it should be individualized [46]. Magnetic resonance imaging (MRI) and ultrasound may need to be used in this situation to plan management approach and can be repeated during pregnancy if necessary (see Table 7.1).

Management

Management generally depends on time of diagnosis, desire for pregnancy continuation, and FIGO stage. As a rule, pregnancy termination is offered before 24 weeks of pregnancy, and pregnancy continuation after 24 weeks due to fetal viability. Pregnancy termination is subject to local laws, and treatment is as in the nongravid patient. When pregnancy is continued, an early cesarean delivery is planned as soon as fetal maturity is reached.

If pregnancy continuation is desired, MRI at diagnosis and at least one more time later in pregnancy is recommended to determine tumor growth. As a rule, cervical cancer growth during pregnancy is slow. Conization during pregnancy should be avoided due to the risk for severe bleeding requiring blood transfusion, spontaneous abortion, premature rupture of membranes, preterm delivery, infection, and fetal loss [47]. Conization (cold knife or loop electrosurgical excision procedure) in the operating room is an option only if absolutely necessary and thought to alter the course of the treatment or delivery. Patients need to be counseled on the risks involved.

In advanced stages, either expectant management until early cesarean delivery or platinum-based neoadjuvant chemotherapy until cesarean delivery are adequate options and depends on patient's clinical condition and extent of disease [46]. The effects of chemotherapy on pregnancy are agent, dose, and gestational age-dependent. In the first 4 weeks of gestation, the pregnancy will result in loss or there will be no effect at all, known as the "all or none" phenomenon. Between 4 and 12 weeks' gestation , teratogenicity may occur depending on the agent used. Chemotherapy is

Table 7.1 FIGO staging of cervical cancer [57]

I	*Cervical carcinoma confined to the cervix*
IA	Invasive carcinoma diagnosed only by microscopy; stromal invasion with a maximum depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less; vascular space involvement, venous or lymphatic, does not affect classification
IA1	Measured stromal invasion ≤3.0 mm in depth and ≤7.0 mm in horizontal spread
IA2	Measured stromal invasion >3.0 mm and ≤5.0 mm with a horizontal spread ≤7.0 mm
IB	Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2
IB1	Clinically visible lesion ≤4.0 cm in greatest dimension
IB2	Clinically visible lesion >4.0 cm in greatest dimension
II	*Cervical carcinoma invades beyond uterus but not to pelvic wall or to lower third of vagina*
IIA	Tumor without parametrial invasion
IIA1	Clinically visible lesion ≤4.0 cm in greatest dimension
IIA2	Clinically visible lesion >4.0 cm in greatest dimension
IIB	Tumor with parametrial invasion
III	*Tumor extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or nonfunctional kidney*
IIIA	Tumor involves lower third of vagina, no extension to pelvic wall
IIIB	Tumor extends to pelvic wall and/or causes hydronephrosis or nonfunctional kidney
IV	*Tumor invades mucosa of bladder or rectum and/or extends beyond true pelvis*
IVA	Tumor invades mucosa of bladder or rectum
IVB	Tumor extends beyond true pelvis

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generally thought to be safe after organogenesis is completed (after 15 weeks). One meta-analysis reported healthy newborns in two-thirds of patients who received chemotherapy for cervical cancer between 17 and 33 weeks of gestation [48].

Obstetrical Implications

No consensus has been reached regarding timing of delivery in those who desire pregnancy preservation. Timing depends on gestational age as well as disease stage at diagnosis. Optimally, a full-term pregnancy is desirable. However, this may not always be feasible, and should be individualized.

In cases of early stage disease, mode of delivery should be as per routine obstetrical indications. In case of macroscopic disease (FIGO stage IB1 or higher), cesarean delivery is preferable due to risk of tumor seeding at episiotomy site, cervical

hemorrhage, infection, and obstruction of birth canal [49]. Definitive surgery for cure may be attempted at time of cesarean delivery in select patients with a cesarean radical hysterectomy.

Pelvic Infection (Pelvic Inflammatory Disease and Tubo-Ovarian Abscess)

Introduction

Pelvic inflammatory disease (PID) is an infection of the upper female reproductive tract, involving the uterus and/or adnexae (see Fig. 7.8). Tubo-ovarian abscess (TOA) is a pelvic abscess that may result from untreated or mismanaged PID (see Fig. 7.9). They are generally a result of a sexually transmitted infection. The incidence of PID and TOA in pregnancy is unknown but exceedingly rare, limited to case reports in the literature [50]. This is thought to be due to the cervical mucous plug that prevents ascending cervical infection into the uterine cavity. Although the initial culprit is commonly a cervicitis due to *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, the etiology of upper genital tract infections is usually polymicrobial [51]. PID may occur in the first trimester before the development of the mucous plug. Severe PID can cause tubo-ovarian abscess and/or sepsis (see Fig. 7.10).

Presentation

Patients with PID typically present with lower abdominal pain, with or without fever, chills, nausea, dyspareunia, or vaginal spotting or bleeding. A ruptured tubo-ovarian abscess (TOA) usually presents with severe acute abdominal pain and possibly peritonitis, but not always. Occasionally, right upper quadrant pain can occur due to perihepatitis (Fitz-Hugh-Curtis syndrome).

Risk factors include young age (less than 25 years), multiple sexual partners, personal history of sexually transmitted infections, or PID [52], as well as assisted reproductive technology [50]. Pregnancy is a protective factor.

Diagnosis

PID is diagnosed clinically. The Center for Disease Control (CDC) diagnostic criterion includes pelvic pain in a sexually active woman with either uterine, adnexal or cervical motion tenderness, and other causes are ruled out [53]. Pelvic tenderness is highly sensitive but not specific. Cervical inflammation may be apparent on speculum exam, with friability and erythema as well as purulent discharge. Cervical nucleic acid amplification test (NAAT) for gonorrhea or chlamydia should be performed. A positive NAAT is useful but not necessary for diagnosis. Besides ruling out other suspected etiologies, laboratory work-up is nonspecific and unnecessary.

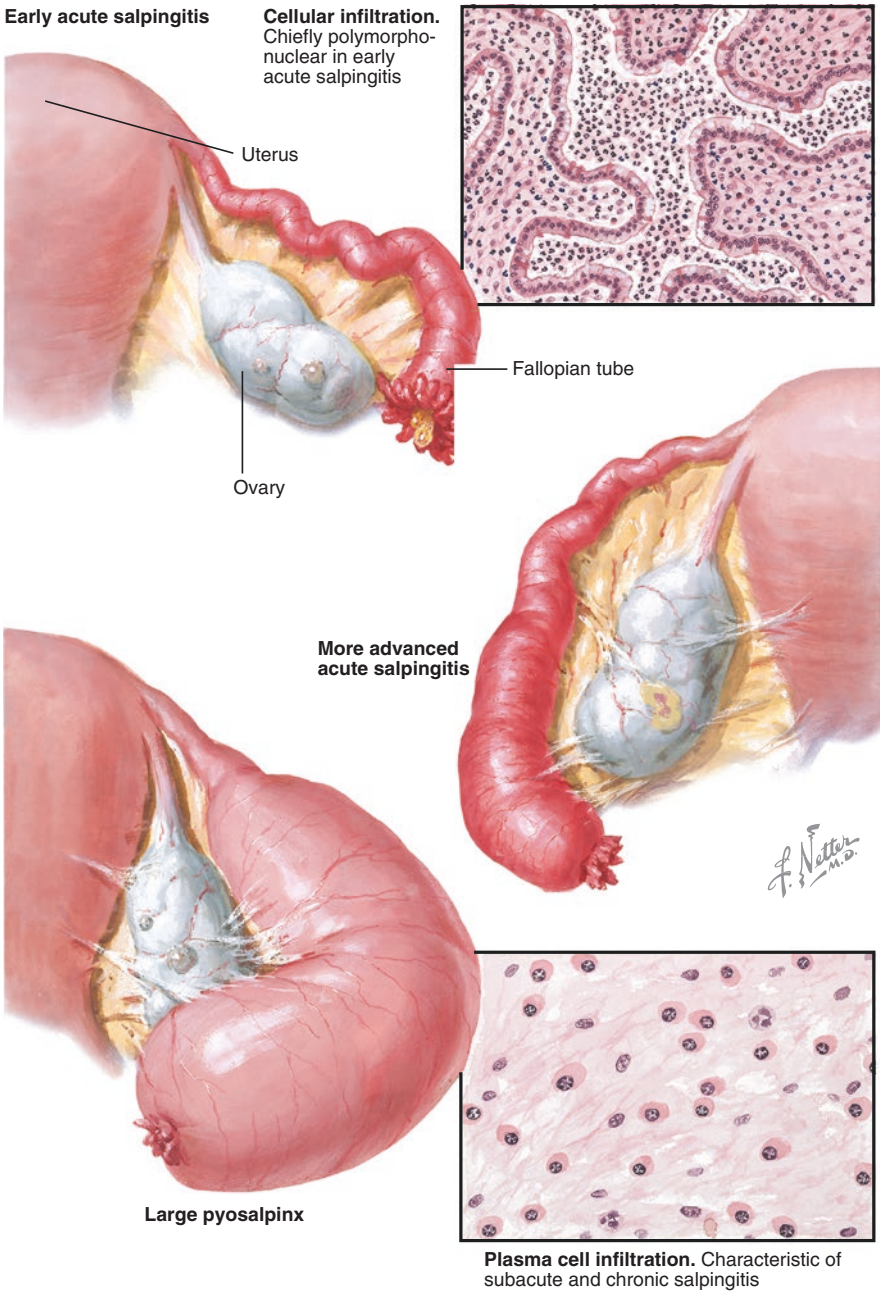

Fig. 7.8 Pelvic inflammatory disease (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

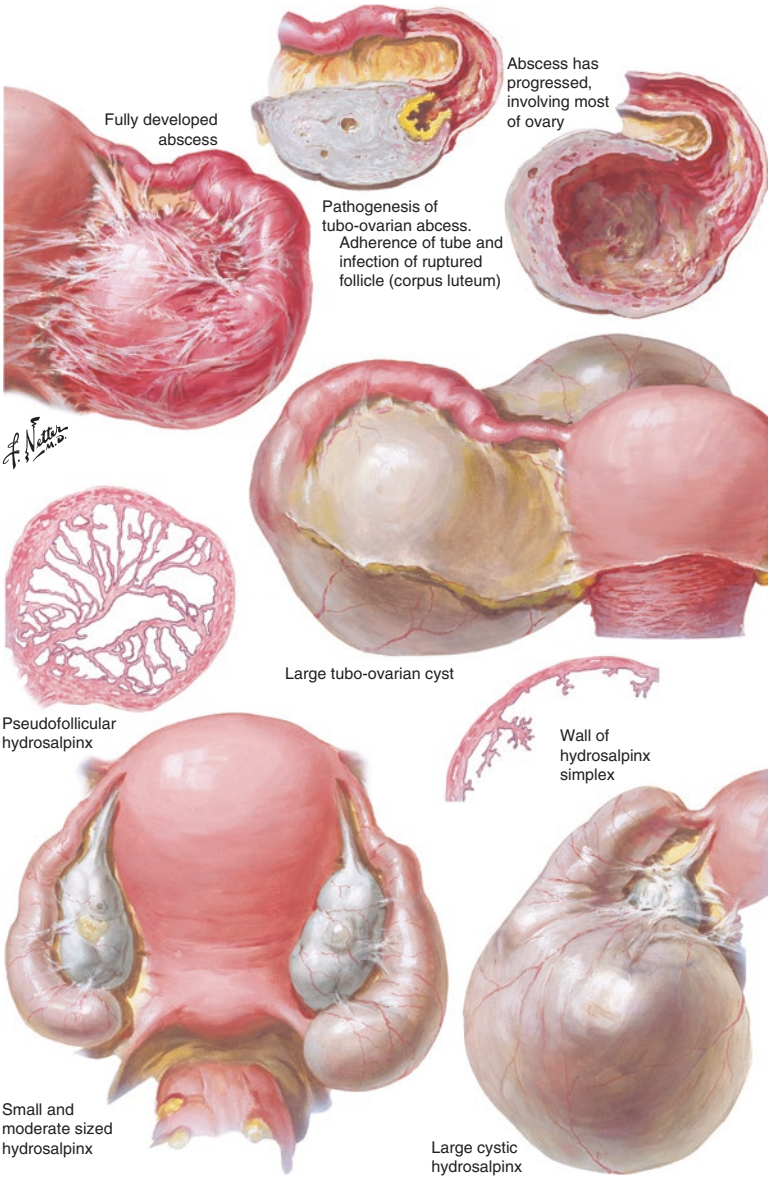

Fig. 7.9 Tubo-ovarian abscess (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

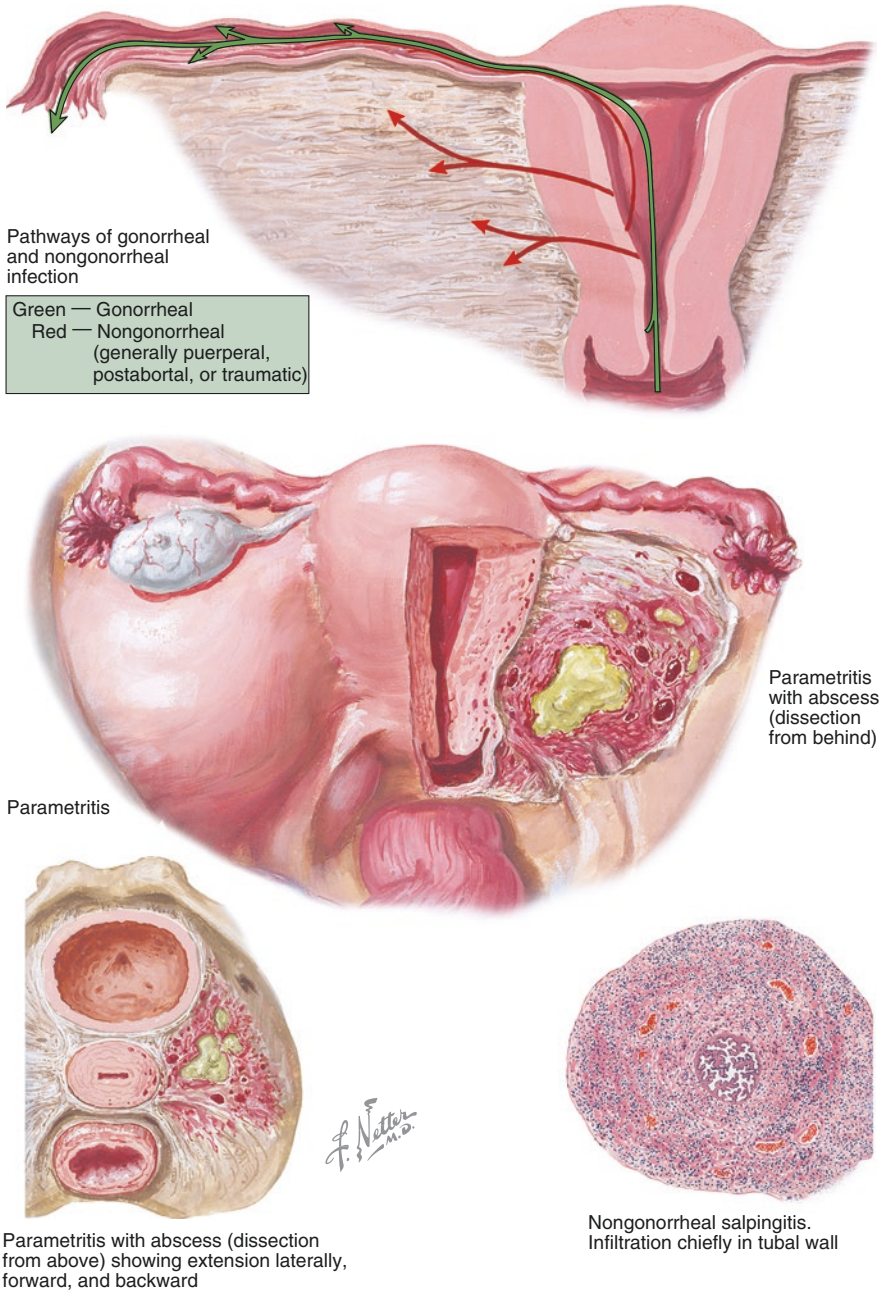

Fig. 7.10 Pelvic abscess (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

Additional imaging is not necessary in the nongravid patient. However, due to the rarity of this condition in pregnancy, we suggest a pelvic ultrasound for fetal assessment as well as to rule out other etiologies. Direct confirmation during surgery is rarely necessary for diagnosis, although has been used historically.

TOA can present the same way. A high index of suspicion is necessary, especially in patients who do not respond to antibiotic treatment for PID. Sonography is first line for diagnosis of TOA. However, magnetic resonance imaging or computer tomography may be necessary with advanced gestation and poor visualization of the adnexa.

We recommend screening for other sexually transmitted infections once the diagnosis is made.

Management

Treatment of PID is with antibiotics. The CDC recommends hospitalization and parenteral treatment for all pregnant women [53]. Note that regimens including doxycycline should be avoided in pregnancy due to its teratogenic effect on fetal bones. Studies are lacking specifically addressing PID in pregnancy, but azithromycin should be used as a substitute for doxycycline. One study showed high PID cure rates in nongravid patients used azithromycin [54], and several randomized controlled trials have shown effectiveness of azithromycin for cervical chlamydial infection in pregnancy [55, 56]. The following outlines our suggested regimens of initial antibiotic in treatment of PID in pregnancy, adapted from the original recommendations of the CDC [53]:

1. Cefotetan 2 g IV every 12 h plus azithromycin 1 g orally or IV every 24 h
2. Cefoxitin 2 g IV every 6 h plus azithromycin 1 g orally or IV every 24 h
3. Clindamycin 900 mg IV every 8 h plus gentamicin loading dose IV or IM (2 mg/kg), followed by a maintenance dose (1.5 mg/kg) every 8 h. Single daily dosing (3–5 mg/kg) can be substituted

Once clinical improvement is noted, the patient may be switched to an oral regimen to continue a total of 14 days of antibiotics, which consists of azithromycin 1 g orally or IV every 24 h for 14 days, with or without metronidazole 500 mg orally twice a day.

TOA can also be managed with antibiotic therapy alone on most occasions. However, if clinical improvement is not seen within 48–72 h, surgical or radiologic drainage of abscess may be necessary. A ruptured TOA needs surgical exploration.

The patient should be counseled on safe sexual practices prior to discharge. Male sexual partners need to be evaluated and treated. Regardless of treatment of their sexual partners, all women with positive chlamydia or gonorrhea should undergo a test-of-cure 3–4 weeks after completion of treatment, preferably with NAAT [53].

Pregnancy Implications

Short- and long-term effects of PID and TOA have been well studied in the non-gravid population, which include infertility, ectopic pregnancy, and chronic pelvic pain. However, much less is known of these conditions in pregnancy, making it is difficult to assess fetal risk. When treated promptly and appropriately, pregnancy outcomes are thought to be good. As long as the patient is clinically stable, the fetus should remain unaffected. A ruptured TOA is a surgical emergency. Sepsis can lead to rapid deterioration of maternal and fetal conditions and preterm delivery.

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Gastrointestinal Etiologies of Abdominal Pain in Pregnancy

8

Farzad Alemi, Teisha Shiozaki, Alexis Graham-Stephenson, and Alexandra Bors

Introduction

While the etiologies of acute abdomen in pregnancy are varied and manifold, among the most common include disorders of the gastroenteric and hepatopancreatobiliary systems (see Fig. 8.1). This chapter systematically reviews both the common and uncommon causes of acute abdomen in the gravid patient due to intra-abdominal etiologies typically evaluated by gastroenterologists and general, colorectal, and hepatobiliary surgeons. Unique considerations in the pregnant patient are explored with respect to diagnosis and management options to provide optimal care to both mother and fetus.

Gastroesophageal Reflux Disease

Background

In the nongravid patient, gastroesophageal reflux disease (GERD) affects close to 40% of patients; during pregnancy, approximately 30–50% of patients are affected [1]. GERD symptoms, including heartburn and regurgitation, most frequently occur in the third trimester of pregnancy [2], but the most important risk factor is preexisting GERD [1]. Interestingly, GERD symptoms can disappear after delivery, and can recur with subsequent pregnancies [3]. This is, perhaps, due to the effects of progesterone which mediates lower esophageal sphincter relaxation leading to a decrease in muscle tone by approximately 33–50% by 36 weeks' gestation [4, 5]. Recent studies have shown the significant impact of GERD on quality of life, with

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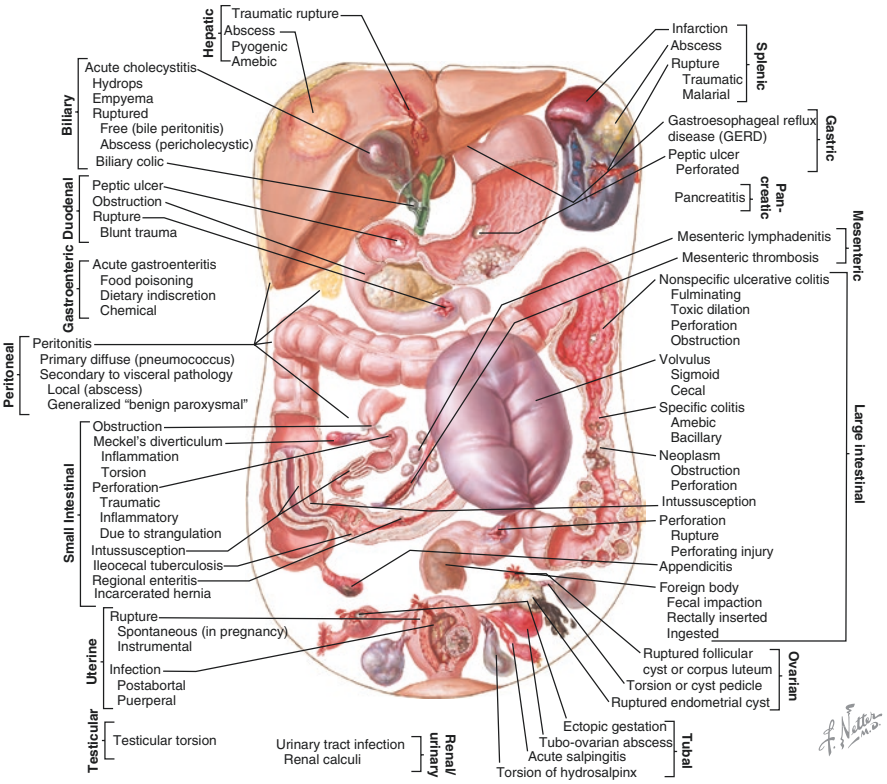

Fig. 8.1 Causes of abdominal pain (© 2016 Elsevier Inc. All rights reserved. www.netterimages.com. Used with permission)

more than 70% of gravid patients reporting heartburn and regurgitation which lead to significant reductions in social and emotional functioning [1].

Diagnosis

Typical symptoms of GERD include heartburn and regurgitation, but it is also associated with nausea and vomiting. Extra-esophageal manifestations are oftentimes present, including asthma (3.5%), chest pain (6%), and cough (1.2%) [6]. Usually the diagnosis of GERD can be made clinically without the use of further imaging. If necessary for intractable cases, endoscopy is the procedure of choice for diagnosis [7]. However, manometry and pH studies can also be performed safely if necessary [5].

Treatment

Lifestyle modifications are the primary modality employed to treat GERD during pregnancy. This includes changes in meal sizes and frequency as well as timing.

Identification of foods which trigger symptoms is critical, and avoidance of those foods is encouraged. If nighttime GERD is problematic, those patients should elevate the head of the bed.

Medical management of GERD is used in conjunction with lifestyle modifications as first-line therapy and effective for most patients [8]. Mild-to-moderate cases of GERD should be treated with H_2 antagonists and antacids. All proton pump inhibitors are classified as safe for consumption during pregnancy with no adverse outcomes reported such as spontaneous abortion or congenital malformations [1].

Surgical management for GERD, such as laparoscopic fundoplication, has not been reported in the gravid population owing to the efficacy of medical management. In some instances, patients with underlying severe GERD have undergone surgery prior to pregnancy, with good results [9].

Peptic Ulcer Disease

Background

The incidence of peptic ulcer disease (PUD) in pregnancy is low, occurring in 78 of 60,994 women with a medically diagnosed ulcer [10]. Peptic ulcer disease, including ulceration of the stomach, duodenum or any combination thereof, often presents with nausea, emesis, and dyspepsia and rarely can be asymptomatic with gastrointestinal bleeding as the presenting symptom [1, 11]. Other conditions that can present similarly include GERD, nonulcer dyspepsia, and hyperemesis gravidarum [12].

There is some thought that PUD improves during pregnancy [1]. Possible explanations include increased prostaglandins and estrogens that offer protective effects to the gastric and duodenal mucosa, immunologic tolerance from pregnancy, healthier lifestyle including reduction in tobacco and alcohol use, diet alterations, and better medical care [1–3].

Diagnosis

Diagnosis of PUD in pregnancy is limited, due in part to self-treatment and decreased reporting, hesitancy of physicians to recommend diagnostic workup during pregnancy, and misdiagnosis with similarly presenting conditions common in pregnancy [3]. While esophagogastroduodenoscopy (EGD) is an accepted and studied diagnostic tool in pregnancy, the use of other studies for nausea and emesis which may otherwise be used for diagnosis, such as the upper GI series, would be contraindicated due to the risk of radiation exposure [3]. The most frequent indications for EGD in pregnancy are refractory dyspepsia and GI hemorrhage [3]. A 2011 European study involving treatment for PUD found that only a small number of those diagnosed with PUD have had an endoscopic exam for diagnosis and the majority of those cases were self-diagnosed [1].

Diagnosis of a perforated peptic ulcer is typically clinical, with findings of peritonitis and acute abdomen. Performance of a plain film to document free intraperitoneal air is critical and not contraindicated in pregnancy [13]. EGD, however, is contraindicated when perforation is suspected.

Diagnosis of a bleeding ulcer is also clinical, with patients presenting with melena, hematemesis, hematochezia, and hypotension. Initial diagnostic maneuvers include performance of nasogastric lavage. Nasogastric decompression is also critical to prevent pulmonary aspiration during subsequent EGD [14].

Treatment

Once diagnosed, recommended treatment for ulcer disease first includes lifestyle modifications. This means smaller, more frequent meals, separate liquid intake from meals, maintaining upright position postprandially, avoiding late night meals, and triggering foods such as caffeine, fatty foods, and if applicable, tobacco, and alcohol [3].

If PUD is refractory to lifestyle modifications, then drug therapies are commonly recommended [1]. Frequently utilized medications include antacids, gastric acid secretion inhibitors (H_2 blocker), proton pump inhibitors, and cytoprotective medications (carafate). Eradication of *Helicobacter pylori*, a treatment option in the nonpregnancy population, should be deferred to the postpartum period [3]). A 2011 European study failed to identify a higher occurrence of congenital abnormalities in women with PUD or those who received drug treatments during pregnancy [1]. Another European study of proton pump inhibitors similarly did not show an increased risk of congenital abnormalities in those exposed [15].

Perforation and bleeding are the two most frequent indications for surgical intervention, and treatment in the gravid patient is the same as in the nongravid patient. A perforated peptic ulcer necessitates emergent surgical intervention with concurrent resuscitation and broad-spectrum antibiotics. Medical management of perforated ulcers is associated with poor prognosis for both mother and fetus, with mortality ranging between 60% and 100% [5]. In the operating room, either Graham patch closure or partial gastrectomy is indicated depending on clinical findings.

Should gastrointestinal bleeding be the presenting symptom, the patient should be hospitalized, observed, and fluid resuscitated as indicated. The bleeding patient should be placed in the left lateral decubitus position to improve venous return through the vena cava and maintenance of uterine perfusion [16]. Endoscopic management with possible therapeutic intervention should be considered first to manage hemorrhage [3]. Indications for surgery for PUD bleeding include failure of endoscopic management, hemodynamic instability, or continued hemorrhage after transfusion of six or more units of red blood cells. As with perforated ulcers, surgical as opposed to medical management of bleeding ulcer disease is associated with improved maternal and fetal outcomes [5].

Hepatic Disease

Fortunately, the etiologies of acute abdomen secondary to hepatic pathology are rare. However, owing to its rarity, the liver may be overlooked as a cause of abdominal pain and this may adversely impact maternal and fetal well-being. The major causes of hepatically induced acute abdomen are hepatic rupture, abscess, and fatty liver of pregnancy.

Hepatic Rupture

Hepatic rupture can occur spontaneously or after an inciting event, such as trauma. The liver is a protected organ owing to its location adjacent to the ribs and diaphragm. Nevertheless, the liver parenchyma itself or lesions within the liver, such as tumors or cysts, can rupture. In the gravid patient, there is an association between pre-eclampsia, eclampsia, and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets) with spontaneous hepatic rupture, with a case-to-delivery ratio of 1:45,000 [17, 18]. In fact, the vast majority (approximately 80%) of spontaneous ruptures are associated with pre-eclampsia [19].

Hepatic rupture usually occurs in the third trimester. In approximately 75% of patients, intraparenchymal hemorrhage occurs in the right lobe; 11% of rupture occurs within the left lobe; and in 14% of patients there is bilateral involvement [20]. Intraparenchymal hemorrhage progresses to contained subcapsular hemorrhage. After the capsule ruptures, the tamponade effect is released, and in patients who are thrombocytopenic, appropriate clotting will not contain progressive hemorrhage [21]. Maternal mortality remains high with this diagnosis, ranging from 25% to 75% [1].

Other rare causes of hepatic rupture include hepatic cysts, which are relatively common and occur in up to 5% of patients [22]. Intraperitoneal or extraperitoneal hemorrhagic cyst rupture is rare, occurring in only 1% of patients. The risk of rupture corresponds to the intracystic pressure and not to the intra-abdominal pressure, so the resultant effects of pregnancy are not necessarily a risk factor [23], and there have only been case reports of ruptured cysts in the gravid population [24].

Diagnosis

Typically, a patient presenting with hepatic rupture is hemodynamically compromised and exhibits peritonitis and abdominal distention on examination. Definitive diagnosis must be made by imaging, usually ultrasound or CT.

Treatment

Hepatic rupture, if the cause is known (i.e., trauma), can sometimes be managed conservatively. Invasive hemodynamic monitoring should be performed, and availability of large volumes of blood products is critical. Coagulopathy must be corrected to prevent further exsanguination, and there have been reports of successful

use of recombinant Factor VIIa to assist with hemostasis, thus averting surgical intervention [25, 26]. Additional trauma to the patient should be avoided (i.e., unnecessary bed transfers, palpation, emesis, etc.).

If conservative management is unsuccessful or the patient presents in extremis, surgical intervention will be required to first control the hemorrhage, which can be achieved with packing. The area of laceration or rupture can then be repaired expeditiously; this may rarely require temporary occlusion of the hepatoduodenal ligament (Pringle maneuver), hepatic artery ligation, or even hepatic resection. In rare scenarios, the need for emergent liver transplant [2] is necessary to control hemorrhage and rupture.

Liver Abscess

Liver abscess is a serious condition which can result from a variety of intra-abdominal processes, such as perforated viscus due to appendicitis or diverticulitis with resultant hematogenous spread to the liver [27]. Not surprisingly, then, enteric bacteria including *Bacteroides* and *Escherichia coli* are the most prevalent causative organisms. In areas where endemic, amoebic liver abscesses (*Entamoeba histolytica*) should also be considered. However, liver abscesses can also occur from liver necrosis secondary to liver infarction resulting from pre-eclampsia.

Diagnosis

Right upper quadrant pain and fever are the most common presenting clinical symptoms. Laboratory analysis is relatively nonspecific, but elevated ALT and thrombocytopenia in pregnancy have been reported [28]. Imaging is key to diagnosis, with ultrasound being of primary consideration with a sensitivity of 86% [29]. In pregnancy, early diagnosis is critical given the high perinatal mortality rate with untreated cases. Additionally, its delayed diagnosis and progression is associated with increased rates of fetal infection and preterm delivery [30].

Treatment

Patients suspected of harboring a liver abscess need prompt resuscitation and commencement of broad-spectrum antibiotics. Definitive aspiration and drainage of the abscess is both diagnostic and therapeutic. This is typically achieved with ultrasound guided percutaneous drainage. It is critical to take cultures from the aspirate to guide the antibiotic regimen.

If percutaneous drainage is unsuccessful or incomplete, surgical drainage may be necessary. Surgical exploration is also necessary in the patient in whom ruptured abscess is suspected; typically these patients will present with peritonitis and sepsis. This intervention is critical for washout of the abdomen, as well as source control and complete drainage of the abscess.

Cholecystitis and Biliary Tract Disease

Biliary Physiology in Pregnancy

Biliary disease is the second most common gastrointestinal disorder requiring surgery during pregnancy [31]. Perhaps, this is due to the changes in biliary physiology induced by the hormones of pregnancy. Increased serum estrogen and progesterone during pregnancy induce metabolic changes in the synthetic and excretory physiology of bile.

Bile, which is composed of bile salts derived from cholesterol, increases in viscosity and volume with elevated estrogen [32]. This risks increased cholesterol crystal aggregation and therefore gallstones. Increased progesterone has been shown to cause relaxation within the smooth muscle of the gallbladder which leads to bile stasis [33]. Studies have widely demonstrated that gravid patients are at increased risk for biliary tract disease, as more than 25% of postpartum patients were demonstrated to have biliary sludge as a result of hormonal changes induced by pregnancy [34].

Cholecystitis

Among the most frequent causes of acute abdomen in pregnancy is acute cholecystitis. Its incidence ranges from between 0.2 and 0.5 per 1000 pregnancies [35]. In the nongravid patient, this typically presents with right upper quadrant pain and fevers, and treatment of cholecystitis can vary, ranging from medical therapy, endoscopic therapy, percutaneous drainage, or surgery depending on the patient's underlying medical conditions and presentation. In the gravid patient, however, the differential diagnosis for right upper pain is broad, and can include uterine contractions, fetal movement, adnexal torsion or rupture, liver hematoma, cholangitis, hepatitis, peptic ulcer, and pancreatitis. It is important then, to first accurately make the diagnosis and then offer the appropriate treatments in a timely fashion.

Diagnosis

To accurately diagnose cholecystitis, it becomes important to "rule out" other confounding causes. Uterine and fetal monitoring should be routinely established to determine maternal and fetal well-being as well as assessing for the possibility of uterine contractions. Clinical history for cholelithiasis and cholecystitis is paramount. Suspicion should be increased in older patients who have a four times increased prevalence of calculi in comparison to younger patients [36]. A previous history of pregnancy is also a risk factor, as multiparous females have a 12-fold increased risk of calculi when compared to nulliparous patients [37].

Otherwise, classic clinical symptoms of postprandial right upper quadrant pain related to fatty foods are diagnostic of biliary colic. When coupled with fevers, chills, nausea, and vomiting, the clinical suspicion for cholecystitis should be elevated.

Delays in diagnosis can ultimately lead to decompensation of the mother and acute perforations of the gallbladder or biliary tree. The unfortunate result of

peritonitis or sepsis may contribute to increased risk of fetal abnormalities, maternal mortality, preterm labor, fetal loss, and death [38, 39]. When suspected, then, proper workup including laboratory analysis and radiographic imaging is critical.

Laboratory Analysis

Liver function tests are sometimes difficult to interpret, given the normal changes seen in pregnancy. Typically, AST/ALT levels should remain normal throughout pregnancy, though bilirubin levels tend to decrease and alkaline phosphatase increases [40]. In addition, given the alterations seen in white blood count, the diagnosis of cholecystitis should not be based on laboratory anomalies alone, but rather the entire clinical picture.

Radiographic Analysis

In gravid and nongravid patients, ultrasound remains the gold-standard diagnostic imaging modality for cholecystitis and biliary tract disease. Its benefits of being quick, noninvasive, and devoid of radiation risk are coupled with its superior sensitivity and specificity for gallbladder disease (typically >97%) [15]. The entirety of the gallbladder and biliary tree can be visualized by ultrasonography, to identify calculi, obstructing stones, biliary sludge, and gallbladder wall thickening. An ultrasonographic Murphy's sign is also highly sensitive for acute cholecystitis.

Treatment

Initial management of the patient with acute cholecystitis should include resuscitation with intravenous fluids and commencement of broad-spectrum antibiotics. In its acute presentation, laparoscopic cholecystectomy should be the standard treatment for cholecystitis. Open cholecystectomy has been shown to result in a higher rate of postoperative premature uterine contractions and use of tocolytic therapy [41]. Laparoscopy has been proven to be quite safe during pregnancy, though care should be taken to enter the abdomen and obtain pneumoperitoneum safely (typically, via Hasson open approach) [42]. Intraoperatively, fetal monitoring should be employed. Pneumoperitoneum should be kept at a maximum of 15 mm Hg, though this may need to be decreased in some instances given patient compliance.

The timing of cholecystectomy is important; in the nongravid patient, patients either undergo operative removal of the gallbladder, percutaneous cholecystostomy tube placement, or medical management with bowel rest and antibiotics. In the pregnant patient, much debate has surrounded whether these approaches are equivalent, especially with respect to the safety of laparoscopic cholecystectomy during the first and third trimesters. Given these uncertainties, some have advocated for temporizing measures such as percutaneous cholecystostomy tube placement in the gravid patient who is not in the second trimester [43]. This allows for safer performance of laparoscopic cholecystectomy during that safe interval (if presenting in the first trimester) or postpartum (if presenting in the third trimester). In nonemergent situations, however, guidelines for laparoscopic treatment of biliary disease recommend elective operations to be performed within the second trimester [27].

Operations performed, even in the second trimester, are not without risk. There have been reports of spontaneous contractions, premature birth, and spontaneous abortions associated with laparoscopic cholecystectomy in the second semester [25, 44]. The alternative of nonoperative management, though, appears to be worse. Collectively reviewed published reports have demonstrated a fetal demise rate of 7% with nonoperative management of acute cholecystitis, compared to 2.2% with laparoscopic cholecystectomy [45]. Moreover, relapse rates of between 40% and 55% were demonstrated with nonoperative management. With this information, decision-tree analysis demonstrates the superiority of operative management in gravid patients with acute cholecystitis, especially in the first or second trimester [30].

Biliary Tract Disease

The biliary tract can be prone to complications from benign and malignant conditions which can cause an acute abdomen in the pregnant patient. The diagnosis and treatment of these conditions should ultimately be undertaken with the health and safety of the mother primarily, but modifications in workup and treatment stratagems can be considered to maximize the chance of successful pregnancy and minimize harm to the fetus.

Choledocholithiasis

As discussed earlier, the pregnant patient is prone to develop gallstones given the effects of hormones on bile stasis and cholesterol crystallization. When the stones are passed into and retained within the common bile duct or common hepatic duct, choledocholithiasis, and the more concerning sequela of cholangitis can result. Choledocholithiasis, though rare, is estimated to affect 1 in 1200 pregnancies [46]. Others have identified that it can complicate up to 12% of pregnancies, and has an increasing incidence with age [47]. Cholangitis is considered a surgical emergency and rapid decompression of the biliary tract is necessary to prevent sepsis from bacterial overgrowth.

Diagnosis

The diagnosis of biliary pathology during pregnancy can be difficult. The clinical symptoms of choledocholithiasis can be nonspecific (nausea, vomiting, anorexia, and pain) and can be masked by the pregnant state. Laboratory analysis, too, can be masked by pregnancy as leukocytosis and elevated liver function tests (especially alkaline phosphatase) can have a placental origin [48].

When suspected imaging becomes critical to rapid diagnosis and treatment. Ultrasound remains the modality of choice given its noninvasiveness, ease of use, and rapidity of results. However, despite its excellent sensitivity for cholelithiasis, its diagnostic ability for choledocholithiasis is limited and sensitivity ranges

between 20% and 38% [49], likely a result of the inaccessibility of the common bile duct by ultrasound given its location and presence of overlying bowel gas and the gravid uterus.

When ultrasound is nondiagnostic, other noninvasive methods can be employed. Cross-sectional imaging using computed tomography (CT) unfortunately has low sensitivity for the diagnosis of common bile duct stones, and furthermore risks radiation exposure to the fetus [50]. Magnetic resonance cholangiopancreatography (MRCP) is an established method of fine detailed analysis of the biliary tree and is routinely used in nongravid patients. It poses no risk to the fetus and has an accuracy of close to 100% in diagnosing the presence and level of biliary obstruction [51]. When negative, it has the benefit of potentially excluding patients who would need endoscopic management of choledocholithiasis, as well as sometimes obviating the need for intraoperative cholangiography during cholecystectomy, thereby reducing the risk of radiation in these patients.

Treatment

Endoscopic Therapy

Medical treatment with endoscopic therapy has become the standard of care to treat choledocholithiasis. With endoscopic retrograde cholangiography, it becomes possible to both diagnose obstructing lesions within the biliary tree and treat them using extraction and stenting techniques.

Endoscopic retrograde cholangiopancreatography (ERCP) does not come without increased risk, however. The ability to visualize the biliary tree requires the use of fluoroscopy, iodinated contrast, radiation, and sedation. In the first trimester, this combination of factors can result in increased complications. Tang and colleagues reported a lower rate of full-term pregnancy (73%), lower birth weight (21%), and higher rate of preterm delivery (20%) in 65 patients who underwent ERCP in the first trimester [30].

The radiation exposure risk from ERCP can be clinically significant. In the pregnant patient, the typical radiation doses using ERCP range from 3.4 mGy to 55.9 mGy [52]. Fortunately, the fetus lies outside the radiation beam during ERCP, but there is potential to exceed the safe clinical radiation thresholds of 50 mGy stipulated by ACOG guidelines [53]. Doses in excess of 100 mGy can result in significant fetal complications, such as growth restrictions, mental retardation, fetal malformations, and intrauterine death [54, 55]. Strategies to mitigate radiation exposure include minimizing fluoroscopic time and performance of ERCP by an experienced practitioner. Smith and colleagues demonstrated that when ERCP was performed by a specialty biliary endoscopist with more than 500 cases yearly, the estimated fetal radiation dose was less than 0.5 mGy [17].

Another strategy that can minimize radiation exposure is performance of endoscopic ultrasound (EUS) to visualize the biliary tree. Only after obstructing stones are located and identified can ERCP and fluoroscopy be performed. Lee and

colleagues demonstrated that this approach led to fewer complications and allowed for proper selection of patients which would benefit from ERCP [37].

Surgical Therapy

When a calculus within the common bile duct is unable to be retrieved endoscopically, a number of options exist. If the stone is partially obstructing, allowing the passage of a plastic stent, that may be a temporizing measure to ensure proper flow of bile. At some point, however, the patient will require removal of the offending obstruction. This will need to be performed surgically in the form of a common bile duct exploration, which can be performed laparoscopically or in an open fashion. Typically, laparoscopic exploration is successful in 80–90% of patients, but does require a skilled surgeon [56]. Laparoscopic exploration can be performed transcystically when the stone burden is low (<5 stones), small (<0.8 cm), not located in the common hepatic duct, and anatomy is favorable (i.e., cystic duct joins common bile duct laterally and not medially) [57]. In cases where the stone is larger and more impacted, a choledochotomy may be necessary to remove the stone [58]. Though the number of laparoscopic common bile duct explorations is limited in the pregnant population, the case reports of such a technique have yielded successful outcomes with no obstetric complications [43, 59].

Surgical Therapy After Endoscopy

The decision to operate after successful ERCP should be made on a case-by-case basis. If ERCP was successful in stone removal and sphincterotomy was performed, the necessity for emergent cholecystectomy to prevent future episodes may be minimized. It seems more advantageous to delay cholecystectomy in this situation until after delivery. On the other hand, if the patient seems to have continued symptoms or develops acute cholecystitis, more immediate surgery should be performed [23].

Pancreatitis

Background

The incidence of pancreatitis in pregnancy varies between 1:882 and 1:4,449 pregnancies [60–64]. Despite the overall low number of cases in the literature, general trends do arise. The most common causes of pancreatitis in pregnancy were related to biliary etiology and hypertriglyceridemia. Acute pancreatitis related to a biliary etiology was estimated 57–73% of the cases studied [46–49, 65]. A variety of less common causes, including alcohol consumption, hypercalcemia, hyperparathyroidism, trauma, anatomic variables, cystic fibrosis, medications, and idiopathic causes, are also known to be causes [46, 49, 50]. There is a trend toward both mild and

severe pancreatitis presenting later in gestation [50], with 43–95% of cases in the third, 5–33% in the second, and 0–24% in the first trimester [45, 46, 48, 50, 66, 67].

Several pregnancy-related risk factors have been identified which predispose one to biliary pancreatitis. Weight gain and hormonal changes associated with pregnancy lead to increased biliary sludge and gallstone production [49, 68]. Hormonal changes also lead to smooth muscle relaxation and bile stasis resulting in reduced gallbladder motility [52]. It is thought that cholesterol secretion increases in the second and third trimesters of pregnancy leading to saturated bile, and that while the fasting and postprandial gallbladder volumes are greater, the emptying rate and volume are reduced [53]. After delivery with normalization of hormones, gallbladder motility normalizes and the stones may disappear as biliary homeostasis is restored [53].

Estrogen is believed to be related to increases in triglycerides during pregnancy, with up to a fourfold increase in levels considered "physiological hyperlipidemia or pregnancy" [69, 70]. Despite this rise, levels generally do not reach above 300 mg/dL, and hypertriglyceridemia is more pronounced during the second and third trimesters [55, 71]. Many cases of hypertriglyceridemic pancreatitis did not have pregestational hyperlipidemia nor familial dyslipidemia [10]; however, an underlying genetic predisposition, obesity, excessive weight gain, diabetes, alcohol consumption, and some drugs may contribute to dyslipidemia [4, 6].

The overall majority of cases of acute pancreatitis were noted to be mild with generally favorable maternal and fetal outcomes [45]. However, in cases of severe acute pancreatitis more than 77% were caused by hypertriglyceridemia [51]. Nonbiliary pancreatitis was associated with more complications, worse outcomes such as preterm delivery when compared to biliary pancreatitis as well [51, 54]. Others have reported biliary and idiopathic causes had better overall outcomes with fewer incidences of organ failure and fetal mortality [50].

In patients with severe pancreatitis, despite the aggressive management required—including mechanical ventilation, hemodialysis, percutaneous drainage, chest drainage, and open necrosectomy—there are no maternal deaths reported [54]. The organ systems most vulnerable to failure are respiratory, renal, and hepatic, with renal and coagulation disorders denoting poor prognosis. Fetal death was more likely when two or more organ systems were affected [50].

Diagnosis

The clinical presentation of acute pancreatitis often elicits complaints of epigastric, right, or left upper quadrant pain, with associated nausea or emesis. The pain is often constant with radiation to the back, chest, and flanks [72]. Despite the common complaints of nausea and emesis in pregnancy, any patient presenting with prolonged nausea and emesis should elicit a pancreatitis workup [17]. Initial workup begins with bloodwork including amylase, lipase, complete blood counts, metabolic panel including liver function testing and a triglyceride level. Serum amylase and lipase continue to be reliable markers during pregnancy, with lipase level unchanged

and amylase remaining normal or mildly elevated [53]. Elevation of serum lipase and amylase to levels three times higher than normal has a good positive predictive value [52]. Elevation of alanine aminotransferase to levels greater than three times normal is a sensitive marker for a biliary etiology of pancreatitis [53]. Triglyceride levels rise gradually and reach a peak during the third trimester, to almost twice nonpregnant levels, then return to prepregnancy levels by 6 weeks postpartum [52]. Nonbiliary causes of pancreatitis have been found to produce worse outcomes and thus screening for these etiologies is of particular importance [50, 55]. The use of serum calcium and triglycerides, parathyroid levels, and discussions about alcohol consumption allow for comprehensive assessment of etiology [46, 50, 55].

Abdominal ultrasonography is a safe and reliable way to diagnose biliary pancreatitis and identifies cholelithiasis or sludge in up to 70% of patients [48]. It can be limited in detection of common bile duct stones; therefore, alternative imaging may be considered when ultrasound or lab findings suggest choledocholithiasis despite an inconclusive ultrasound [53]. Due to concerns of radiation exposure related to computed tomography (CT) imaging and endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasonography (EUS) should be considered for diagnosis [49, 52, 53]. Additionally, MRCP use can limit the use of ERCP to therapeutic procedures only [53, 55], given concerns about radiation exposure to the fetus.

Treatment

Treatment of pancreatitis in pregnancy generally follows similar principles to that in the nonpregnant population. Hospitalization is indicated for diagnosis, pain management, aggressive rehydration, electrolyte replacement, nasogastric decompression, and, in limited cases, hyperalimentation [17]. Following the American College of Gastroenterology (ACG) guidelines, aggressive hydration is most beneficial and of vital importance in the first 12–24 h [56], with lactated ringers as the choice crystalloid replacement fluid. Frequent reassessment within the first 48 h and use of BUN, creatinine, and hematocrit as surrogate markers for successful rehydration are standard means to follow the clinical course of pancreatitis.

Bowel rest is indicated though nutrition is of obvious importance to the pregnant state. According to the ACG, bowel and pancreatic rest until complete resolution of pancreatitis is no longer indicated. Current guidelines indicate that complete bowel rest is associated with intestinal mucosal atrophy and increased infectious complications [56]. There is some suggestion that the frequency of maternal complications secondary to central venous catheters is higher in the pregnant population [53]. While studies are limited in addressing this factor specifically during pregnancy, general principles for the nonpregnant population recommend enteral feeding over parenteral feeding when possible [56]. Enteral nutrition has recognized benefits including maintenance of the gut flora and mucosal barriers, promoting of gut immunity, and reduction of bacterial translocation [48, 54]. For patients with mild pancreatitis, immediate refeeding with a soft, low-fat, low residual diet is safe and

may lead to shorter hospitalization than advancing through from the clear liquid diet [56]. Early enteral nutrition (within 1–3 days) in severe pancreatitis was initiated in a 2010 study where 18 of 69 cases were deemed severe, there were no maternal deaths reported in the study nor feeding-related complications [54].

It is believed that early diagnosis, aggressive treatment and intervention, and improvements in intensive care for both mother and fetus have played a role in the decrease in morbidity and mortality associated with pancreatitis [55]. The main causes of perinatal mortality were preterm delivery, while additional risks include threatened preterm labor and in utero fetal death [52, 55]. Intensive fetal monitoring has been suggested when recurrence or prolonged disease is encountered. This may consist of nonstress testing and serial ultrasounds for fetal growth as well as biophysical profiles [17].

Biliary Etiologies

Definitive management of biliary pancreatitis includes the decision on timing of cholecystectomy and disease management in the interim. Optimal timing of cholecystectomy needs to be considered in the context of best outcomes for the mother and the fetus, taking into account gestation age, recurrence rates, and pregnancy outcomes. One-third of patients experienced between two and five recurrences during the same pregnancy, with 50% of those in the biliary pancreatitis group who had been managed conservatively experiencing recurrence [49]. Similar results were noted in other studies which confirmed a higher relapse rate, as high as 55% [17, 47].

Given that recurrence of pancreatitis is more likely in patients with gallstone pancreatitis [47], management strategies aimed at definitive intervention need to be considered. The gestational age at which pancreatitis presents can assist with choice of therapy [47]. As a surgical concept is it advisable to undertake surgical intervention in the second trimester, when the fetus has completed the organogenesis of the first trimester and while the uterus is still sufficiently small such as to avoid interfering within the surgical field. A simple algorithm devised by Swisher et al., suggests that pancreatitis presenting in the first or third trimester be treated medically until surgical intervention can be performed in the second trimester or postpartum period, respectively; second trimester pancreatitis should be treated with surgical intervention after initial resuscitation[47]. By this stratagem, there was no fetal or maternal mortality attributed to surgical intervention, nor was there any difference in premature labor compared to the medically treated group.

ERCP with sphincterotomy and clearance of the bile duct offers an alternative until surgical intervention is possible [52, 53]. A 2004 study on the safety of ERCP during pregnancy with concurrent literature review concluded that with appropriate monitoring and adjustments in technique to minimize fluoroscopy time, ERCP is both safe and efficacious in pregnancy [73]. Other groups have reported an absence of serious complications and a relative low (<5%) risk of fetal complications related to ERCP [52]. The danger in not treating biliary pancreatitis surgically or endoscopically was highlighted by a 2008 study at 15 Midwestern hospitals, where patients treated conservatively (without antepartum cholecystectomy or ERCP) demonstrated significantly higher rates of fetal demise, preterm delivery, and recurrence of pancreatitis [46].

Delivery

Delivery has been suggested as a treatment option for severe pancreatitis, particularly when organ failure in two or more systems was observed [50, 54]. With severe disease serving as a surrogate for worse fetal outcomes, pregnancy termination may improve maternal outcomes while allowing for enhanced fetal survival rates, by removing the fetus from an environment with an increasingly mounting inflammatory response [54]. It is thought that the state of hypovolemia, hypercoagulability, and intimal inflammation may be associated with a decline in placental blood perfusion, while pancreatitis may directly irritate the uterus leading to contractions [50]. Termination of pregnancy has been recommended in extreme cases when homeostatic conditions cannot be achieved rapidly in the mother. While minimal discussion exists regarding delivery methods during acute pancreatitis, it is suggested that vaginal delivery is preferable to cesarean section where possible in order to limit the risk of infection to any existing pancreatic necrosis [52].

Mesenteric Ischemia

Background

Mesenteric venous thrombosis (MVT) is the least common form of mesenteric ischemia, occurring in approximately 5% of the population, with an average age at presentation of 45–60 years. However, in younger patients without cardiovascular disease, it is the major cause of acute small bowel ischemia [74]. In a large percentage of patients with MVT, a previous history of deep vein thrombosis has been reported, as well as underlying acquired and inherited risk factors that predispose patients to the disorder. Local intraperitoneal inflammatory processes (i.e., pancreatitis, cirrhosis, and portal hypertension) and trauma generally affect the larger veins, thereby increasing the risk of mesenteric thromboembolic complications, while nephrotic syndrome, malignancy, and other systemic hypercoagulable states generally affect the distal, smaller vessels. In pregnancy, high levels of factors VII-X and fibrinogen reduced fibrinolytic activity, venous stasis, and blood pooling, and other factors result in increased morbidity [58].

Underlying hereditary coagulopathies significantly increase the maternal risk of thromboembolic episodes, including mesenteric and portal vein thromboses [75]. Additionally, repeated abdominal surgery, cesarean section, appendectomy, elective laparoscopic cholecystectomy, inflammatory bowel disease (IBD), and continued oral contraceptive use during gestation have all been associated with mesenteric venous thrombosis in the absence of any heritable thrombophilia [58]. In the majority of cases, MVT involves the distal small intestine (superior mesenteric venous drainage) and rarely involves the colon, which drains through the inferior mesenteric vein.

Diagnosis

Early acute mesenteric venous thrombosis is characterized by the insidious onset of diffuse, colicky abdominal pain that is out of proportion to physical examination. Pain is often dull with a less sudden onset than other forms of acute mesenteric ischemia, and 75% of patients with MVT report a least a 2-day history of symptoms before pursuing medical care [76]. Nausea, vomiting, and abdominal distension are common, and can be accompanied by gastrointestinal bleeding, diarrhea, and/or leukocytosis, although the latter is a nonspecific finding in pregnancy and generally does not aid in the diagnosis. In later stages, bowel edema, infarction, and necrosis develop, and classic findings of peritonitis are observed.

Definitive diagnosis of mesenteric venous thrombosis is best seen with MR venography, although CT with and without oral and IV contrast is the initial screening study of choice due to widespread availability. Findings suggestive of acute mesenteric ischemia include the presence of venous filling defects or absent flow in the mesenteric veins, severe bowel wall thickening (>3 mm) secondary to mural edema and hemorrhage, and poor mucosal enhancement, suggesting infarction [77]. Pneumatosis intestinalis, portal vein gas, and unexplained ascites may be seen in patients with advanced ischemia. In pregnant patients with a nondiagnostic CT and strong clinical suspicion of mesenteric vein thrombosis, CT angiography with delayed imaging is recommended [58]. Suggestive findings on angiography include late filling or thrombus in the superior mesenteric vein, arterial spasm, a prolonged vascular blush, and reflux of IV contrast into the aorta due to resistance to venous flow.

Treatment

Mesenteric venous thrombosis is generally managed conservatively, using systemic anticoagulation, bowel rest, and serial abdominal exams [78]. Thrombolytics, although used in nonpregnant patients, are not recommended during pregnancy [79]. If mesenteric venous thrombosis without evidence of bowel infarction is confirmed or strongly suspected, therapeutic anticoagulation with low molecular weight heparin (LMWH) or intravenous unfractionated heparin should be initiated immediately. Initial dosing is weight based, with subsequent dose adjustments depending on anti-factor-Xa levels and aPTT, respectively. Altered LMWH metabolism due to the physiologic changes of pregnancy results in lower peak levels and a higher clearance rate; thus, greater or more frequent doses may be required [63]. If heparin is chosen as the initial agent, transition to therapeutic LMWH is appropriate after several days. In patients with signs of bowel infarction or necrosis, surgical exploration and resection of nonviable bowel are performed, with a goal of conserving as much bowel as possible [80].

Therapeutic anticoagulation after an initial thrombotic event during gestation should be maintained for at least 3 months. Postpartum, continued anticoagulation is essential, as approximately one-third of thromboembolic events occur during the

puerperium until 6–12 weeks after delivery [58]. Transition to oral anticoagulants is possible during this time. Although warfarin may appear in small amounts in breast milk, it is considered compatible with breastfeeding and has not been associated with adverse events in newborns [63]. In patients with a history of MVT or other thromboembolic complication during pregnancy, hypercoagulable testing is recommended for preconception management of subsequent pregnancies, including prophylactic anticoagulation in certain high-risk populations.

Small Bowel Obstruction

Background

Small bowel obstruction (SBO) in pregnancy is the third most common cause of acute abdomen in pregnancy, following acute appendicitis and acute cholecystitis [81]. The incidence is estimated at 1:1500 to 1:16,000 [45]. The most common cause is related to postsurgical adhesions, accounting for 50–60% of small bowel obstruction [45, 82]. Other causes include volvulus, internal hernia, intussusceptions, carcinoma, hernia, and appendicitis [45, 46, 83]. It is suggested by case studies that the majority of patients with small bowel obstruction have prior abdominal or pelvic surgical history [84]. In patients who have had previous Roux-en-Y-gastric bypass surgery, for instance, the majority of which are women of child-bearing age, an internal hernia is a recognized complication. In a review of 46 cases of SBO in pregnancy, 50% were found to be caused by adhesions, followed by volvulus 15%, and internal hernia 13% [46].

A high index of suspicion is needed to diagnose bowel obstruction, as there is a high rate of associated maternal morbidity, mortality, fetal loss, and premature onset of labor, especially when diagnosis is delayed. The overall risk of fetal loss is estimated to be as high as 17% [46]. It is estimated that only one-third of pregnant patients with bowel obstruction complete term pregnancies after operative intervention [47].

Diagnosis

The most common presenting symptoms are the same as in nonpregnant patients, including spasmodic abdominal pain, nausea and vomiting, abdominal distension, and obstipation. A careful history and physical examination should be obtained focusing on vital sign abnormalities, signs of sepsis, abdominal tenderness, and any previous abdominal or pelvic surgeries, which will often point to a specific cause. Abdominal wall laxity may delay peritoneal signs [85].

While the symptoms can be atypical, a pregnant patient with intractable vomiting and new onset abdominal pain should be assessed with further imaging. A plain abdominal radiograph will show dilated loops of bowel and air fluid levels [45, 86]. Abdominal ultrasound is often utilized for initial workup. Specific sonographic

findings include small bowel wall edema and diameter of >25 mm; a small bowel transition point may also be visualized [87]. Ultrasound is thought to be more accurate than X-ray; however, diagnosis is more difficult during pregnancy [88]. CT scan may not be necessary for diagnosis, unless X-ray and ultrasound show no abnormalities and clinical suspicion is still high. However, in patients with severe abdominal pain, a CT scan should not be delayed if deemed necessary. MRI may also be used and can help distinguish between adhesive disease and volvulus or internal hernia which is more likely to require surgery [46].

Treatment

Treatment in the pregnant patient mirrors that of the nonpregnant patient with mainstay conservative management of bowel rest, correcting fluid and metabolic derangements, and nasogastric decompression. Treatment of hypovolemia and correction of electrolyte abnormalities should also be prompt as fetal death from hypoxia secondary to maternal hypovolemia and shock has been reported [48]. Typically, if there are no signs or symptoms of systemic illness to suggest impending bowel compromise, then expectant management is initially undertaken. The decision to operate will depend on patient clinical resolution of obstruction; those patients who fail to resolve or worsen will necessitate surgical intervention.

However, in patients with signs of intestinal ischemia, peritonitis, worsening pain, and imaging findings suggestive of bowel strangulation, urgent surgical exploration is indicated. This is also especially true if peritonitis, closed loop obstructions, or volvulus is suspected. In these patients in whom bowel ischemia is suspected, broad-spectrum antibiotics and resuscitation should immediately precede operative exploration.

The most common postoperative complication is premature labor [46]. In patients with signs or symptoms of premature labor, tocolysis may be indicated [48]. Early surgical intervention may decrease occurrence, as there is an association between longer delays before surgery and premature labor [46]. Favorable fetal outcomes are associated with early diagnosis, early surgical intervention when indicated, and avoidance of maternal hypotension and hypoxia [48].

Hernias and Incarceration

Background

A hernia is a defect in the body wall and can occur through the body wall, diaphragm, pelvic floor, and through internal abdominal viscera [89]. Due to increases in intra-abdominal pressure, abdominal wall hernias may become visible that are not apparent in the nongravid state.

Inguinal hernias are rare in adult women, with a lifetime risk estimated at 3%, and even more so in pregnant women, with prevalence estimated at 1:2000 [90, 91].

Umbilical hernias, caused by failure of closure of the umbilical ring, account for about 10% of primary hernias in adults [92].

When hernias do occur in pregnant women, they present a unique challenge as risk of incarceration could result in a high level of morbidity to the mother and fetus. In a retrospective review, the occurrence of incarceration is exceedingly rare, accounting for <5% of intestinal obstruction in pregnancy [93]. There have also been reports of incisional hernias complicating pregnancy which can manifest as a gravid uterus herniating through an incisional hernia [94].

Diagnosis

The diagnosis of inguinal hernia in pregnant women is made by the presence of a new, symptomatic groin mass groin, which may or may not be reducible [90]. The differential diagnosis should include round ligament varicosities, lipoma, vascular aneurysm, hematoma, and abscess [95]. Round ligament varicosities, similar to inguinal hernia, can present with swelling and tenderness in the groin, can be reducible, or nonreducible, and are more common in pregnancy due to pelvic vein enlargement related to smooth muscle relaxation, increased venous return, and pelvic venous obstruction from a gravid uterus; the diagnosis can be confirmed with duplex ultrasound showing prominent venous plexus [96]. Patients are more likely to become symptomatic with groin or umbilical hernias in the second trimester [56].

Treatment

Traditionally, hernia repair in pregnancy has been reserved for cases of strangulation or incarceration. This has been supported by contemporary studies showing low rates of incarceration with conservative measures, namely, weight loss, abdominal binders, and stool softeners aimed at reducing intra-abdominal pressure [56]. In a retrospective study of 12 gravid patients with hernia, a watchful waiting strategy is supported for reducible groin masses, with a plan for postpartum herniorrhaphy. This approach has been supported, as none of the patients followed had any perioperative or postoperative complications [56].

Colitis

Background

Inflammatory bowel disease(IBD) is among the most common causes of intestinal inflammation in pregnancy. Two conditions, ulcerative colitis (UC) and Crohn's disease (CD), are the most common and their peak incidence occurs between ages 15 and 30, and therefore often affect women during pregnancy [97].

Compared to the general population, women with inflammatory bowel disease are at risk for worse medical and pregnancy-related outcomes, such as preterm birth, antepartum hemorrhage, and low birth weight infants. These patients should be considered high-risk [98]. Active disease at the time of conception is associated with an increased risk of active disease during gestation, contributing in part to worse obstetric outcomes [99, 100]. The risk of relapse is highest in the first trimester, and up to one-third of patients with quiescent disease at conception relapse over the course of their pregnancy and during the postpartum; this risk is especially high among women with ulcerative colitis [101]. Preconception counseling should be undertaken to identify risk factors and optimize control of disease activity, as well as to discuss the potential risk of medications usage during pregnancy to maintain remission.

Diagnosis

The diagnosis of IBD is typically made prior to pregnancy and is similar to those in nonpregnant patients. During pregnancy, the gravid uterus makes physical examination difficult. Endoscopy may be indicated for the diagnosis of IBD or the management of complications in patients with established disease. However, due to limited evidence regarding safety and efficacy, it should generally be postponed until the second trimester [102]. Similarly, limited evidence exists for colonoscopy in pregnant patients. Flexible sigmoidoscopy, however, is low risk in pregnancy in any trimester, and can be done without colonic preparation or sedation.

Treatment

Ultimately, treatment depends on patient severity and disease process. Absolute indications for surgery are the same as in nonpregnant patients, and include obstruction, perforation, severe hemorrhage, increasing transfusion requirements, acute refractory colitis, and abscess formation. However, medical management should be attempted whenever possible. Surgery in the gravid female has been associated with higher rates of preterm labor and fetal loss (especially when peritonitis is present), but there is limited data regarding the risk to pregnant patients with IBD [103].

In patients with fulminant colitis with or without toxic megacolon, prophylaxis with broad-spectrum antibiotics is indicated in anticipation of perforation. High-dose intravenous corticosteroids (hydrocortisone 400 mg/day or equivalent) should be administered to treat the underlying inflammatory bowel disease, resulting in a resolution of the majority of cases of fulminant colitis [85]. If colonic distension is not resolved after 48 to 72 hours, colectomy is recommended before perforation occurs. Other medications designed for treatment of ulcerative colitis or Crohn's disease should be avoided until the acute process has begun to resolve; even then, their use may be limited in pregnancy due to adverse effects on the fetus. Patients with symptomatic fistulas not amenable to bowel rest and spontaneous closure

should undergo resection of the affected intestine. In patients with colitis or colonic hemorrhage requiring urgent or emergent surgery, subtotal colectomy with end-ileostomy is the procedure of choice. Regardless of disease process, early surgical consultation should be obtained to mitigate poor outcomes.

Diverticulitis

Background

Colonic diverticular disease represents a clinical condition often seen in developed countries, although reports during pregnancy remain exceedingly rare [104, 105]. Generally seen in aging populations, its prevalence reaches about 75% in adults over the age of 80 years. In young adults, diverticulosis is uncommon. As such, it is not routinely considered in pregnant women with abdominal symptoms.

Small bowel diverticula are generally asymptomatic and found incidentally on routine imaging studies. Like colonic diverticula, their incidence is increased with age, and thus is rare in pregnancy. An exception in pregnant women is Meckel's diverticulum, which has been described in several case reports as a source of abdominal symptoms [106].

Diagnosis

A very limited number of case reports have described right-sided colonic diverticulitis during gestation [89, 90]. Right-sided diverticula are more common in non-Western countries, and most patients are younger compared to those with left-sided disease. The majority are asymptomatic, likely due to increased fluid consistency of stool in the right hemicolon. Decreased colonic motility in pregnancy can predispose patients to constipation and diverticular inflammation, which most commonly presents as localized abdominal pain in the right lower quadrant; other symptoms include changes in bowel habits, nausea, anorexia, fever or chills, or urinary urgency secondary to bladder irritation. Diagnosis is often difficult due to nonspecific symptoms, baseline elevation in white blood cell count during pregnancy, and decreased peritoneal signs in the gravid female. Since right-sided diverticulitis mimics acute appendicitis, accurate clinical diagnosis is difficult. Abdominal imaging with ultrasonography, computed tomography, or magnetic resonance imaging may be helpful, and can be used in the pregnant patient.

Meckel's diverticula are most commonly associated with gastrointestinal bleeding due to the presence of ectopic gastric mucosa. Others remain asymptomatic or may present with bowel obstruction secondary to torsion, incarceration, or peptic ulceration. Obstruction and bacterial overgrowth can result in diverticular inflammation, or perforation, with patients exhibiting symptoms similar to acute appendicitis with or without rupture. As with other causes of obstruction, abdominal distension, nausea, vomiting, and obstipation are common presenting symptoms.

Abscesses and ectopic peptic ulceration, as well as Littre's hernia—an incarcerated Meckel's diverticulum in an abdominal wall or internal hernia—can also occur.

Several imaging studies may be useful in establishing a diagnosis of Meckel's diverticulum. Similar to right-sided diverticula, Meckel's can be found using ultrasonography followed by computed tomography or magnetic resonance of the abdomen and pelvis. Radionucleotide imaging with technetium 99 m (i.e., a Meckel's scan) can also be used during gestation, with whole fetal exposure doses of less than 0.5 rad, well within the known safe range of 0–5 rad throughout the course of pregnancy. Prior to performing the study, a nuclear medicine consultation should be considered.

Treatment

Management of colonic diverticulitis depends on patient presentation, and ranges from conservative antibiotic therapy to surgical resection. In the absence of frank peritonitis or diffuse dissemination, conservative management (antibiotics and percutaneous drainage) may be attempted, but data regarding outcomes are limited. Surgical options include isolated diverticulectomy, ileocecal resection, or right hemicolectomy. Concurrent appendectomy during surgical exploration is often recommended if the base of the appendix and cecum are not inflamed [107]. Abdominal exploration and resection of the Meckel's diverticulum is the treatment of choice.

Appendicitis

Background

Acute appendicitis is the most common cause of acute abdomen in pregnancy, and the most common reason for nonobstetric surgical intervention [108]. The incidence is estimated at 0.15–2.1 cases with appendicitis per 1000 pregnancies. Appendicitis can occur at any time during pregnancy, though cohort studies suggest a preponderance for the second trimester with reports of 40% of cases compared to 25% and 34% in the first and third trimesters, respectively [109, 110]. The perforation rate is up to 25% higher if surgery is delayed, with rates reported of up to 65% when delayed more than 24 h. In cases where the appendix is perforated, the rate of fetal loss is up to 36% in comparison to 3–5% in cases of early diagnosis where the appendix is nonperforated [53–55]. Therefore, early surgery is advisable to prevent the morbidity associated with perforation.

Cohort studies have compared the rate of acute appendicitis during antepartum and postpartum periods and have found pregnant women to be slightly less likely to be diagnosed with acute appendicitis than nonpregnant women [111]. A case-control of 53,000 age matched controls corroborated the inverse relationship between pregnancy and appendicitis, especially in the third trimester [112].

Diagnosis

Appendicitis continues to be a diagnosis that is best made on clinical suspicion. The most common presenting symptom is abdominal pain, which is located in the right lower quadrant at McBurney's point in the majority of cases, regardless of trimester of pregnancy [113]. Abdominal guarding and percussion tenderness may be more difficult to detect in the late stages of pregnancy due to abdominal wall laxity [53]. The patient may also complain of nausea and vomiting; however, nausea by itself is common in normal pregnancy, especially during the first trimester.

Attention has been given to diagnostic difficulties given the common atypical presentation, and differentiating appendicitis among other common gastrointestinal complaints of pregnancy. While a mild leukocytosis is common in pregnancy, the mean WBC for patients with proven appendicitis is higher—16.4, compared to 14 for patients without appendicitis [57]. Ultrasonography is often considered a safe imaging modality in the workup of acute abdominal pain and can aid in the differentiation of many gynecologic and nongynecologic intra-abdominal processes. However, ultrasonography is often operator dependent, has a limited field of view, and may delay diagnosis and treatment when inconclusive [114]. MRI has the potential to give more diagnostic information, and simultaneously limit radiation. Although ultrasound and MRI may be the primary imaging modalities when evaluating pregnant patients with abdominal pain, when a rapid diagnosis is necessary for a potentially lifesaving treatment, CT is the primary imaging tool as it is rapidly available.

Treatment

The treatment of appendicitis is the same as in nonpregnant women, with practice guidelines supporting laparoscopy as safe and effective in any trimester of pregnancy [115]. Access to the abdomen is based on the size of the uterus, with both the use of the Hasson trocar and the Veress needle being supported as safe approaches, although there have been reports of Veress placement into the amniotic cavity resulting in fetal loss [116]. Historically, there has been concern regarding the increase in intra-abdominal pressure during laparoscopy resulting in decreased maternal cardiac output, as well as fetal acidosis from carbon dioxide pneumoperitoneum. Current guidelines from the Society of American Gastrointestinal and Endoscopic Surgeons report that routine blood gas monitoring is sufficient and 10–15 mmHg intra-abdominal pressure should be maintained. Intraoperative and perioperative fetal monitoring should be used in pregnancies over 24 weeks. A normal appendix at the time of surgery is an acceptable tradeoff given the high morbidity in pregnancy associated with treatment delay.

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Urological Etiologies of Abdominal Pain

9

Joshua A. Broghammer and Marcus Austenfeld

Introduction

Urological causes of pain during pregnancy are common and can be caused by both normal physiological changes of pregnancy and by newly acquired pathological processes. Care of the pregnant patient must take into account the health of the mother and the fetus. A firm understanding of the normal urological anatomical changes during pregnancy will help with determining the etiology of the pain. Imaging of the urinary tract must be done in a safe but efficient manner to minimize the radiation exposure required to make the correct diagnosis. Finally, surgical intervention can be performed when required with minimal risk to the mother and fetus.

Physiological Changes to the Urinary Tract in Pregnancy

Lower Urinary Tract

Changes to the bladder are somewhat limited during the first trimester. As the pregnancy progresses, increased pelvic vascular congestion results in increased mucosal vascularity. The bladder begins to change with a widening of the trigone, elevation of the ureteral orifices, and compression of the bladder dome from the gravid uterus [1]. Urodynamic studies during pregnancy reveal increased bladder pressures of up to 20 cm H_2O at term [2]. This increased pressure would normally result in episodes of stress urinary incontinence, but there is a compensatory increase in urethral length and urethral closure pressure as the pregnancy progresses [2]. In contrast,

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those women who did experience more stress incontinence showed less overall increase in urethral length and decreased urethral closing pressures [3].

Urinary frequency is considered normal during gestation and worsens as pregnancy progresses [1]. By the 12th week of gestation, urinary urgency and frequency are at a high of 63% and 74%, respectively [4]. Nocturia occurs in over 90% of women during gestation [5]. Lower urinary tract symptoms are common and quality of life questionnaires indicate that nearly half of all women were generally dissatisfied with their urinary symptoms [6]. The majority of symptoms will resolve after pregnancy but stress incontinence in early pregnancy and advanced maternal age was predictive of stress incontinence a year after delivery. Urge incontinence was found to be more predominant after Caesarean section [7]. Lower urinary tract symptoms are commonplace during pregnancy and do not require treatment, but other causes must be considered.

Upper Tract Changes

The kidney and collecting system undergo dynamic changes during gestation. Pregnancy causes plasma volume expansion due to retention of sodium [8]. The renal parenchyma begins to expand due to increased intravascular volume, and uptake in renal perfusion contributes to an increase in renal length of 1 cm [9]. This is not a true renal hypertrophy but rather an expansion of interstitial volume. Pregnancy results in a state of renal hyperfiltration with a 80% increase renal plasma flow by second trimester and an increase in glomerular filtration rate of 50% [10]. These changes result in an alteration in renal substrates and solutes processing.

The kidney is not the only genitourinary organ which increases in size. There is a slow and steady dilation of the collecting system which occurs throughout advancement of the pregnancy. The exact etiology for this is unclear. This is thought to be due to several factors which are both mechanical and hormonal. Compression of the ureters by the gravid uterus occurs above the pelvic brim, but the ureters remain undilated distally, in the lower pelvis [11]. Interestingly, quadruped animals do not develop hydronephrosis as the weight of the ureters is borne on the anterior abdominal wall and is not seated in the pelvis. There is a more pronounced dilation of the right side compared with the left side [12]. Many theories exist for this preferential dilation including compression of the right ureter by the more dilated right ovarian vein complex, dextro-rotation of the ureters, and cushioning of the left ureter by the sigmoid colon [13, 14]. Progesterone likely plays a role as it stimulates muscle atony in other organs during pregnancy. Van Wagenen et al. demonstrated that the removal of a monkey fetus mid pregnancy with retention of the placenta revealed continued ureteral dilation. This is not without controversy as the studies were repeated by Roberts et al. Intraureteral pressure catheters were placed in rhesus monkeys, and when upper tract ureteral pressures increased, laparotomy was performed, the uterus was elevated off the ureters, and the pressure readings returned to normal [15]. No matter what the etiology, hydronephrosis of pregnancy has implications on clinical conditions causing pain in the pregnant patient.

Acute Urinary Retention

Acute urinary retention is rare among pregnant women. Patients present with the inability to void, abdominal distention, and suprapubic pain. A population-based study on Taiwanese women showed that the incidence of overall acute urinary retention (AUR) is 0.47% [16]. The peak risk of AUR occurred between the 9th and 16th weeks. Preterm delivery posed the highest risks at 2.18% [16]. There have been many case reports of a retroverted, incarcerated (impacted) uterus causing AUR [17]. Physical exam findings include a low fundal height, fetal position deep in the pelvis, and no detectable uterine cervix [18]. Ultrasound findings indicate that the uterine fundus lies posterior to the cervix and the bladder is enlarged and distended [19]. The mainstay of treatment is catheterization of the bladder and manual manipulation of the uterus into its correct position. The use of a pessary has also been described [17].

Infections of the Urinary Tract

Asymptomatic Bacteriuria

The incidence of asymptomatic bacteriuria (ASB) during pregnancy is roughly 2–7% [20, 21]. The definition of ASB is the development of 10^5 colony-forming units of asingle bacterium on two consecutive voided cultures or alternatively, a single catheterized specimen with 10^2 colony-forming units [22]. Women with diabetes mellitus and a previous history of urinary tract infection are at higher risk for ASB [23] as well as those of lower socioeconomic status [24] and increased parity [25]. The most common bacteria associated with ASB are coliform bacteria from the gastrointestinal tract. *Escherichia coli* is the most common cause of ASB [26], but other Gram-negative rods include *Klebsiella*, *Enterobacter*, *Proteus*, and *Pseudomonas* are all associated [25, 26]. Group B *Streptococci* is the most common Gram-positive bacteria) and is seen in up to 10% of ASB patients [25].

ASB has been associated with an increased risk of pyelonephritis in up to 30% pregnant patients [27]. There is also an association with low birth weight and preterm labor [27]. Given these findings, both the United States Preventative Services Task Force (USPTF) and the American College of Obstetricians and Gynecologists (ACOG) recommend for the routine screening for ASB with a single urine culture [28, 29]. The relationship between preterm labor and ASB is controversial and may simply be a side effect of the increased risk of pyelonephritis with the associated risk of systemic infection [25, 27]. A recent study in the Netherlands screened pregnant women in the 16th to 22nd week of pregnancy for ASB. Those with ASB were randomized to treatment with nitrofurantoin versus placebo for 5 days. The authors concluded that ASB did not create an increased risk for low birth weight, but the study was underpowered to detect this difference. There was no difference in preterm labor rates between the groups. There was, however, a lower rate of

pyelonephritis in the treated cohort (0.6%) compared with the untreated, placebo group (2.4%) [30].

Treatment of ASB is dependent on the organism detected during screening urine culture and tailored to the safety in the current stage of pregnancy. Therefore, no single agent can be recommended in all occurrences of ASB. The duration of treatment is controversial, and many single dose regimens have been reported, but a recent Cochrane database review suggests that a 7 day course of therapy is more efficacious than shorter therapies. More studies are needed to determine actual cure rates [31]. A repeat urine culture is recommended after a course of therapy to assure clearance of the bacteria) [32]. Recurrent infections may suggest an anatomical abnormality or other process, and thus, the recommendation is for a further urological workup after delivery.

Acute Cystitis/Pyelonephritis

Acute cystitis is a symptomatic infection of the bladder. Symptoms are the same in both pregnant and nonpregnant women and generally include dysuria, frequency, and urgency. Systemic infections do not generally occur. Frequency is common during pregnancy, and its presence alone should not be an indication of infection [1]. Dysuria is not a normal finding in pregnancy and as such should mandate an evaluation. Microscopic hematuria is often positive on urinalysis. Gross hematuria may be present in more severe cases of cystitis but is rare and necessitates a more extensive urological workup including cystoscopy. A urinalysis with signs of pyuria indicates an infection. All cases of cystitis can be treated with empirical therapy, but a culture should be obtained to determine the causative bacteria. The duration of treatment is similar to that of ASB and should be 7 days [31]. A repeat urine culture is required after treatment to confirm clearance of the bacteria.

Pyelonephritis is associated with fever, flank pain, nausea, vomiting, and costovertebral angle tenderness on examination. The incidence of pyelonephritis in pregnancy is 0.5% [33]. Women with pyelonephritis were more likely to be smokers, present late for prenatal care, belong to African American and Hispanic populations, and have less education [33]. Patients should be promptly evaluated, admitted to the hospital, and administered intravenous antibiotics. A urine culture prior to initiating antibiotic therapy is obtained. Parenteral antibiotics are continued until the patient remains afebrile for 48 h. Transitioning to oral antibiotics can be performed once culture-directed therapy is available. Twenty percent of patients will progress to severe infections and develop septic shock [34]. Women with pyelonephritis suffered more complications with their pregnancy including sepsis, anemia, acute respiratory failure, acute renal failure, and preterm birth.

Those with complex urological histories such as renal stones, ureteropelvic junction obstructions, prior surgery on the urinary tract, and those not responding to antibiotic therapy should be screened with upper tract imaging to rule out urinary tract obstruction. Renal and bladder ultrasound serves as a safe baseline study that

poses minimal risk to the fetus. Cultures confirming clearance of bacteria should be performed after treatment to reduce the risk of recurrence.

Hydronephrosis of Pregnancy

The ureters and renal pelvis undergo dilation in up to 80% of pregnant women [13]. This phenomenon is called hydroureter and hydronephrosis, respectively. The dilation is more prominent on the right than the left. Ultrasonographic studies can demonstrate these changes by the second trimester and may persist until 12 weeks postpartum. The dilated ureters can retain as much as 200–300 mL of urine, producing stasis which can result in a bacterial reservoir, thus, contributing to an increased risk of pyelonephritis during gestation.

Hydroureter and hydronephrosis in pregnancy may be a result of hormonal influences, physical compression, and intrinsic alterations in the walls of the ureters [35]. In addition, high concentrations of progesterone reduce ureteral tone, peristalsis, and contraction pressure. The typical dextrorotation of the gravid uterus by the sigmoid colon helps explain the more likely involvement of the right ureter. In some cases, this effect can kink the right ureter as it passes over the right iliac artery. Furthermore, the enlargement of the ovarian infudibulopelvic ligament vessels may cause ureteral compression at the sacroiliac articulation. In addition, the gravid uterus, as it enlarges, may produce elongations and tortuosity of the ureters, displacing them more laterally. Albeit rare, these changes may produce maternal pain and true urinary obstruction.

The connective tissue that surrounds the ureters (Waldeyer's sheath) undergoes hypertrophy which may have a protective effect of preventing hormone-induced dilation below the pelvic brim [36]. Obstructive uropathy, from nephrolithiasis or stricture, will produce ureteral dilation. This causes flank pain. Typically, it can be distinguished from physiological hydronephrosis on imaging studies which may identify a cause for obstruction.

Patients presenting with symptomatic hydronephrosis should be managed with conservative measures including analgesics, hydration, and repositioning [37]. The lateral decubitus position can help to unload the compressive weight of the gravid uterus on the posterior pelvis and thus decompress the ureters. Multiple studies have shown that conservative treatment is effective in over 90% of patients [38, 39]. Renal and bladder ultrasound is used to evaluate the severity of hydronephrosis and the presence of obstruction. Ureteral jets are easily seen during pregnancy by performing an ultrasound of the bladder [40]. The absence of a ureteral jet is consistent with renal obstruction (Fig. 9.1). Color Doppler can aid in the diagnosis. A renal arterial resistive index of >0.70 and a difference of 10% compared with the contralateral kidney or reduced ureteral jet is indicative of ureteral obstruction [41].

Patients failing conservative treatment for symptomatic hydronephrosis and demonstrating obstruction should be managed with the placement of an indwelling ureteral stent [39], although this is not without controversy. One group reported that the degree of hydronephrosis did not actually correlate with pain scores in patients

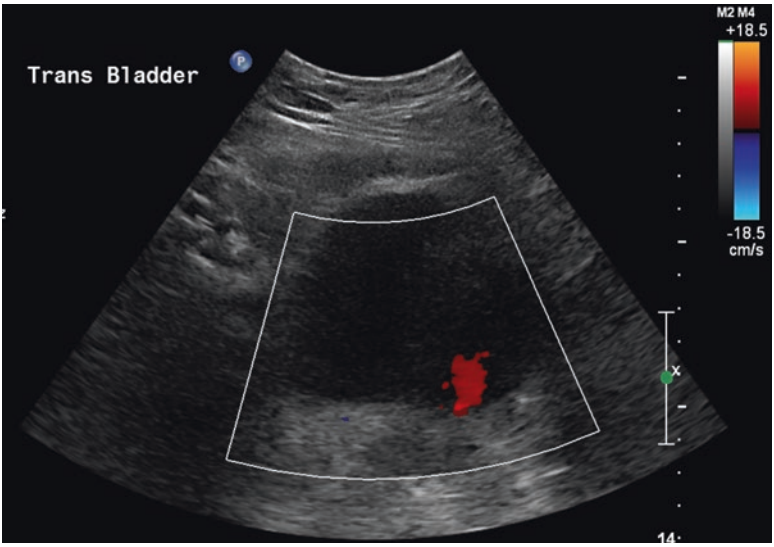

Fig. 9.1 Ultrasound of a pregnant patient presenting with flank pain, nausea, and vomiting with a right-sided ureteral stone. *Color Doppler* indicates the loss of a right ureteral jet, consistent with obstruction

presenting with flank pain [42]. Caution must be exercised in not underdiagnosing obstructed patients with less severe forms of hydronephrosis. One case-controlled study showed no difference between conservative treatment and ureteral stent placement, noting that both had similar pain scores before therapy and a week after. However, a randomized trial of conservative therapy or stent placement for symptomatic hydronephrosis revealed that stent placement has a lower failure rate in moderate to severe cases of hydronephrosis. The authors noted that 16% of patients with ureteral stents complained of stent-related discomfort, and they felt that conservative management should be attempted first [43]. Rare cases of renal pelvis rupture have been reported due to obstruction which can mimic normal symptomatic hydronephrosis of pregnancy [44]. This is also treated with ureteral stent placement.

Pregnancy causes the bladder mucosa to become edematous and hyperemic. High levels of progesterone cause bladder wall relaxation and increased bladder capacity. However, the enlarging uterus displaces the bladder superiorly and anteriorly, thus, flattening it, and in effect, reducing capacity. The flaccidity of the bladder may produce incompetence of the vesicoureteral valve. The combination of increased intravesical and decreased intraureteral pressures may cause transient vesicoureteral reflux [45, 46].

Nephrolithiasis

Symptomatic nephrolithiasis is a common nonobstetric cause of hospital admission for pregnant patients [47]. Although the rates vary within the literature, roughly 1 in 1500 pregnancies is affected by stones, but the overall rate of symptomatic stones remains the same between pregnant and nonpregnant women; 0.03–1% [48]. Presenting symptoms are similar to the general population: nausea, flank pain, urinary frequency, microscopic, and even gross hematuria are common. The vast majority of patients can be managed expectantly but cautiously; pregnant women admitted for renal colic associated with kidney stones have a higher risk of preterm delivery [49–51].

Beginning in the first trimester, gestational hydronephrosis is seen in 80% or more of pregnant women and should resolve in the postpartum period [50]. The right ureter is typically more dilated than the left, but symptomatic stone frequency is the same bilaterally [52]. This is felt to be primarily the result of compression by the dextrorotated uterus and dilation of the right ovarian vein, although serum progesterone levels may contribute to ureteric smooth muscle relaxation [53]. Hydronephrosis and resultant urinary stasis can produce a lithogenic environment.

Renal blood flow in pregnant women increases as does overall kidney size [54]. As the glomerular flow increases, the serum levels of creatinine, blood urea nitrogen, and uric acid decrease [55]. Pregnant women are at risk of stones due to this increased urinary uric acid as well as increased calcium excretion, but the risk is offset by excretion of other factors such as citrate and magnesium. Hypercalciuria is secondary to the elevation of 1, 25-dihydroxyvitamin D in the maternal bloodstream as the fetus removes calcium across the placenta; hypercalciuria is seen in all trimesters but should return to normal levels after birth [56].

Although calcium oxalate stones are the most common type of kidney stone regardless of age and gender, a greater proportion of women in childbearing years develop calcium phosphate stones than at later ages. Studies of symptomatic pregnant women suggest that calcium phosphate stones are much more common than calcium oxalate stones, at rates of 65–70% [57, 58]. The exact etiology behind this difference is still under investigation, but it has been suggested that the increased urinary calcium and slightly higher urine pH of pregnant women in the third and second trimester, in addition to increased urinary stasis, may be linked.

The medical and surgical treatment of nephrolithiasis in the pregnant patient should be coordinated between the urologist and obstetrician [59]. The rate of spontaneous passage of stones is high: from 64% to 81%, and pregnant women are often able to pass stones at an increased rate compared with nonpregnant women [52, 58]. Due to the risks of anesthesia, conservative trials for passage with opiate pain medication are often recommended as a first-line intervention [59]. Tamsulosin, an alpha-1a antagonist, is commonly prescribed as part of medical expulsive therapy; in nonpregnant patients, it has been shown to decrease pain and decrease time to stone passage [60]. It is rated as a pregnancy category B (no adequate and well-controlled studies in pregnant women) by the Food and Drug Administration; thus, its use in the pregnant population is controversial. Animal studies in rats and rabbits

demonstrated no evidence of fetal harm [61]. Data in pregnant women are sparse, but Bailey et al. found that in a retrospective review of 27 women treated with Tamsulosin for symptomatic stones, women on Tamsulosin had an increased rate of spontaneous stone passage compared with controls without increased rates of obstetric or perinatal complications [62]. The majority of women in the study had symptomatic stones and subsequent Tamsulosin exposure in the second and third trimester, consistent with usual stone presentation. While later use of Tamsulosin would ideally prevent fetal exposure at the most vulnerable times of pregnancy, Tamsulosin's use for medical expulsive therapy in the pregnant patient is off-label and must be associated with careful counseling between physician and patient, particularly before of the third trimester. The counseling must be accompanied by clear documentation in the medical record.

Imaging options for the pregnant woman with flank pain and concern for stones are often limited due to concern for fetal safety. Ultrasonography is a natural first-line choice without any concern for side effects, although long durations of Doppler signals can cause temperature elevations and should be limited during the first trimester. Unfortunately, hydronephrosis is common in pregnant women and, especially in the late term, is not specific for nephrolithiasis and can have a sensitivity as low as 34% in the detection of kidney stones [63]. The distal ureter can be evaluated with transvaginal ultrasound; this is tolerable by patients and can complete the evaluation of the entire ureter; physiological compression of the ureter should not occur below the pelvic brim in pregnancy [64]. Ureteric jets may be helpful in determining if a ureter is obstructed, although 15% of asymptomatic pregnant women may not have detectable jets [65].

Noncontrast magnetic resonance imaging (MRI) avoids radiation exposure and can help with stone identification as well. Although noncontrast computerized tomography (CT) remains the most accurate imaging modality for stone identification, MRI can detect a filling defect signifying a stone (Fig. 9.2) and also other secondary signs that suggest the presence of nonphysiological obstruction [66]. A standing column of urine within the ureter, ending at an abrupt transition point, is indicative of obstruction (Fig. 9.3) [67]. Physiological obstruction is often more tapered in shape and should not extend beyond the pelvic brim; perinephric and periureteral edema, as well as pyelonephritis, can also be seen on MRI. In the middle of the night, however, on-call radiologists may not read MRI studies, and smaller hospitals may not have MR imaging available. Gadolinium contrast increases the specificity of MRI but is not recommended in pregnant patients; it is water soluble and can cross the placenta into the fetal circulation. The risks to fetal exposure are not known, but the American College of Obstetricians and Gynecologists recommends against its use unless benefit clearly outweighs risk [68].

Noncontrast CT is an ideal method for imaging stones but exposes the fetus directly to ionizing radiation. According to the ACOG guidelines, radiation exposure through CT scans is much lower than the exposure associated with fetal harm, and if the safety of the pregnant woman is in question, CT studies should not be withheld from the patient. However, for routine imaging or equivocal cases where ultrasound or MRI is possible, CT should be avoided. The American College of

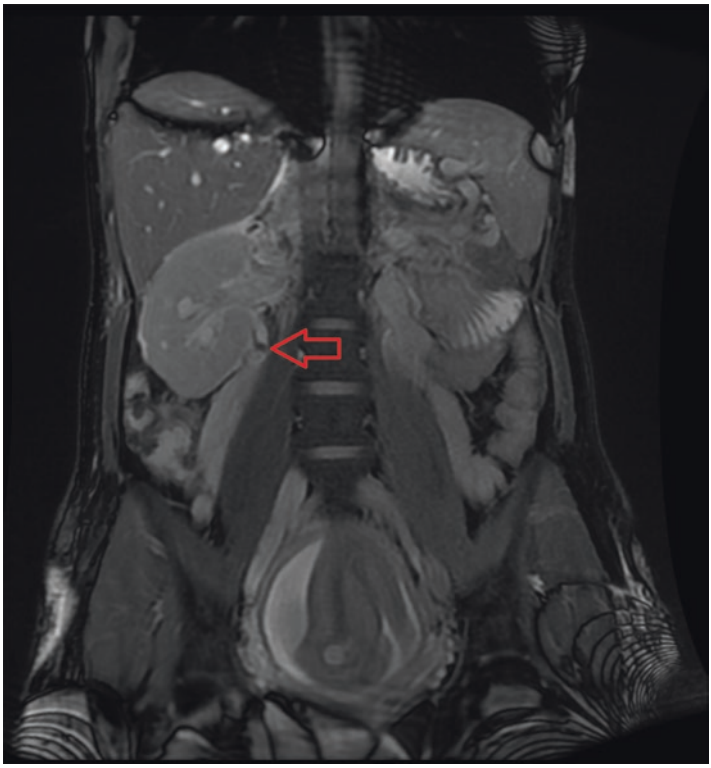

Fig. 9.2 Magnetic resonance imaging (MRI) in a pregnant patient with a right-sided, symptomatic, obstructing stone. The *arrow* indicates a filling defect consistent with a proximal ureteral stone

Radiology guidelines support these recommendations; the risks of fetal damage by low-dose noncontrast CT are exceptionally low, particularly at doses of radiation less than 100 mGy and/or after 15 weeks of conception [69].

Stone disease which is not responsive to hydration and analgesics requires surgical intervention [59]. Cystoscopy and stent placement rapidly relieve the ureteral obstruction [37]. Likewise, those with obstruction and signs of urinary tract infection require emergent decompression via ureteral stenting. Septic patients with hemodynamic instability should undergo percutaneous nephrostomy placement to decompress the collecting system [70]. Percutaneous nephrostomy placement avoids general anesthetic and can be performed under local analgesia. Ureteral stent placement should be done using the ALARA (as low as reasonably achievable) principles. Most urological cases can be performed with ultrasound guidance rather than fluoroscopy [71–73]. In cases where fluoroscopy is required, it should be performed with minimal fluoroscopy usage and lead shielding of the fetus (Fig. 9.4).

Once the stone is treated acutely, long-term management is dependent on the risks associated with treatment and the stage of pregnancy. Ureteral stents placed to

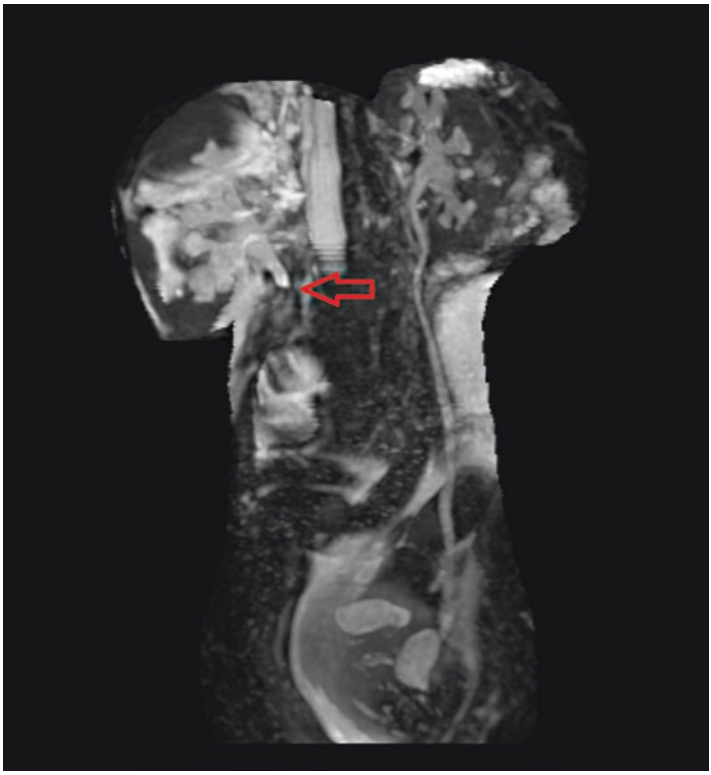

Fig. 9.3 Reconstructed magnetic resonance imaging (MRI) in a pregnant patient with a right-sided, symptomatic, proximal ureteral stone. The *arrow* indicates a fluid column in the right ureter with an abrupt transition point and is indicative of obstruction

relieve the obstruction of stones typically last 3–6 months in a nonpregnant patient before requiring replacement. In the pregnant patient, ureteral stent dwell times are much shorter and may require frequent changes due to encrustation in a mere 4–6 weeks [59]. These stent changes lend themselves to increased exposure to both anesthesia and radiation. A growing body of literature suggests that ureteroscopy with holmium laser lithotripsy may be a safe and effective alternative to repetitive stent changes [59, 74, 75]. Analytical models demonstrate that stone treatment with ureteroscopy is more cost-effective than stent changes alone regardless of gestational age [76]. Ureteroscopic management should only be performed at centers capable of providing specialty services and the ancillary equipment required to handle pregnant stone patients [59].

Extracorporeal shock wave lithotripsy (ESWL) is commonplace in the treatment of renal stones but is contraindicated in the pregnant patient. Larger stones in the kidney which are not amenable to ureteroscopy should be managed expectantly until after delivery in most cases. There are newer studies which indicate that percutaneous nephrolithotomy is feasible in the pregnant patient [70, 77]. Positioning of

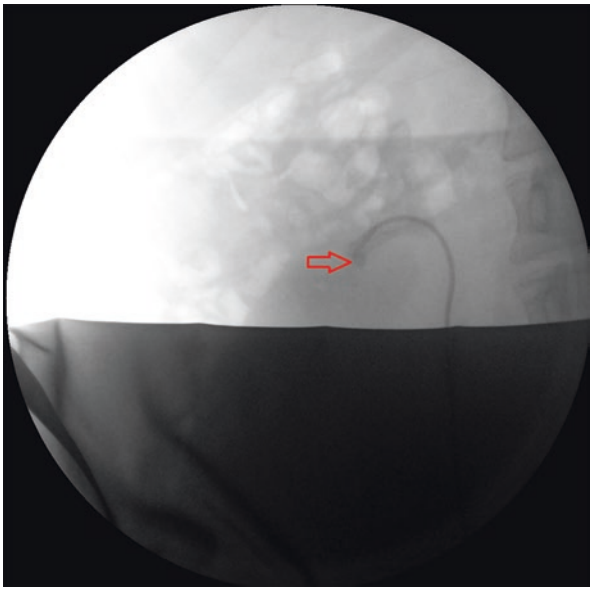

Fig. 9.4 Lead shielding placed over the mid and lower abdomen during the placement of a right ureteral stent under fluoroscopic guidance. The *arrow* indicates a renal stone

the patient in the prone position is difficult in the later stages of pregnancy. Complex surgical intervention such as this should be left to centers of excellence familiar with the technique and proper resources for both mother and fetus.

Summary

The genitourinary system undergoes extensive changes during pregnancy. Many alterations of normal function such as infection, dilation, or obstruction of the urinary tract, and formation of renal stones can all lead to abdominal pain in the pregnant patient. Imaging strategies use ultrasonography as the main modality with the addition use of MRI when appropriate, minimizing fetal exposure to the risks of ionizing radiation. Patient management is dependent on the stage of the pregnancy and overall maternal health. Core principles include treatment of infection, drainage of the collecting system, and treatment of the offending obstruction. The majority of urological issues in the pregnant patient can be managed both safely and effectively with minimal risk to both mother and child.

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Trauma During Pregnancy

10

Stanley M. Augustin, Maxwell Almenoff, and Aaron Sparks

Introduction

Trauma in pregnant women presents a unique problem. The addition of a second patient adds a layer of complexity to management. Trauma is a significant cause of morbidity and mortality to both the mother and fetus. Trauma represents the leading cause of death in women under the age of 35 [1]. Six to seven percent of pregnancies are complicated by trauma [2]. Common causes include motor vehicle collisions, falls, and assaults. Trauma is a leading cause of death during pregnancy and is related to 50% of maternal deaths [3]. The fetal death rate has been reported at 6.5 per 1000 live births [3]. The primary cause of fetal death is maternal death.

Trauma represents a significant burden to the pregnant patient and fetus. This chapter will explore relevant anatomical and physiological changes, injury prevention, injury patterns, initial and operative management, specific obstetrical complications, and outcomes.

In general, the initial management of pregnant trauma patients mirrors the management of nonpregnant trauma patients. The relevant differences and important distinctions in the pregnant patient will be highlighted.

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Anatomy and Physiology of Pregnancy

A complete discussion of the physiological changes in pregnancy is discussed elsewhere. The relevant factors to the trauma patient are discussed here. The pregnant patient can be expected to have increased minute ventilation. A study of the blood gases will reflect the changes in ventilation. The pregnant trauma patient may have an elevated diaphragm. Chest tube placement may need to be 1 to 2 intercostal spaces higher in the pregnant patient. A decrease in lower esophageal sphincter pressure increases the risk of aspiration. Early placement of a nasal or oral gastric tube should be considered in those gravid patients who are without a protected airway.

Cardiovascular vital signs are altered in the pregnant population. An increased heart rate and altered blood pressures are considered to be normal physiological alterations in gravid women. The blood pressure decreases in the first trimester and reaches a low point in the second trimester. It returns to near normal in the third trimester. However, attributing tachycardia and hypotension to normal physiology represents a potential pitfall in the pregnant trauma patient. Plasma volume expands and results in a relative anemia (RBC mass increases by a lesser value). Plasma expansion increases the loss of blood volume necessary to cause clinical hypotension. A relatively "minor" blood loss results in shunting blood away from the placenta. Thus, the fetus may be experiencing shock in a mother with normal or near normal vital signs. The gravid uterus exerts pressure on the inferior vena cava and decreases preload which can result in hypotension when supine.

Injury Prevention

Trauma represents a serious cause of morbidity and mortality in pregnancy. Simple interventions, however, can protect both the mother and fetus. The utilization of a seat belt is paramount in the pregnant patient. Correct placement and usage of both the lap belt and the shoulder harness provide the best protection. The lap belt should be placed under the abdomen and across the upper thigh. The shoulder harness is placed between the woman's breasts. Placing the lap belt across the abdomen may result in injury to the uterus and fetus during motor vehicle collision. Nonuse of the shoulder harness exposes the uterus to flexion/compression injuries and increases risk of maternal injury. The greatest benefit of a seat belt is not being ejected from the vehicle.

Domestic violence represents another source of trauma in the pregnant patient. The incidence of domestic violence varies by study and may be as high as 30% [2]. The primary care physician, obstetrician, and trauma team have a duty to identify and recognize warning signs (inconsistent injury/history, frequent hospital/ED/office visits, substance abuse, depression, partner unwilling to leave during examination). Involvement of the appropriate agencies, interventions, and counseling provides safety to mother and fetus. In addition, substance abuse represents an increased risk of trauma along with the additional negative side effects on the fetus. Screening

and intervention of at- risk individuals provide another opportunity to intervene before a trauma occurs.

Injury Patterns

Pregnancy changes the patterns of injury in trauma. However, it does not affect the morbidity or mortality. The changes in injury patterns include more severe abdominal injuries, higher percentage of extremity injuries, and less severe head injuries [4]. Depending on the size of the uterus, the fetus may be more likely to be injured than the mother. The incidence of trauma and the likelihood of injury to the fetus increases with an increase in gestational age. Half of all traumas in the pregnant population occur in the third trimester [5].

The most common cause of injury is blunt trauma as a result of motor vehicle collisions, falls, assaults, automobile striking pedestrians, and domestic violence.

Penetrating injuries include stab wounds, gunshot wounds, and impalement. Stabbing wounds are generally better tolerated than gunshot wounds [2]. Domestic violence is common during pregnancy with a rate of 10–30% [3]; fetal death occurs in 5% of these cases [3].

Imaging Issues

Trauma patients frequently require multiple imaging modalities. Exposure of the fetus to ionizing radiation represents an obvious concern. However, the risk of ionizing radiation should not outweigh the benefits of imaging in pregnant trauma patients. The imaging necessary to identify injury and treat the mother is obtained. The threat of a missed or misdiagnosed injury represents great harm to the mother and fetus. Despite the concern about ionizing radiation, routine imaging in pregnant trauma patients presents a low risk to the fetus. The typical dose of ionizing radiation to the fetus in a CT study of the abdomen and pelvis is 25 mGy [6]. The dose may be lower with modern CT scanning and the use of automated exposure control [6]. "In 1977, the National Council of Radiation Protection and Measurement issued the following policy statement with regard to radiation and pregnancy: 'The risk [of abnormality] is considered to be negligible at 50 mGy or less…'" [6]. The American College of Obstetricians and Gynecologists offered a similar statement in 2004: "Women should be counseled that x-ray exposure from a single diagnostic procedure does not result in harmful fetal effects. Specifically, exposure to less than 5 rad [50 mGy] has not been associated with an increase in fetal anomalies or pregnancy loss" [6]. Routine trauma imaging does not appear to increase the risk of radiation-induced diseases. However, it is prudent to limit exposure without compromising patient care. Shielding the uterus is appropriate, when possible, and limitation of the number of nonessential radiographic studies is advisable.

Primary and Secondary Survey

The gravid uterus does not alter the primary survey of the injured patient. The mother takes precedent over the fetus. Standard trauma resuscitation utilizes the ABCDE's to identify and treat life-threatening injuries. A patent airway is confirmed or secured based on the patient's clinical status. Supplemental oxygen is administered to prevent maternal and fetal hypoxia. Breath sounds are auscultated bilaterally (and confirmed with a chest X-ray as an adjunct to the primary survey). Pulses are palpated, and hemorrhage is controlled to confirm and protect cardiovascular circulation. The liberal use of intravenous fluids and blood products should be administered through large bore peripheral intravenous accesses. The physiological volume expansion of pregnancy can obscure hypovolemia so a clinically high index of suspicion is required to assess fluid status. The gravid patient should be placed on their left side to avoid obstruction of the inferior vena cava. Alternatively, if the patient must be maintained on a backboard due to concern for spinal injury, a wedge can be placed under the patient's right hip and flank. A rapid neurological assessment provides a measure of disability. The patient is rolled and completely exposed to identify further injury.

The secondary survey contains a head-to-toe physical examination as in the nonpregnant patient. Injuries should be identified and addressed. The secondary survey should contain a thorough obstetrical history and formal pelvic examination unless vaginal bleeding is observed. An obstetrical consultant should be obtained and remains readily available to the trauma team.

It is important to identify vaginal lacerations/bleeding, fluid indicating possible rupture of membranes, early contractions/labor, placenta previa, placental abruption, prolapsed cord, and any fetal heart rate abnormalities. If available, sonography of the abdomen should be liberally applied.

The initial fetal evaluation takes place after the mother's primary survey and stabilization. It is important to initially establish an estimation of the gestational age. The gestational age addresses the important question of viability and dictates management. Fetal heart rate auscultation, fundal height measurement, presence of and frequency of contractions and sonographic evaluation of the placenta and fetus are important aspects of the evaluation [1]. Early initiation of continuous electronic fetal monitoring is important way to assess fetal distress [7].

The diagnostic workup for the mother should proceed in a manner to address her injuries. Routine trauma lab studies should be obtained. In addition, Kleihauer-Betke acid elution testing (KB) should be performed and $Rh_o(D)$ immune globulin given if appropriate. KB testing helps to identify those patients at higher risk of abruption and preterm labor [5]. Radiographic imaging should be obtained as indicated by the mother's injury pattern, just as for a nonpregnant patient. Ultrasound can be used to evaluate the fetal gestational age and injuries and assess amniotic fluid volume. Continuous electronic fetal monitoring is the standard of care in patients with a viable fetus. Monitoring should be a minimum of 6 h in the absence of no concerning findings and up to 24–48 h with uterine contractions, nonreassuring fetal heart rate patterns, vaginal bleeding, uterine tenderness, and rupture of membranes or with

serious maternal injury [5]. The setting for continuous fetal monitoring depends on the mother's injuries and may include the intensive care unit, operating room, and/or obstetrical unit.

Operative Intervention

The operative indications are the same for the pregnant and nonpregnant trauma patients. The presence of a gravid uterus should not alter the decision to proceed with exploratory laparotomy. Penetrating abdominal trauma violating the peritoneal cavity should proceed to the operating room. Some penetrating trauma (knife wounds not penetrating peritoneum) may not need laparotomy. Blunt abdominal trauma with a positive physical exam (peritonitis), hemodynamic instability, and those patients requiring continuing resuscitation should proceed to laparotomy. Specific findings on CT scan may dictate further management per trauma guidelines. The fetus should tolerate the operation well, if appropriately resuscitated [1]. It is paramount that the mother, and by extension the fetus, receive appropriate resuscitation. The operation should proceed as in a nonpregnant patient. The tenets for operative intervention include hemorrhage control, contamination control, identification of injuries, and repair/reconstruction. An important distinction includes management of the injured uterus. In a viable pregnancy, abdominal delivery should be considered in patients with an injured uterus and evidence of fetal intolerance to the intrauterine environment [1]. The injured uterus can then be repaired or excised if necessary. If the pregnancy is nonviable, the uterus can be repaired and managed expectantly in many cases [1].

Obstetric Emergencies in Trauma

Abruption of the placenta is the 2nd most common cause of fetal death in trauma patients [2]. Placental separation represents a cause of significant morbidity and mortality to the fetus. The rate of placental abruption is 5% in minor injuries and increases to 50% in patients with severe injuries [2]. The overall fetal mortality rate may be as high as 60% [2]. Placental abruption, of clinical significance usually presents within 24–48 h after the initial trauma [2]. As in nontrauma patients, symptoms include painful vaginal bleeding. It can lead to premature labor and disseminated intravascular coagulation. Continuous fetal monitoring is the most sensitive diagnostic test and should be maintained for a minimum of 6 h per Eastern Association for the Surgery of Trauma (EAST) guidelines [5]. In the absence of symptoms, monitoring can be discontinued after 6 h [4]. Ultrasound can also aid in diagnosis but does not rule out abruption in some cases secondary to low sensitivity [4].

Uterine rupture represents a rare event and occurs in less than 1% of traumas [4]. The most significant risk factor for rupture is a prior cesarean section [4]. It occurs after direct abdominal trauma in the late second and third trimesters. The maternal mortality rate approximates 10%, and the fetal morality approaches 100% [2].

Physical examination demonstrates abdominal tenderness, uterine irregularity, and palpable fetal parts. Early recognition may increase maternal survival. The treatment is emergency laparotomy and possible hysterectomy.

Fetal injury should be suspected when the uterus has sustained a penetrating injury. The fetus is injured in 2/3 of cases with penetrating uterine trauma [1]. Fetal skull and brain injury are common in pelvic fractures when the head is presenting at the pelvic inlet and is engaged in the pelvis [1].

Umbilical cord prolapse into the vagina can occur with spontaneous rupture of membranes when there are no fetal parts engaged in the pelvis. The potential sequelae include fetal hypoxia and death. The treatment is emergent abdominal delivery for viable gestations.

Urgent abdominal delivery is considered on an individualized basis. Abdominal delivery should be considered in all patients over 26 weeks with fetal intolerance to the intrauterine environment [2]. The risk of prematurity should be weighed against the fetal compromise and need for delivery. Other indications for delivery include a gravid uterus preventing repair of maternal injuries, unstable spinal injuries, and if maternal demise is imminent [2]. In the event of maternal death or failure of resuscitation, emergent abdominal delivery should be considered in all fetuses over 24 weeks [2]. The best results occur if the fetus is delivered within 4 min of maternal demise [5].

Outcomes

Trauma is a leading cause of maternal death and accounts for over 5% of fetal deaths. Interestingly, the overall morbidity rates are similar to those of nonpregnant patients and the mortality rate of pregnant patients may actually be lower in the setting of trauma [4, 7, 8]. Pregnancy-related morbidity occurs in approximately 25% of trauma patients [9]. Maternal mortality is associated with amniotic fluid embolism, deep vein thrombosis/pulmonary embolism, and infections [3]. Even pregnant patients with minor traumatic injury have increased risk of preterm delivery and a low birth weight infant [4]. Trauma patients should be monitored more closely throughout their pregnancy as the associated risks are both short and long term [10].

The maternal injury severity score correlates well with adverse fetal outcomes. A score of over 25 is associated with a 50% fetal mortality rate. Risk factors for fetal death include maternal death, overall maternal injury, ejection from a motor vehicle, pelvic fracture, severe abdominal injury, and hemorrhagic shock. Maternal shock is associated with preterm labor and fetal intolerance to the intrauterine environment resulting in an 80% fetal mortality [5].

The presence of disseminated intravascular coagulation represents a major predictor of fetal mortality and consideration should be given to imminent delivery of a fetus with viable gestational age [4]. Additional factors associated with fetal mortality include decreased Glasgow Coma Scale, maternal acidosis, decreased serum

bicarbonate, maternal hypoxia, fetal heart rate under 110 beats per minute, maternal malperfusion, maternal death, pelvic fracture, ejection from a vehicle, direct uteroplacental injury, and severe maternal head injury [3, 4]. Composite morbidity models using third trimester trauma, hospital length of stay greater than 2 days, abdominal trauma, an injury severity score of greater than 2, or a positive Kleihauer-Betke test identifies those at risk for adverse perinatal outcomes [11]. Both major and minor injury places the fetus at increased risk for fetal demise, premature delivery, and low birth weight [12].

Summary

Trauma represents a significant cause of morbidity and mortality in pregnancy. The presence of a second patient presents unique management challenges. However, the initial management of a pregnant trauma patient is unchanged. The mother should be treated as in a nongravid patient. A good outcome for the mother is the best chance for fetal survival.

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Recommended Reading

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Surgical Principles in the Gravid Female

11

Peter Bogach Greenspan

Introduction

Surgical intervention in the gravid female does not appreciably result in adverse outcome for the mother or the fetus. Risks may be increased, however, if complications arise. For example, peritonitis from a perforated appendix produces significant maternal and fetal morbidity and mortality, despite appropriate anesthesia and surgical intervention. Nonetheless, gravid women do not seem to have significant untoward complications when compared with non-gravid women undergoing similar procedures [1].

General Principles

Nonobstetric surgery during pregnancy is a significant issue for providers who care for women. Large-scale randomized clinical trials in this population are difficult to perform; therefore, no data are available to allow for specific recommendations.

It is important for a provider to seek obstetrical consultation prior to performing nonobstetric surgery and certain invasive procedures (e.g., cardiac catheterization or colonoscopy) because obstetricians are uniquely qualified to discuss aspects of maternal physiology and anatomy that may affect intraoperative maternal–fetal well-being.

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The following generalizations outlined in American College of Obstetricians and Gynecologists (ACOG) Committee Opinion #696 may be helpful to guide decision-making:

- No currently used anesthetic agents have been revealed to have any teratogenic effects in humans when using standard concentrations at any gestational age.
- Fetal heart rate monitoring may assist in maternal positioning and cardiorespiratory management and may influence a decision to deliver the fetus [2].

The following recommendations represent the consensus of the ACOG committee:

- A gravid woman should never be denied indicated surgery, regardless of trimester.
- Elective surgery should be postponed until after delivery.
- Whenever possible, nonurgent surgery should be performed in the second trimester when preterm contractions and spontaneous abortion are least likely [2].

When nonobstetric surgery is planned by a nonobstetric provider, an obstetric care provider should be consulted, if possible. If such a health care provider is not at the institution where surgery is to be performed, another obstetric care provider with privileges at another institution should be involved.

If fetal monitoring is to be used, consider the following recommendations:

- Surgery should be done at an institution with neonatal and pediatric services.
- An obstetric care provider with cesarean delivery privileges should be readily available.
- A qualified individual should be available to interpret the fetal heart rate patterns.

General guidelines for fetal monitoring include the following:

- If the fetus is considered previable, it is usually sufficient to determine the fetal heart rate by Doppler before and after the procedure.
- If the fetus is considered to be viable, simultaneous electronic fetal heart rate and contraction monitoring should be performed before and after the procedure to assess fetal well-being and the status of contractions.

Intraoperative electronic fetal monitoring may be appropriate when all of the following apply:

1. The fetus is viable.
2. It is physically possible to perform intraoperative electronic fetal monitoring.
3. A health care provider with obstetric surgery privileges is accessible and willing to intervene during the surgical procedure for fetal indications.

4. When possible, the gravida should be given informed consent for emergency cesarean delivery.
5. The nature of the planned surgery will allow the safe interruption or alteration of the procedure to provide access to perform emergency delivery.

In select circumstances, intraoperative fetal monitoring may be considered for previable fetuses to facilitate positioning or oxygenation interventions.

The decision to use fetal monitoring should be individualized and, if used, should be based on gestational age, type of surgery, and facilities available. Ultimately, each case warrants a team approach (anesthesia and obstetric care providers, surgeons, pediatricians, and nurses) for optimal safety of the woman and the fetus.

Optimal Timing for Surgery

There are little data to support optimal timing for surgery in a gravid woman. Modern surgical practice, combined with extremely safe anesthesia support and an understanding of maternal and fetal physiology, allows for surgery to occur essentially at any time during gestation.

Conventional wisdom and experience point to the optimal timing for nonemergent surgery occurring between 16 and 20 weeks. This allows time for resolution of benign cysts and reduces rates of preterm labor associated with surgery later during pregnancy [3].

Consideration of Delivery of the Fetus

The delivery of the fetus in an acutely ill surgical patient is incumbent on multiple factors. One important consideration is the morbidity that the condition is producing in the gravid woman. The physiological alterations that result in the disease process may impose physiological limitations on the mothers' ability to oxygenate her fetus. Hemodynamic status of the mother is an important consideration.

Proper positioning of the gravida during surgery is imperative. The operative management of pregnant patients must include interventions that prevent maternal hypotension, hypoglycemia, hypothermia, and hypoxia.

The Four H's of surgery on pregnant patients:
1. Prevent maternal hypotension
2. Prevent maternal hypoglycemia
3. Prevent maternal hypothermia
4. Prevent maternal hypoxia

The patient should be positioned in a partial left lateral tilt to reduce pressure on the vena cava and maintain adequate venous return. Reese and Willis determined that a tilt at 27 degrees was optimal for cardiopulmonary resuscitation and would also be sufficient for general operative procedures on patients beyond the first

trimester [4]. This concept is universally practiced in the abdominal delivery of fetuses at term or otherwise, for any indication mandating delivery.

The Swedish Birth Registry as described by Mazze and Källén provides the most extensive data regarding anesthetic and surgical risks to pregnant women [5]. The analysis of the effects on pregnancy outcomes of 5405 nonobstetrical surgical procedures performed in 720,000 pregnant women from 1973 to 1981 was reported. General anesthesia was administered for approximately half of these procedures and frequently involved nitrous oxide supplemented by another inhalation agent or intravenous medications. These procedures were performed on 41 percent of women in the first trimester, 35 percent in the second, and 24 percent in the third (Fig. 11.1). Twenty-five percent were abdominal operations, and 20 percent were gynecological or urological procedures. The most frequently performed procedure was laparoscopy, and appendectomy was the most common second-trimester procedure.

Increased perinatal morbidity related to nonobstetrical surgery is often attributable to the underlying disease process rather than to adverse effects of surgery and anesthesia. The Swedish Birth Registry again provides valuable data [5].

The incidence of newborns with congenital malformations or those stillborn was not considerably different from that of nonexposed control neonates. However, there were significantly increased incidences of low birth weight, preterm birth, and neonatal death in infants born to women who had undergone surgery. Increased neonatal deaths were mainly due to preterm birth. These investigators concluded that these adverse outcomes likely were due to a synergistic effect of the maternal morbidity in conjunction with the surgical procedures. Hong reported that there was an increased preterm delivery rate in 235 women undergoing adnexal mass surgery [6].

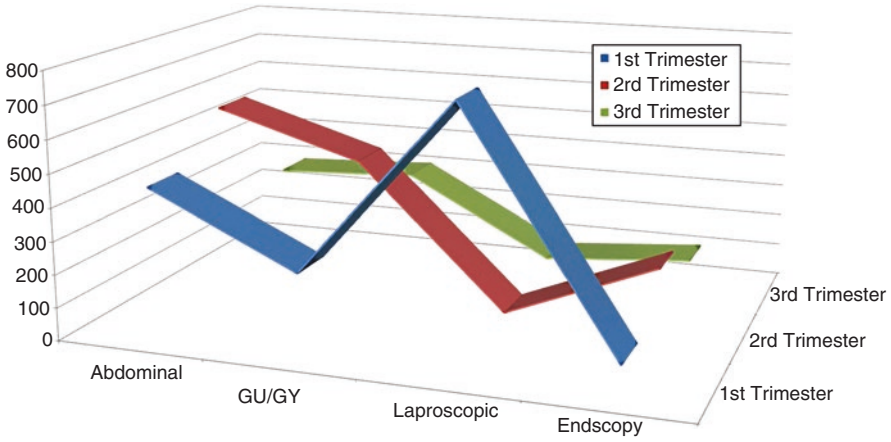

Fig. 11.1 Percentage of surgical procedures by trimester

The Role of Minimally Invasive Technologies

Pelviscopy, originally termed laparoscopy, was considered to be absolutely contraindicated in pregnancy until 1990. Nezhat et al. reported the first pelviscopic cystectomy in a gravid woman in 1991. Technology since then has led to the development of myriad endoscopic procedures as the safety of the technique in the pregnant population has been very widely appreciated [7].

Pelviscopy is now considered the standard of care in the management of much of the pathology in the gynecologic and obstetric populations. Examples include total pelviscopic hysterectomy, salpingectomy, oophorectomy, endometriosis resection, ovarian cystectomy, appendectomy, bowel resection, and ovarian detorsion. Several müllerian anomalies may be managed pelviscopically. Single-incision pelviscopy is emerging as an even less invasive operative intervention in treating the array of gynecological pathologies that afflict women.

Fatum et al. have shown that the benefits of pelviscopy in the nonpregnant patient can be applied to the gravid woman [8]. The pelviscope affords a magnified, improved, and wide view of the operative field. The smaller incisions for the ports into the abdomen result in lesser postoperative pain and more rapid postoperative recovery. Reduction in postoperative pain leads to a decreased postoperative narcotic consumption, earlier ambulation, and a reduced risk of thromboembolism. Fetal depression is also less likely with reduced maternal narcotic use. Bowel manipulation is usually minimal during pelviscopy, which benefits a quicker return to bowel function, and a possible diminution in postoperative adhesions, ileus, and bowel obstruction [9–11]. The smaller scars from pelviscopy result in less incisional hernias, lower the risk of wound complications, and create less opportunity for wound dehiscence as the gravid uterus distends the abdomen. Women undergoing pelviscopic procedures also experience shorter hospital stays and promptly return to regular activities [12].

Visualization and performance of pelviscopic procedures require pneumoperitoneum. The cardiovascular and respiratory adaptations observed with pneumoperitoneum during laparoscopy are heightened in the pregnant patient compared with the general population [13]. The combination of the enlarging uterus which mechanically displaces the diaphragm together with pneumoperitoneum produces decreased compliance of the thoracic cavity, a decrease in the functional reserve capacity, an increase in peak airway pressure, ventilation–perfusion mismatching, increased alveolar–arterial oxygen gradient, and increased pleural pressure. These changes are further accentuated by the Trendelenburg position commonly employed in pelviscopy [9, 13, 14]. The arterial carbon dioxide partial pressure is increased with pneumoperitoneum because of absorption of carbon dioxide from the peritoneal cavity. This increase and the concomitant decrease in arterial pH is of concern in that it may adversely affect the fetus because fetal arterial CO_2 is directly related to maternal arterial CO_2. Bhavani-Shankar et al. investigated this in eight gravid women at 17–24 weeks' gestation that underwent pelviscopic surgery with carbon dioxide pneumoperitoneum [15]. The minute ventilation was adjusted to keep the end tidal CO_2 at 32 mmHg, and arterial blood gas was measured at preinsufflation, insufflation, postinsufflation, and

postoperatively. There were no differences observed in the partial pressure of arterial CO_2 to end-tidal CO_2 gradient, or the partial pressure of arterial CO_2 and pH during the different phases of monitoring. The investigators concluded that end-tidal CO_2 correlated with arterial CO_2 and that optimal maternal arterial CO_2 could be maintained during pelviscopy by adjusting minute ventilation. Blood gas monitoring may not be necessary in healthy patients undergoing pelviscopy [15].

Cardiovascular and hemodynamic changes that occur with pneumoperitoneum are the result of a combination of the physiological effects of patient positioning, anesthesia, and carbon dioxide absorption. Insufflation decreases cardiac output, with a concomitant increase in systemic and pulmonary vascular resistance and blood pressure [13, 16]. The reverse Trendelenburg position has been shown to intensify the cardiovascular changes observed with general anesthesia and pneumoperitoneum with a reduction in the cardiac index of up to 50%. Significant hypotension is also detected resulting from aortocaval compression by the pregnant uterus in conjunction with the other cardiovascular changes induced by pneumoperitoneum [13, 16]. After 15 min of insufflation, a study investigating the hemodynamic changes in laparoscopic surgery in pregnant women revealed that the cardiac index dropped to 21% below baseline. Systolic blood pressure 20% below baseline was aggressively managed with intravenous ephedrine to minimize any decrease in uterine perfusion [15]. Left uterine displacement and limiting the intra-abdominal insufflation pressure to 12 to 15 mmHg are essential to minimizing these cardiovascular changes [15].

Pelviscopy during pregnancy is not without controversy. Timing, the safest method of abdominal cannulation, and appropriate fetal and maternal monitoring are issues that have been raised over time. Pregnancy in the first trimester poses the least technical challenges during abdominal and pelvic surgery. The first trimester uterus is well below the point of initial trocar entry, and visualization of the pelvis and adnexa is optimal. Teratogenesis risk, however, is greatest during this trimester. Second trimester operations pose less risk to the fetus but are technically more difficult, requiring greater surgical skill. The third trimester is attendant with a greater potential for preterm labor, and visualization difficulties are further pronounced by the enlarging uterus. The safest interval for operative intervention for elective cases is during the second trimester. This is explained by the decreased rate of spontaneous abortion, and the risk of premature labor increases as the gestation progresses [9].

Trocar placement and insertion of the pelviscope are determined by uterine size and gestational age. Many surgeons utilize the open Hasson technique when operating in the second and third trimesters; however, studies have shown that closed-entry techniques are undertaken by others [17]. The left upper quadrant (Palmer's point) entry is frequently chosen for insertion of the Veress needle in the closed-entry technique, beyond the first trimester. With this approach, the primary trocar is placed in the midclavicular line, 2 cm below the ribcage. Ultrasound guidance has been utilized to improve the safety of Veress needle and trocar insertion. Similarly, a subxyphoid entry can be undertaken with the trocar placement 2–6 cm above the umbilicus, varying with the fundal height. The additional trocars are then placed under direct visualization. The use of vaginal instrumentation, cervical clamps, and uterine manipulators is contraindicated in the pregnant patient [18].

Because there are a large number of physiological changes seen with gestation and the cardiovascular and pulmonary changes induced by laparoscopic surgery, optimal perioperative monitoring is unclear. The standard precautions that apply to pregnant women undergoing surgery should be sustained in laparoscopic surgery. End-tidal CO_2 should be maintained between 32 and 34 mmHg when using CO_2 insufflation by increasing respiratory rate and tidal volume and systolic blood pressure should be kept within 20% of baseline [14].

There are surgeons who have reported the use the apneumatic approach due to concerns as to the effects of CO_2 pneumoperitoneum. With this technic, pelviscopy is performed using epidural anesthesia, and abdominal access is achieved by mechanical lifting of the abdominal wall with wire spokes [19, 20]. Because this option eliminates the effects of carbon dioxide insufflation seen with general endotracheal anesthesia and is an appealing option for patients with preexisting cardiopulmonary disease, further study is needed to validate its efficacy.

No intraoperative fetal heart rate abnormalities have been reported. When urgent abdominal surgery is indicated during pregnancy, fetal monitoring is sufficient in the preoperative and postoperative periods. There has been no increased fetal morbidity reported using this approach [21].

The positioning of the patient is important in pelviscopic procedures. The bowel and omentum, the gravid uterus, and maternal obesity can make visualization of pelvic organs difficult. Trendelenburg positioning is essential for pelviscopic surgeries. The gravida should be placed in the supine position with a leftward tilt to reduce further compression of the inferior vena cava by the uterus, thus, allowing maximized venous return to the heart and uterine perfusion. Trendelenburg position should be accomplished to reduce the effect on hemodynamic stability.

The Society of American Gastrointestinal Endoscopic Surgeons Guidelines for Laparoscopic Surgery during Pregnancy recommends the following:

- Gravid patients should be placed in the left lateral decubitus position to minimize compression of the vena cava.
- Initial abdominal access can be safely performed with an open (Hasson) technique, Veress needle, or optical trocar if the location is adjusted according to fundal height and previous incisions.
- Intraoperative CO_2 monitoring by capnography should be used during laparoscopy in the pregnant patient.
- Intraoperative and postoperative pneumatic compression devices and early postoperative ambulation are recommended prophylaxis for deep venous thrombosis in the gravid patient.
- Fetal heart monitoring should occur preoperatively and postoperatively in the setting of urgent abdominal surgery during pregnancy.
- Obstetric consultation can be obtained preoperatively and/or postoperatively based on the severity of the patient's disease and availability.
- Tocolytics should not be used prophylactically in pregnant women undergoing surgery but should be considered perioperatively when signs of preterm labor are present [22, 24].

Extrapolation of the success of pelviscopy in the pregnant population has been hindered by the lack of prospective trials and understudied risks. Pelviscopic surgery has been performed safely on gravid women for more than 30 years. There are numerous examples of women suspected of having ectopic pregnancies with subsequent findings of normal first trimester pregnancies that underwent pelviscopy and have progressed to normal gestation and birth. Rizzo studied the effects of pelviscopic surgery during pregnancy with patient and child follow-up during a 1–8-year period [23]. Eleven pregnant women underwent pelviscopic procedures with only 1 conversion to laparotomy. The surgeries were accomplished in the first through third trimesters of pregnancy (10–28 weeks) for acute cholecystitis, chronic cholecystitis and biliary colic, appendicitis, and bowel obstruction. The operative protocol was similar for all patients. All patients received general anesthesia, an open Hasson entry technique, end-tidal CO2 monitoring, insufflations pressure of 10 mmHg, and left lateral positioning. Operative time ranged from 25 to 90 min. Postoperative fetal monitoring was performed for a total of 24 hours. There were no cases of fetal intolerance to the intrauterine environment, need for tocolysis, or fetal demise. The gravidas and their offspring were followed for 6 years. None of the offspring failed to thrive or developed any medical issue [23].

At times, pregnancy is complicated by pathologies and diseases necessitating surgical intervention. The evidence, thus, far indicates that pelviscopic surgery can be safely performed with clear benefits for gravid women.

Antibiotic Prophylaxis, Glucocorticoids, and Tocolytics

Antibiotic prophylaxis at the time of surgery on a gravid female depends on the specific procedure. Antibiotics that have a good safety profile in gravid women include the cephalosporins, penicillins, erythromycin (except the estolate), azithromycin, and clindamycin. Aminoglycosides are relatively safe, but there remains the risk of fetal (and maternal) ototoxicity and nephrotoxicity. Doxycycline is contraindicated and should be avoided during pregnancy. Other tetracyclines have been proven to cause transient suppression of bone growth and staining of developing teeth, although available data do not implicate teratogenic effects from doxycycline. Trimethoprim and nitrofurantoin are not recommended in the first trimester because of a potential increased incidence of congenital malformations. Fluoroquinolones are toxic to developing cartilage in experimental animal studies and are, therefore, usually avoided during pregnancy and lactation. However, these adverse effects on cartilage or an increase in congenital malformations from utilization during human gestation has not been documented.

The standard practice of administration of antenatal glucocorticoids 24–48 h prior to surgery between 24 and 34 weeks of gestation can reduce perinatal morbidity/mortality if preterm birth occurs. However, the American College of Obstetricians and Gynecologists recently published a Practice Advisory entitled “Antenatal Corticosteroid Administration in the Late Preterm Period.” This advisory proposes that with new data and until further guidance is released,

administration of betamethasone may be considered in woman with a singleton pregnancy between 34 0/7 and 36 6/7 weeks at imminent risk of preterm birth within 7 days [25]. Utilization depends upon the urgency of the surgery, and the provider's estimate of whether the gravida is at increased risk of preterm birth due to the underlying disease or the planned procedure. Although there are potential benefits to the fetus, however, antenatal glucocorticoids should be avoided if there is evidence of systemic infection (such as sepsis or a ruptured appendix), because the steroids may impair the ability of the maternal immune system to contain the infection.

The routine administration of prophylactic perioperative tocolytic therapy has no proven benefit. Tocolytics are indicated for treatment of preterm labor until resolution of the underlying, self-limited condition that may have caused the contractions.

Minimizing uterine manipulation may reduce the risk of development of uterine contractions and preterm labor.

Thromboprophylaxis

The increase in the majority of coagulation factors and the decrease in protein S levels during gestation result in a hypercoagulable state. This effect safeguards against excessive blood loss at delivery but contributes to the risk of a thromboembolic event in the postoperative period [16].

Randomized trials on the use of unfractionated or low molecular weight heparin or intermittent pneumatic compression for venous thromboembolism prophylaxis in pregnant patients undergoing pelviscopy provide no data at this time.

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) recommends applying pneumatic compression devices on the lower limbs of gravid women undergoing pelviscopic procedures for surgical problems [17].

The 2012 American College of Chest Physicians (ACCP) clinical practice guideline on prevention and treatment of thrombosis recommends mechanical or pharmacological thromboprophylaxis for pregnant patients undergoing surgery [26]. For any pelviscopic operation likely to take more than 45 min, the use of low molecular weight heparin is recommended; mechanical thromboprophylaxis is a practical alternative for shorter procedures.

Wound Care

The management of surgical wounds in gravid patients does not differ from that which is administered to non-gravidas. The general principles of wound care such as meticulous hemostasis and prevention of infection are universal. Closure of operative wounds is usually left to the discretion of the operator; however, the routine use of sterile surgical staples in no longer advised. Furthermore, the routine placement of surgical drains is discouraged.

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Principles and Practice of Anesthetic Management in the Gravid Patient Undergoing Abdominal Surgery

12

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Maternal Physiologic Considerations

Physiologic adaptations to pregnancy are described in detail in Chap. 1. Table 12.1 summarizes the physiological alterations that have specific implications with respect to anesthesia. They include the following:

The *maternal airway, nasopharynx, and laryngeal* structures are more edematous, and the mucus membranes are more friable than in the nonpregnant state, especially near term. Typically a smaller sized endotracheal tube (6.5–7.0 mm) is used for endotracheal intubation. Extreme caution is used if placing anything through the nares. The nares should be treated with a nasal decongestant spray prior to inserting a nasogastric tube, especially if one is deemed necessary prior to intubation. Likewise, nasotracheal intubation is fraught with the potential for significant epistaxis in the pregnant patient. Pregnant patients have higher incidence of *difficult intubation* because *enlarged breasts* and excess soft tissue can make insertion of the laryngoscope into the oropharynx, and visualization of the glottis difficult. A short-handled laryngoscope and video laryngoscopy should be readily available. In the obese patient, it is important to "ramp" them by placing several blankets underneath the back and neck, placing the operating room table in reverse Trendelenburg position, and asking an assistant to retract the breasts downward during laryngoscopy.

Respiratory changes in the parturient include a higher minute ventilation and a significant reduction in functional residual capacity (FRC), or oxygen reserve. In addition, the maternal "set point" with respect to normal PaCO2 is lowered to

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Table 12.1 Physiologic alterations of pregnancy and anesthetic implications

System	Maternal physiologic alterations	Anesthetic management
Airway	Mucous membranes are more edematous and friable Breasts are enlarged	Use smaller sized ETT (6.0–7.0 mm) Use short-handled laryngoscope or video laryngoscopy Pretreat with nasal decongestant before placing anything through the nares Use ramp and/or Reverse Trendelenburg position Ask an assistant to retract the breasts downward
Respiratory	Lower FRC and higher oxygen consumption leads to rapid desaturation "Normal" maternal PaCO2 is 30–32 mmHg	Preoxygenate prior to induction of GETA with three vital capacity breaths or 3 min of tidal breathing of 100% FIO2 With controlled ventilation, use higher minute ventilation with target ETCO2 of 25–28 mmHg
Cardiovascular	40% increase in cardiac output by 28 weeks gestation Higher maternal HR Lower SVR Lower baseline MAP Aortocaval compression in the supine position	Decreased vascular responsiveness to vasopressors Ephedrine and phenylephrine first line therapy for hypotension Norepinephrine also acceptable to use Maintain left uterine displacement after 20 weeks gestation
Gastrointestinal	Increased gastric acid production Decreased lower esophageal sphincter tone Upward displacement of the stomach by the gravid uterus Volume of gastric content may be difficult to assess	Rapid sequence induction of GETA should be performed on all parturients after 16 weeks. Consider NG tube placement prior to induction in the presence of significant gastric volume.
Hematologic	Dilutional anemia from increased plasma volume relative to red cell mass "Normal" maternal Hb value 10–12 mg/dL Hypercoagulable from increased synthesis of clotting factors	Blood transfusion should be guided by knowledge of lower baseline maternal Hb. DVT prophylaxis with pneumatic compression stockings, SQ heparin or enoxaparin.
Renal/Hepatic	Increased renal blood flow Decreased hepatic synthesis of albumin and glycoproteins Increased hepatic synthesis of coagulation factors	Drugs that are excreted by the kidney will undergo rapid elimination. Elevation of "free" fraction of drugs that are protein bound will occur
Neurologic	Endogenous endorphins, progesterone, and estrogen cause increased sensitivity to anesthetic agents. Nerves are more sensitive to blockade by local anesthetics Increased emotional lability	MAC is lowered Use smaller doses of sedatives and narcotics Local anesthetic dose should be decreased by 25% Emotional support is essential in the setting of emergency surgery

30–32 mmHg. Reduced FRC, combined with the high oxygen consumption of the fetal-placental unit, results in rapid maternal desaturation during periods of apnea or hypoventilation. It is extremely important to provide adequate preoxygenation prior to induction of anesthesia using 3-4 vital capacity breaths or 3 min of normal tidal breathing of 100% oxygen by mask. Mechanical ventilation requires both a larger tidal volume and respiratory rate than in the nonpregnant state, with the target end-tidal pCO_2 value of 25–28 mmHg.

Gastroesophageal changes make ALL parturients after 16 weeks gestation at higher risk of *pulmonary aspiration* and *"full stomach"* precautions should be initiated regardless of NPO status. Decreased lower esophageal sphincter tone, higher gastric acid production, and upward displacement of the stomach by the gravid uterus all contribute to this phenomenon. In the presence of an "acute abdominal" process, administration of narcotic pain medications, administration of oral contrast during the diagnostic workup, delayed gastric emptying, and overt bowel obstruction significantly exacerbate the risk of pulmonary aspiration. The degree of gastric distention may not be apparent on physical exam due to the presence of a gravid uterus. The practitioner should review the CT/MRI results and consult with the surgeon prior to induction of anesthesia to better approximate the volume of gastric contents. If significant gastric content is present, placement of a nasogastric tube and decompression of the stomach should *strongly be considered* before proceeding with induction of general anesthesia. The nares should be treated with a nasal decongestant spray prior to placement of a nasogastric tube, as mentioned above.

Cardiovascular changes in the parturient include a higher cardiac output and circulatory volume by approximately 40% above baseline at 28 weeks gestation. The pregnant state is characterized by increased heart rate, increased stoke volume, and decreased systemic vascular resistance. Elevated heart rate and low systemic vascular resistance would be easy to misinterpret as a manifestation of sepsis, if the practitioner did not have an understanding of what constitutes "normal values" during pregnancy. Because of hormonal changes, the parturient also exhibits *decreased responsiveness to vasopressors* and requires larger doses for therapeutic effect. Both indirect acting (ephedrine) and direct acting vasopressors (phenylephrine) administered to treat hypotension and maintain uteroplacental perfusion are considered safe to use in pregnancy. Because the gravid uterus can cause *aortocaval* compression by about 20 weeks of gestation, it is imperative to perform *left uterine displacement* preoperatively, intraoperatively, and postoperatively to ensure adequate maternal venous return from the lower half of the body to maintain maternal blood pressure and uteroplacental perfusion.

Hematological adaptations to pregnancy include an increased plasma volume relative to the increase in red cell mass, resulting in a *dilutional anemia.* Normal maternal hemoglobin values range from 10–12 mg/dL. Maternal dehydration should be suspected when the hemoglobin level is in a "normal" physiological range. In addition, if surgery involves significant blood loss, blood transfusion should be guided by the knowledge that the pregnant woman has a lower hemoglobin level at baseline. Increased hepatic synthesis of coagulation factors renders pregnancy a *"hypercoagulable state,"* making the parturient high risk for developing deep vein

thrombosis and pulmonary embolism. *Pneumatic compression* stockings should always be applied during surgery and continued well into the postoperative period. Subcutaneous heparin or low molecular weight heparin should be administered in the perioperative period to patients confined to bed. Other hematological findings in the parturient include *increased concentration of fibrin degradation products and plasminogen,* suggesting that systemic fibrinolysis is occurring to some extent. During pregnancy, the diagnosis of disseminated intravascular coagulation should not be based on these lab values alone.

Renal blood flow is dramatically increased during pregnancy causing drugs that are primarily excreted by the kidney to undergo rapid elimination. *Hepatic synthesis* of serum proteins, especially albumin and glycoproteins, is diminished. This causes a slight decrease in maternal colloid osmotic pressure. More importantly, elevated free fractions of drugs that are highly protein bound will exist in the serum, increasing their potential for toxicity.

Finally, *neurological changes* that occur include increased emotional lability which, especially in the setting of impending emergency surgery, can lead to hysteria, inability to cooperate, and irrational behavior. Minimum alveolar concentration (MAC) is thought to be reduced by 40% due to hormonal changes (estrogen, progesterone) and increased levels of endorphins. Sensitivity of nerves to local anesthetic blockade is enhanced, and the dosages of all anesthetic agents should be adjusted accordingly.

Fetal Considerations

Several different types of drugs will most likely be administered to a pregnant patient with an acute abdomen should surgery become necessary. Multiple concerns arise with respect to the fetus at this point.

- Do anesthetic agents have harmful effects on fetal growth and development?
- How might they affect the fetal status during emergency abdominal surgery?
- Are there any particular anesthetics or medications that should be avoided?
- How should we monitor the fetal status during surgery?

The potential for teratogenic effects of anesthetic agents on the developing fetus has long been a concern. Teratogenicity depends on dosage, duration of exposure to the agent, the susceptibility of the species studied, and the timing of exposure with respect to organogenesis. In humans, organogenesis is generally during the first trimester, approximately 15–60 days post conception. It is essentially impossible to conduct controlled, randomized studies in humans due to ethical concerns, and thus, available data are derived from animal studies and from retrospective human studies. Since 1979, the FDA has used a letter risk classification system (A, B, C, D, and X) to categorize the teratogenic risk of medications (see Table 12.2). In 2015, that system was abandoned and replaced by a narrative risk summary contained in the Pregnancy and Lactation Labeling Rule (PLLR) [1]. However, most clinicians

Table 12.2 United States food and drug administration category ratings of drugs during pregnancy

Risk Category during Pregnancy	Outcome
A	Controlled studies show no risks
B	No evidence of risks in humans
C	Risk cannot be ruled out
D	Positive evidence of risk
X	Contraindicated in pregnancy

PDR [5]

continue to use the letter categories as a quick reference. In animal models, MOST anesthetic agents have been found to be teratogenic, though the doses used clinically are MUCH lower, and thus, the data are of limited value for the anesthesia practitioner (Tables 50.2 and 50.4 in [2]).

With the exception of muscle relaxants, most anesthetic agents, including volatile anesthetics, readily cross the placenta and are present in the fetal bloodstream. Suggested to be teratogenic in animal models with prolonged use (greater than 24 h) is nitrous oxide. The associated teratogenicity of nitrous oxide was thought to be a result of oxidation of vitamin B12 and the subsequent dysfunction as a coenzyme for DNA synthesis (decreased methionine synthase and thus decreased tetrahydrofolate production) leading to neurological and hematological symptoms. More recent evidence suggests a more complex and multifactorial etiology, including postulated mechanism of decrease in uterine blood flow and overstimulation of certain membrane signal pathways. Despite the fact that nitrous oxide has not been found to be associated with congenital anomalies in humans, most clinicians avoid its use especially during the first and second trimesters.

Intravenous opioids easily cross the placenta and may cause decreased heart rate variability if fetal monitoring is being used during surgery or in the perioperative period. If delivery of the fetus occurs after opioid administration to the mother, significant respiratory depression may be observed in the newborn for several hours. The respiratory-depressant effects are variable and depend upon the narcotic used. Long-acting opioids such as morphine result in more significant respiratory depression than shorter acting opioids such as fentanyl. Opioids administered by the neuraxial route (epidural or spinal) have little effect on the newborn.

Induction agents which include propofol, etomidate, and ketamine cross the placenta and are present in the fetal circulation. Although ketamine has been shown to cause a dose-dependent increase in uterine tone in vitro, all these induction agents are considered safe to use in the fetus.

Therapy with benzodiazepines is controversial. Several studies reported a correlation of maternal diazepam administration and infants with cleft lip. In one study, 278 mothers whose infants had major malformations, diazepam ingestion was four times more common among mothers of infants with oral clefts than mothers of infants with other defects [3]. Other studies have failed to show a correlation. Although the consensus is that diazepam is not a proven human teratogen, the risk/benefit ratio should be considered before starting chronic benzodiazepine during the first trimester.

Due to their molecular size and ionized state, muscle relaxants DO NOT cross the placenta to an appreciable extent. Placental transfer of local anesthetics depends on several factors; route of metabolism, degree of protein binding, pKa, and maternal and fetal acid base status. Because chloroprocaine undergoes rapid metabolism by maternal plasma cholinesterase, minimal fetal transfer occurs. Highly protein bound local anesthetics (bupivacaine and ropivacaine) undergo less fetal transfer than local anesthetics that are less protein bound such as lidocaine. However, keep in mind that serum protein levels are decreased in pregnancy, which can potentially lead to increased concentrations of "free", unbound drug in the maternal circulation. This may result in enhanced fetal transfer of local anesthetics. Once these drugs cross the placenta and enter the fetal circulation, they can potentially be converted into an ionized form in the presence of fetal acidosis and remain "trapped" in the fetal circulation, thus, increasing the potential for toxic effects.

Other medications that may be used when caring for a parturient undergoing emergency abdominal surgery include medications with cardiovascular effects. Vasopressors, beta-blockers, vasodilators, and atropine all cross the placenta. However, glycopyrolate, a quaternary ammonium compound, does not. Expect to see fetal heart rate effects when drugs that have the potential to cross the placenta are administered to the parturient.

Finally, the use of ketorolac and other nonsteroidal anti-inflammatory agents are generally avoided during pregnancy, especially during the third trimester due to the concern about premature closure of the fetal ductus arteriosus.

Should the fetus be continually monitored during emergency abdominal surgery? This decision should be made in consultation with the Obstetrician caring for the parturient and the surgeon performing the surgery. ACOG states "The decision to use intraoperative fetal monitoring should be individualized and, if used, should be based on gestational age, type of surgery, and facilities available" [4]. It is unlikely to be of benefit and not possible to do before 18 weeks gestation. It requires the presence of personnel trained in interpretation of fetal monitoring, such as the obstetrician or labor and delivery nurse. It also requires a plan in place for emergency cesarean section should fetal compromise be detected. Proponents of continuous intraoperative fetal monitoring feel that it allows for optimization of the fetal status should heart rate abnormalities be detected. Maternal blood pressure, hemoglobin, and oxygen concentrations can be augmented to improve uteroplacental perfusion. When perioperative fetal heart rate monitoring is performed, clinicians should have a thorough understanding of the fetal effects of maternally administered medications.

Anesthetic Recommendations

Regional Versus General Anesthesia

The type of anesthetic chosen will depend upon several factors: the site and nature of the surgery, maternal factors, and patient preference. The use of regional anesthesia (spinal, epidural, or peripheral nerve block) will almost always be the preferred

method in a pregnant patient, EXCEPT when presenting for acute abdominal surgery. However, a strong argument may be made that a spinal or epidural anesthetic COULD be performed in a handful of cases provided that there was not significant bowel obstruction present. Examples might include

- Open repair of incarcerated inguinal hernia
- Open repair of incarcerated umbilical hernia
- Open repair of a ventral hernia
- Open appendectomy

Contraindications to regional anesthesia would include

- Patient refusal
- Coagulopathy
- Maternal hypotension, hypovolemia, and sepsis
- Evidence of significant bowel obstruction or bowel infarction
- Potential for significant blood loss

When spinal or epidural anesthesia is chosen for these procedures, keep in mind that the abdominal viscera is innervated by nerve fibers that enter the spinal cord and travel cephalad, synapsing within the sympathetic ganglia in the high or mid-thoracic region. Thus, to truly provide adequate intraoperative anesthesia, the level of epidural or spinal blockade must reach the T4-T6 dermatomes. This CAN be accomplished using either a hyperbaric spinal anesthetic or an epidural anesthetic, much like what is done when performing anesthesia for cesarean section. However, high spinal blockade will increase the risk of pulmonary aspiration of gastric contents in the setting of acute abdominal surgery. In addition, if maternal hypovolemia or sepsis is present, significant hypotension would result from the sympathectomy caused by this level of neural blockade and would therefore be contraindicated.

The vast majority of operations involving the abdomen and viscera will require the use of general endotracheal anesthesia. The following are specific recommendations for the perioperative care of the parturient and her fetus.

Preoperative Preparation

Regardless of the type of anesthetic used, all patients undergoing surgery for an acute abdominal procedure should undergo a thorough history and physical examination. In addition to gestational age, history of prior medical problems such as asthma, hypertension, or diabetes should be elicited, as well as medication allergies, or problems with prior anesthetics. Physical examination should focus on the patient's airway, heart, and lungs, and estimation of gastric content. Fetal heart tones should be documented and a decision should be made whether intraoperative continuous fetal heart rate monitoring is feasible. ALL parturients should receive a 30 ml dose of a nonparticulate antacid, such as sodium citrate, within 30 min of induction. In addition, a promotility agent such as metoclopramide, an H2 receptor antagonist such as

famotidine, or proton pump inhibitor such as pantoprazole should be administered intravenously 30–60 min prior to induction in patients with increased risk of pulmonary aspiration. A small dose of a short-acting benzodiazepine such as midazolam is considered safe to use as a premedication to allay anxiety. Anti-emetic prophylaxis with 4 mg of dexamethasone should also be administered preoperatively, as well as 4 mg of ondansetron prior to emergence from anesthesia.

Intraoperative Management

Standard monitors should include electrocardiography, pulse oximetry, noninvasive blood pressure measurement, capnography, as well as temperature and neuromuscular blockade monitoring. Invasive blood pressure measurement in the setting of hypovolemia or sepsis is considered. Continuous fetal heart monitoring should be utilized when feasible according to ACOG guidelines. Left uterine displacement (after 20 weeks gestation) and pneumatic compression stockings should be applied and maintained throughout the postoperative period. Preoxygenation followed by rapid sequence induction of general endotracheal anesthesia should be performed on all patients beyond 16 weeks of gestation and in all patients with evidence of increased gastric content, regardless of gestational age. Propofol is the most common agent used for induction, but using etomidate or ketamine with preexisting hypotension or hypovolemia is considered. Despite a lower plasma pseudocholinesterase concentration in pregnancy, a smaller induction dose of succinylcholine should not be used because clinical prolongation of neuromuscular blockade rarely occurs. Anesthesia using volatile agents, narcotics, and nondepolarizing muscle relaxants is maintained, keeping in mind that MAC is reduced by 20–40% during pregnancy. An inspired oxygen concentration greater than 50% is used, and nitrous oxide during abdominal surgery is avoided. The fetal heart rate tracing will likely exhibit decreased beat-to-beat variability due to the effects of narcotics and volatile agents. However, if persistent fetal heart rate decelerations occur, every attempt to optimize the fetal status by increasing maternal blood pressure and oxygenation is made.

Because many of these acute abdominal surgeries will be performed laparoscopically, it is important to anticipate the cardiorespiratory changes that are likely to occur. Hypotension and decreased uteroplacental perfusion from increased intra-abdominal pressure caused by carbon dioxide insufflation are common. The reverse Trendelenburg position will enhance venous pooling and worsen maternal hypotension. Carbon dioxide insufflation will also cause increased peak airway pressures, decreased lung compliance, and decreased functional residual capacity. Respiratory changes will be exacerbated in the Trendelenburg position, with obesity, and with advanced gestational age. It is important to support maternal blood pressure with appropriate fluid therapy and vasopressors and to attempt to maintain end-tidal carbon dioxide between 32 and 36 mm HG. At the end of the procedure, the patient must be fully conscious before extubation to ensure return of protective airway reflexes.

Table 12.3 Summary of Anesthetic Recommendations

Preoperative preparation	Intraoperative management	Postoperative management
Perform thorough history and physical examination, paying close attention to the airway and estimation of gastric contents	Monitors to include standard ASA; pulse oximetry, EKG, NIBP, capnography, temperature, neuromuscular blockade, and FHR monitoring according to ACOG guidelines.	Monitor FHR and observe for signs of increased uterine activity
Document fetal heart tones and determine if continuous fetal heart rate monitoring is feasible	Preoxygenation followed by RSI and GETA	Provide postop analgesia using neuraxial and/or TAP blocks
Consider aspiration prophylaxis with any/all of the following: 30 ml sodium bicitrate within 30 min of induction Metoclopramide 10 mg IV Famotidine 20 mg IV Pantoprazole 40 mg IV	Maintain anesthesia with volatile agent, muscle relaxants, and narcotics, keeping in mind that MAC is reduced by 20–40% Aggressively treat hypotension/hypovolemia to maintain uteroplacental perfusion Decreased FHR variability will likely be observed secondary to anesthetic agents.	Consider multimodal analgesics such as acetaminophen and gabapentin administered on a scheduled basis Use reduced doses of narcotics and sedatives Avoid NSAID's during the third trimester Institute DVT prophylaxis

Postoperative Management

In addition to maternal vital signs, fetal heart tones and uterine activity should be monitored for several days during the postoperative period. The risk of preterm labor is increased after abdominal surgery, irrespective of anesthetic technique. Nevertheless, prophylactic tocolytic agents are not routinely administered (see Chap. 13). Postoperative analgesia in patients who have undergone laparotomy can be provided by TAP blocks or thoracic epidural analgesia using a dilute infusion of local anesthetic with fentanyl. Oral and parenteral opioids, as well as acetaminophen, usually provide adequate analgesia after laparoscopic procedures. Nonsteroidal anti-inflammatory agents should be avoided during the second half of pregnancy due to concerns of premature closure of the fetal ductus arteriosus. Pneumatic compression stockings should be continued well into the postoperative period and thromboprophylaxis with subcutaneous heparin or enoxaparin should be instituted as soon as possible. Table 12.3 presents a summary of anesthetic recommendations to follow when providing general anesthesia to a parturient and her fetus.

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Postoperative Care Issues

13

Peter Bogach Greenspan

Monitoring the Fetus and Timing of Delivery

Monitoring the fetus of a gravida who is undergoing surgery is addressed in the ACOG Committee Opinion No. 696 on Nonobstetrical Surgery during Pregnancy [1]. The status of the fetus is important in the postanesthesia care unit as well. Depending on the fetal gestational age, the monitoring may only entail intermittent fetal heart tone documentation or the fetus may require continuous electronic monitoring, especially in the later stages of pregnancy.

Pre-viable fetuses generally tolerate anesthetics and surgery very well; however, if the fetal heart tones indicate fetal compromise, little can be done to manage that other than correction of respiratory and metabolic problems in the gravida.

Viable fetuses that are demonstrating persistent intolerance to the intrauterine environment may require intervention including interruption of the pregnancy, if the offense causing the intolerance is irreversible with intrauterine resuscitative measures.

It is preferable to have an obstetrical provider with surgical privileges available in the postoperative period to intervene with emergent delivery if need be.

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Route of Delivery

The determination of delivery route is entirely dependent upon the urgency to remove the fetus from a hostile intrauterine environment. In most cases, albeit rare, the most expeditious route of delivery is abdominal, hence subjecting the gravida to another surgical procedure. In rare instances, the delivery of the fetus coincides with the surgical procedure being performed for the pathology that is causing the indication for surgery. In that case, the delivery of the fetus via Cesarean section, if indicated, can be expedited through the same incision.

When continuation of the pregnancy is warranted, then the patient can be followed for the pregnancy as she recovers from her surgery, until such time that a fetal and/or maternal indication for delivery arises or the patient's gestation reaches term status.

General Postoperative Principles [2, 3]

Immediate postoperative care in most patients, pregnant or otherwise, is supportive care with the goal of emerging the patient from the anesthetic that was provided for the surgery. This includes maintenance of the patients' airway with supplemental oxygen, as needed.

The first 24–72 h of the postoperative period are the most critical. During this time, monitoring of the patient for complications is essential.

The gravidas' hemoglobin and hematocrit should be followed, most importantly when the surgery was indicated for acute blood loss, such as trauma or abruption. Maintenance of the intravascular volume may require replacement of blood products by transfusion, etc. The clinical presentation of the patients' hemodynamic status will determine what treatment is required.

The evaluation of fluids and electrolytes should be carefully considered especially when the procedure is lengthy and/or if there was a considerable preoperative or intraoperative blood loss. Fluid management may also be a part of the nonsurgical care of the patient.

Care should be taken postoperatively to avoid emesis. In some cases, intraoperative and postoperative gastrointestinal decompression with nasogastric suction may be warranted. Once the gravida is alert and able to swallow, and any nausea and/or vomiting has resolved, then nasogastric suction should be discontinued, as it is very uncomfortable and may be of limited value in the prevention of postoperative ileus.

Indwelling Foley catheterization is helpful during and immediately following a procedure to monitor urinary output and to assist the patient in emptying her bladder until such time that she is stable and can void spontaneously on her own. The more critically ill gravida who has undergone surgery may require bladder drainage for longer periods of time. Furthermore, a catheter may prove to be useful since the gravid uterus may predispose the patient to urinary retention.

Postoperative antibiotic therapy is appropriate in select patients who are preoperatively infected, but the use of prophylactic antibiotics in the postoperative phase of recovery is not indicated.

The implementation of a protocol for the prevention of venous thromboembolism is very important especially in gravid women. Most institutions have order sets or electronic medical record prompts that assist the clinician in choosing what type of prophylaxis to implement. In almost all cases, the use of sequential compression devices is appropriate.

Incentive spirometry and other forms of pulmonary support are recommended in the postoperative gravid patient as would be in any other patient. These measures are vital in the deterrence of atelectasis and pneumonia.

Early postoperative ambulation is encouraged if the gravida and her fetus are otherwise found to be stable.

Very rarely is it necessary for a gravid postoperative patient to receive total parenteral nutrition. Parenteral nutrition requires expertise in multiple fields. Most clinicians would obtain consultation from other specialists if this were warranted.

Wound care in pregnant women does not differ from that in nonpregnant patients.

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Legal Concerns in Complicated Obstetrical Cases

14

Marilyn M. Pesto, Janet I. Mittenfelner, and Andrew Spaedy

Abbreviations

EHR	Electronic Health Record
EMTALA	Emergency Medical Treatment and Labor Act
FCA	False Claims Act
HIPAA	Health Insurance Portability and Accountability Act
OCR	Office of Civil Rights
PSDA	Patient Self-Determination Act
PVS	Persistent Vegetative State

Introduction

The last thing healthcare providers want to think about is the legal implications of practicing medicine. Most practitioners are attracted to the art and science of medicine, and they are motivated by the altruistic notion that the long, hard years they devote to the study and practice of medicine will improve the health and well-being of their patients. In a perfect world, healthcare providers would go about their day doing what they do best, without the worry of being sued for malpractice,

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committing a HIPAA violation, or otherwise being held legally liable. Unfortunately, medicine is not practiced in a perfect world. Legal and regulatory issues in the healthcare arena continue to expand and evolve, making the environment in which patient care is provided ever more complex and cumbersome.

The objective of this chapter is to educate and empower the healthcare provider by highlighting some of the legal issues one can expect to encounter when caring for the gravid patient with acute abdominal pain. The risks are particularly high when the gravid patient presents because there are two patients instead of one and, whether realistic or not, patients have a near universal expectation of a perfect outcome with the birth of their child. Obstetrics is a lightning rod for litigation and accounts for a large percentage of all medical malpractice lawsuits. Ob/Gyns and surgeons are the most likely to be sued among all physicians [1, 2]. A survey conducted in 2015 revealed that 85% of Ob/Gyns and 83% of general surgeons have been sued at some point in their career [3]. By extension, the various settings in which care is provided to the gravid patient with acute abdominal issues expose the practitioner to a higher level of risk.

The number one rule of any practitioner is simple: always practice good medical care. But just as litigators lose some trials they never should have lost, healthcare providers lose some patients they never expected to lose or their patients experience less than optimal outcomes, despite the best efforts of the provider. Unanticipated outcomes are an inevitable fact of life from which no healthcare practitioner is immune. It does not necessarily mean the practitioner was wrong, but poor outcomes, regardless of fault, often lead to litigation. Similarly, a well-meaning practitioner can unintentionally commit a regulatory infraction, but still be held legally liable. With such high stakes associated with caring for the gravid patient, it is prudent for practitioners in the various settings described in this book to arm themselves with the basic legal knowledge necessary to avoid legal pitfalls. The ultimate goal is to provide the highest quality care to the patient while simultaneously protecting oneself from legal liability, both civil and criminal.

Professional Negligence

The legal concept with which healthcare providers are most familiar, and which creates the most dread, is professional negligence, also known as medical malpractice. No practitioner sets out to harm a patient, so the prospect of being sued for a poor outcome is difficult to accept as an occupational hazard. Yet it makes sense to hold professionals with specialized training and knowledge to a high standard of professional practice. Without such standards there would be no protection of patients from medical error or unreasonable risk of harm. Indeed, as a form of self-policing of sorts, physicians serve as expert witnesses against other practicing physicians in order to establish the necessary legal elements of a medical malpractice case. While no practitioner should be crippled by a concern of being sued, familiarity with the elements of professional negligence and knowledge of how to minimize the risk of malpractice are essential components of the healthcare provider's professional toolbox.

Elements of Medical Negligence

Negligence is what is known in the law as a type of tort. This is a wrongful act or failure to act, by a party, for which the injured party is entitled to compensation. In order for the injured party (known as a plaintiff in a lawsuit) to obtain a judgment in their favor, they must establish four essential elements of negligence: duty, breach, causation of injury, and resulting damages.

Elements of Medical Negligence

1. *Duty*
   Obligation owed by a healthcare provider to the patient to provide that degree of medical care which a reasonably prudent provider would exercise in the same or similar circumstances.
   Also known as the standard of care.
2. *Breach*
   Violation of the duty owed to the patient. The healthcare provider failed to meet the standard of care.
3. *Causation*
   The causal link between the patient's injury and the healthcare provider's action. "But for" the negligence of the healthcare provider, the patient would not have been injured.
4. *Damages*
   Economic or noneconomic harm arising from the injury to the patient. Damages can be monetary or nonmonetary (pain and suffering).

The plaintiff has what is known as the burden of proof. In other words, the defendant does not have to prove that these elements do not exist; the plaintiff has to prove that they do. In the context of medical negligence, duty is the obligation owed by a healthcare provider to his or her patient to provide that degree of medical care which a reasonably prudent provider would exercise in the same or similar circumstance. This is also known as "the standard of care." By virtue of entering into a healthcare provider-patient relationship, a duty to the patient is created. If a provider's treatment falls below the standard of care, it is considered a breach of that duty. If the breach causes injury to the patient resulting in damages, then the four elements of medical negligence have been established. Physician expert testimony about the standard of care must be entered into evidence for the jury to render an opinion.

Not all breaches of the standard of care cause injury to the patient. For instance, a provider may fail to respond to critical lab values in a gravid patient, but if neither the mother nor the baby suffers any harm from that failure to respond, the four elements of negligence have not been established. While the elements of duty and breach are present in that example, the breach did not cause an injury. Similarly, if a provider fails to recognize a placental abruption on an ultrasound, but it can be proven that the baby's demise was due to a nuchal cord which preceded the

abruption, then there is no causation between the breach of the standard of care and the poor outcome for the baby. In that example the elements of duty and breach exist, but the elements of causation of injury and damages are missing because the breach did not cause the harm suffered by the baby. While both examples represent suboptimal practice, neither can be proven as medical malpractice in a court of law, and thus, are not compensable. In other words, whatever the practitioner did or failed to do caused no impact.

In medical malpractice cases, expert witnesses are utilized to establish standard of care and causation. Practitioners in a same or similar field as the defendant offer opinion testimony about whether or not the defendant breached the standard of care and whether the injury was a direct result of the breach. The burden of proof for the plaintiff is "more probable than not" or, stated another way, "to a reasonable degree of medical probability." The reason expert testimony is used is because most jurors do not have the knowledge of complex medical concepts presented at trial in order to draw conclusions about liability. The exception to that rule is when the evidence is so common that even a lay person would understand the medical issues in the case. The most common example in the context of a medical malpractice case is when a foreign object, such as a sponge or instrument, is unintentionally left in a patient after surgery. Even a lay person, with no medical knowledge or training, can conclude that such an error is below the standard of care. Proving a breach of the standard of care in that example does not require expert opinion testimony. This concept is known in the law as *res ipsa loquitur*, which is Latin for "the thing speaks for itself."

Implicit in its definition, the standard of care will always evolve because the practice of medicine is always evolving. With advances in drugs, procedures, diagnostic tools, and knowledge about disease processes, the standard of care for treating a pregnant woman 5 or 10 years ago is not the same as today. It is essential that practitioners stay current in their field via continuing education because what a reasonably prudent provider would do yesterday is not necessarily the same as what one would do today or tomorrow. For example, until recently it was completely within the standard of care to routinely perform an episiotomy during a delivery, but today that practice has changed due to studies showing episiotomies can, under certain circumstances, increase the risk of perineal lacerations as opposed to protecting against lacerations. The importance of evidence-based practice cannot be overstated when it comes to a practitioner guarding against future lawsuits where it will be alleged that the standard of care was breached.

Types of Torts

The tort of medical negligence described above is only one of several torts for which a healthcare provider might be responsible. Other types of torts include intentional torts and strict liability.

Types of Torts

1. *Intentional Tort* – an overt act which is done intentionally and causes harm.
2. *Negligence* – a breach of the duty of care owed to another that occurs with factual and proximate cause and creates damages.
3. *Strict Liability* – liability that arises from certain actions without a showing of actual negligence. Fault is not an issue.

An intentional tort is an overt act which is committed deliberately and causes harm to another. In other words, it must be shown that the person committing the tort, also known as the tortfeasor, intended to commit the act. Examples include assault, battery, false imprisonment, abandonment, defamation, deceit, fraud, and misrepresentation.

Intentional Torts

- Assault
- Battery
- False Imprisonment
- Abandonment
- Defamation
- Deceit
- Fraud and Misrepresentation

Assault is the threat to cause harm to another without any actual contact or harm taking place. Battery is the intentional touching of another without that person's consent. A common example of battery in the medical context is performing a procedure on a patient without their consent, or going further with the procedure than what the consent authorized, such as removing both an ovary and a fallopian tube when the patient only consented to a salpingectomy. Abandonment is another tort which often arises in the context of providing healthcare. When a physician-patient relationship has been established, and the physician unilaterally terminates that relationship without the patient's consent and without giving reasonable notice to the patient, and the patient is somehow harmed, the physician can be held liable for abandonment.

The tort of strict liability is liability that arises from certain actions without a showing of fault or actual negligence. This type of tort is more likely to arise in the context of consumer products such as medical equipment or drugs where the manufacturer is held strictly liable for some kind of defect in the product, or for a lack of warning about the dangers of the product, if the user suffered harm caused by the product.

Damages

Damages are what an injured party can recover as compensation for their loss. Basic types of damages include nominal damages, compensatory damages, and punitive damages.

Types of Damages in Medical Negligence

1. *Nominal Damages*
   A slight or token payment to demonstrate that, while there may not have been any physical harm done, the patient's legal rights were violated.
2. *Compensatory Damages*
   Special compensatory is for actual economic loss.
   General compensatory is for noneconomic loss such as pain and suffering.
3. *Punitive Damages*
   Damages awarded to punish the defendant and to serve as a deterrent.

Nominal damages are simply a small or token payment made to a litigant, often to demonstrate that, while there may not have been any physical harm done; the patient's legal rights were violated. Alternatively, nominal damages are sometimes paid in an effort to resolve a lawsuit where the defendant may have a good defense, but the cost or inconvenience of litigating the case is higher than the value of the case, so a token or nominal payment is offered to settle out of court. This is frequently referred to as the "cost of defense."

In a medical negligence claim, there are a wide variety of compensatory damages that can be paid which fall into two main categories: special compensatory and general compensatory damages. The former relates to actual economic loss, such as past and future medical bills or lost wages, whereas the latter relates to noneconomic loss, such as pain and suffering experienced due to a medical injury. In a trial the plaintiff must introduce evidence of actual economic loss in order for a jury to award money to compensate for those special damages. However, a jury is free to award whatever amount they see fit to compensate for noneconomic loss based on the plaintiff's testimony about the pain and suffering they experienced. Because the jury is not confined to a particular dollar amount with noneconomic damages, and because jurors can be easily influenced by emotion, there is the potential to get a "runaway jury" which awards an amount far beyond what may seem as reasonable compensation. In an obstetrical case, the most costly claim frequently involves a neurologically impaired infant. In such a case, both special and general compensatory damages can be very high because the damages may cover the entire life span of the child (calculated by creating a life care plan) and because juries tend to be sympathetic toward an injured baby and its family.

Punitive damages are awarded for the purpose of punishing a defendant and to serve as a deterrent of future behavior. In order for a plaintiff to be awarded punitive

damages, they must demonstrate that the behavior of the defendant was so egregious as to warrant punishing him or her with a monetary sanction. The standard of proof varies throughout the country but typically involves a showing of reckless, wanton or malicious behavior which has a high likelihood of resulting in substantial harm, or behavior which shows complete disregard for the health and safety of the injured party. This standard of proof goes well beyond ordinary negligence or failure of a healthcare provider to meet the standard of care in a medical malpractice case. An example would be a provider conducting a cesarean section while under the influence of alcohol or drugs. Depending on the circumstances, the plaintiff might be able to establish that such behavior showed a complete disregard for the health and safety of the patient. Punitive damages are serious because, as they are typically excluded from professional liability coverage, they place the provider at risk of personal liability exposure. If a jury awarded punitive damages to a plaintiff, which frequently are higher than other damages in a case, the provider would personally be responsible for paying those out of his or her own assets.

Professional Liability Cost

The cost associated with professional liability is a topic well known to most healthcare providers as it is frequently in the news and is the subject of much debate about the rising cost of liability insurance and healthcare. In 2015, the total medical malpractice payout in the United States was $3,954,339,750, which represents an increase of 1.68% over the prior year. Per capita by state, New York had the highest payout and Wisconsin had the lowest. The most severe outcome as a result of medical malpractice in 2015 was death, constituting 30% of the cases and resulting in an average payout of $374,944. The outcomes of quadriplegia, brain damage, and lifelong care constituted 16% of the cases, and resulted in an average payout of $1,086,711, which was the highest average payout for all outcomes [4].

In an effort to control the cost of professional liability awards and the resultant effect on medical malpractice insurance premiums, many states have passed tort reform legislation which caps noneconomic damages at a certain dollar amount. However, such caps do not limit what a plaintiff can be compensated for economic damages.

Disclosure of Adverse Outcomes

Some literature advocates that disclosure of adverse events has benefits for the patient and the physician [5] and that a patient is less likely to pursue litigation if they perceive that the event was honestly disclosed. A formal Sentinel Event Policy was adopted by The Joint Commission on Hospital Accreditation in 1996. The policy was developed to help hospitals improve patient safety, prevent further harm, and learn from sentinel events (adverse outcomes). A sentinel event is a Patient Safety Event that reaches a patient and results in:

1. Death
2. Permanent harm, or
3. Severe temporary harm and intervention is required to sustain life [6]

The AMA Code of Ethics states, "The physician is ethically required to inform the patient of all the facts necessary to ensure an understanding of what has occurred" [7]. Although studies show that disclosure of adverse events promote patient-physician trust, there are many barriers to disclosure. A culture of blame, fear of retribution, and fear of lawsuits have caused physicians great concerns [5]. Some states have enacted legislation to provide protection from liability if the physician offers acknowledgment of the patient suffering, expressions of sympathy or empathy, or if appropriate, an apology.

Sample State Statute

Certain Statements, Writings, and Benevolent Gestures Inadmissible

Missouri Revised Statutes, Chapter 538, Tort Actions Based on Improper Health Care

Section 538.229. August 28, 2016

538.229. Certain statements, writings, and benevolent gestures inadmissible, when--definitions.

1. The portion of statements, writings, or benevolent gestures expressing sympathy or a general sense of benevolence relating to the pain, suffering, or death of a person and made to that person or to the family of that person shall be inadmissible as evidence of an admission of liability in a civil action. However, nothing in this section shall prohibit admission of a statement of fault.
2. For the purposes of this section, the following terms mean:
   (1) "Benevolent gestures," actions which convey a sense of compassion or commiseration emanating from humane impulses;
   (2) "Family," the spouse, parent, grandparent, stepmother, stepfather, child, grandchild, brother, sister, half brother, half sister, adopted children of a parent, or spouse's parents of an injured party.

(L. 2005 H.B. 393)

Medical Records and Associated Topics

Documentation

In a legal context, the medical record can be considered a "silent witness" [8]. How care is documented can be the best defense should a legal action arise because it is rare that a healthcare provider will have an independent recollection

of the details surrounding the care of a patient by the time a lawsuit is eventually filed. More often than not, providers do not even remember the patient, let alone what was said and done to the patient. Thus, the medical record is typically the key evidence upon which a legal defense is built. On the other hand, the medical record can also be the best witness for the plaintiff, particularly when there is a failure to document [8]. Plaintiff attorneys love to assert that "if it wasn't documented it wasn't done." While technically this is not true because it is unnecessary, impractical, and impossible to document every single thing that is done for a patient, the reality is that if key information is missing from the record it will typically work to the plaintiff's advantage and against the healthcare provider. The jury may presume that if something was omitted from the record, it should have been done but was not. A healthcare provider's testimony that he or she has a custom and practice of doing things, regardless of whether it is written down, can be used as evidence in a lawsuit, but it is always best to preserve the key aspects of patient care by making a written record.

Take, for example, the case where the provider allows his patient to be removed from the fetal monitor because she needs to go to the bathroom and after 10 min she returns to her bed. The monitoring is resumed with the strip suddenly indicating late decelerations, but there is nothing in the medical record documenting the patient's trip to the bathroom. Several years hence when a lawsuit is filed because of fetal demise, the defendant healthcare provider and his attorney will attempt to piece together what happened, but there will be no explanation in the medical record for why the patient was off the monitor for 10 min. Unless the provider specifically remembers the incident, there can only be speculation as to why there is a gap in the fetal monitoring. The plaintiff's attorney will assert that the patient was experiencing late decelerations during the time she was off the monitor, and he will argue that the defendant was negligent because, had there been continuous monitoring, the fetal compromise would have been caught sooner and more timely intrauterine resuscitation would have saved the baby's life. A simple entry by a provider about why the patient was off the monitor for 10 min would save a lot of headache down the road.

Practice Tips for Documentation

Documentation serves the dual purpose of making a record of a patient's healthcare while communicating important details to other providers, so there is continuity of care for the patient. Given the importance of medical record documentation, it is helpful to cultivate good practice habits for documentation which will serve a provider well over time. The acronym CART, which stands for complete, accurate, rationale, and timely, is a useful tool when documenting in a patient record.

Complete A good patient record is comprehensive in order to be complete, but it should also be concise. The goal is to cover everything pertinent to a particular exam, treatment, or consultation in a format that is easily and readily reviewed by subsequent providers without getting bogged down in superfluous information.

Accurate Accuracy should go without saying in medical record documentation, yet far too often in litigation a patient's chart contains inaccuracies. Sometimes those inaccuracies are ultimately not relevant to the issue in the case, yet they create a poor image in the mind of the jury. If a provider or facility seems sloppy in its documentation, then were they sloppy in their care? To be accurate, the medical record needs to conform to the facts of the patient's care and be as free from error as possible.

Rationale A provider's rationale should be apparent when reading the medical record. In order to illustrate that the standard of care was met when caring for a patient, the provider should document the logic behind his or her diagnosis and plan of care. Unfortunately, when a medical record is reviewed down the road, it can be difficult to understand the justification for a particular treatment or course of action. Setting forth the reasons for a plan of care demonstrates that a provider took into account the objective and subjective information in a patient's case and drew logical conclusions from that information.

Timely The general rule with documentation is that the closer in time it is done with the care provided the more accurate and complete it will be. Documenting contemporaneously can be difficult in the busy life of a healthcare provider who is under tremendous pressure in an increasingly complex healthcare environment. However, making a habit of quickly capturing what has been done with a patient will pay off in both the short run and the long run. In the short run, it saves the provider time by not having to reconstruct what was done with a patient when the facts are not fresh in one's mind, and in the long run it creates a reliable record for future reference.

Sometimes it is necessary to make a late entry in a record. This situation often occurs when an emergency arises, such as a caesarean section, and there is no time to document contemporaneously. Obviously, patient care takes priority over charting, so "hands on the patient, not on the computer" is always a good rule for providing excellent and safe patient care. But those are exactly the kind of circumstances where it is essential to have complete and accurate documentation which explains the rationale behind the patient care. Regardless of the reason for the late entry, be it an emergency or simply forgetting to put something in the chart, always indicate that a late entry is being made as opposed to making it appear that the entry was contemporaneous or made at some time other than the actual time it is being made. Most entries in the electronic record have an internal time and date stamp associated with them which will contradict an entry that is purposefully timed or dated differently. In the legal context, it is always easier to explain why a late entry was made rather than explain why an entry was dated and/or timed inaccurately.

Liability Issues with Medical Records

Tampering with medical records, such as falsification or spoliation, can expose the healthcare provider to civil or criminal liability. Spoliation is "the destruction or

significant alteration of evidence" [9]. Spoliation of evidence is usually done solely, or primarily, to deprive an opposing party of its use. Spoliation can take many forms but in a medical legal context it usually involves destroying a document or record or the alteration of a record. However, spoliation can also take the form of concealment of physical evidence or tampering with witnesses. A classic example is set forth in the film, *The Verdict*, where a doctor ordered a nurse to change a 1 to a 9 in order to bring the doctor's actions within the standard of care for that particular case.

While most states refuse to recognize a claim for intentional spoliation, there are a few that do allow the claim as a separate cause of action. However, even if it is not recognized as a separate cause of action, it is condemned in every jurisdiction in the United States. Most states utilize jury instruction and negative inferences to address the issue if a case is being tried. Spoliation is an all too frequent occurrence. It has been estimated that as many as 50% of medical malpractice cases involve altered records [10]. The most common actions involve altering the records, adding to the record at a later time, deletion and/or substitution, insertion of false information, and destruction or loss of X-rays, lab reports, or other physical evidence.

Historically there have been two remedies for spoliation. First, and most common, is the court directs a jury to infer that the altered or missing evidence was legally harmful to the spoliator. This inference only applies where the spoliator is a party or its agent. The second remedy is monetary or nonmonetary discovery sanctions imposed by the court during the discovery phase of a lawsuit. Monetary sanctions include compensating the injured party for discovery costs, the cost of reconstructing evidence, and attorney's fees. Nonmonetary sanctions include precluding the evidence from being used [11], deeming certain facts established [12], dismissing the action [13], entering a default judgment against the party who committed the spoliation [13], and holding the offending party in contempt [14]. Additionally, spoliation can cause the burden of proof to shift from the plaintiff to the defendant.

Electronic Health Record Issues

With the advent of the electronic health record (EHR), there has been an unfortunate tendency for healthcare providers to "copy and paste" from other providers' notes into their own notes in an effort to save time. This is frequently seen when a provider is writing a progress note or consultation and they copy information from a prior progress note, or history and physical, into their own note. While there is nothing inherently wrong with repeating information already documented by another provider, a problem arises when the copied material contains information about the patient that is no longer pertinent to their current status, or was mistaken when originally written. For example, if a physician is creating a progress note on day three of a pregnant patient's admission for contractions, which have now subsided due to treatment with terbutaline, and he copies and pastes some of the patient's history from a prior day's progress note without noticing that it states the patient is still

experiencing contractions, then his current progress note is immediately inaccurate because it is inconsistent with the patient's status. Not only is this dangerous in terms of potential mistreatment of the patient due to a mistaken record, it is also a legal liability should a lawsuit be filed down the road. You can be sure a jury will see an exhibit comparing the two progress notes word for word, often including the exact same typos or misplaced punctuation, and they will conclude that the copying physician was lazy and sloppy, either because he did not bother to read the original note to ensure its current applicability, or he did not bother to conduct his own complete assessment of the patient, or both. Regardless of whether the copying physician met the standard of care in the underlying issue of the case, the jury will develop an unfavorable view of that physician, or worse, question his credibility, which can be fatal when it comes to returning a favorable verdict.

Another example of how copying and pasting can be risky is when one provider documents an inaccurate assumption about a patient, such as assuming the patient is a recreational drug user, or otherwise makes an error in his documentation, such as transposing two digits of a lab value, and a subsequent provider copies and pastes that information into her own note. It is not uncommon to see the same error repeated over and over again in the patient's chart by numerous providers because nobody is actually making the effort to ensure the copied information is accurate. Rather, they skim the record for a convenient summary of the patient's history, so they do not have to recreate it on their own, and then copy it verbatim into their own note. Again, not only is this unsafe for patient care, it can be embarrassing and damaging in subsequent litigation.

While traditional documentation in the paper medical record had its own inherent issues such as illegibility, the EHR has risks associated with it. Some examples are:

1. Inadequate training on use may lead to upcoding
2. Over-documentation or "note bloat"
3. Unauthorized prescribing and ordering
4. Lack of access to all patient data
5. Inaccurate time and date stamping
6. Pop-up reminder fatigue
7. Computer crashes and power outages
8. Vulnerable security
9. Errors caused by misuse of copy and paste (cloning)
10. Automatic coding features

Unfortunately, auto-coding, record cloning, and software prompts have made it easy to achieve inflated upper-level coding and additional payment for services. Billing and coding errors, whether intentional or unintentional, have led to a substantial attack on providers for healthcare fraud.

Those involved in healthcare fraud are vigorously pursued by The Department of Justice- Health and Human Services Medicare Fraud Strike Force. This

multiagency team of federal, state, and local investigators was designed to combat Medicare fraud. The False Claims Act (FCA) prohibits individuals from submitting, or causing someone else to submit a false or fraudulent claim for payment, to the government. It applies to all government programs including Medicare. The two most common violations of the FCA are the fabrication of records to get a false claim paid and the submission of false claims to the government. The False Claims Act is discussed later in this chapter.

Privacy and Protection of Health Information

Medical records and medical information are protected by a multitude of laws including the Health Insurance Portability and Accountability Act (HIPAA). HIPAA ensures (1) privacy and (2) protection of health information that is individually identifiable health information maintained or transmitted in any form. Required disclosures under HIPAA are limited to (1) disclosures to the individual who is the subject of the information and (2) disclosures to the Office of Civil Rights (OCR) to determine compliance. All other uses and disclosures are permissive.

The patient's rights under HIPAA include [15]:

1. Right to inspect and copy protected health information
2. Right to amend the record
3. Right to an accounting of disclosures
4. Right to have reasonable requests for confidential information accommodated
5. Right to file a complaint with the OCR or with a covered entity
6. Right to written notice of information practices from providers and health plans

HIPAA has placed additional burdens on healthcare providers and institutions to safeguard the confidentiality of medical records and has created civil and criminal penalties for violations. The OCR is responsible for administering, investigating, and enforcing the HIPAA privacy standards. The American Recovery and Reinvestment Act created a tiered penalty configuration for HIPAA violations. But the OCR determines the amount of each penalty, and it is dependent upon the nature and extent of harm that results from a breach (see Table 14.1).

Table 14.1 Tiered penalties for HIPAA violations

Category	Fine range
Did not know of breach	$100–50,000
Had reasonable cause to know	$1000–50,000
Willful neglect, corrected	$10,000–50,000
Willful neglect, not corrected	$50,000

Informed Consent

Informed consent is a doctrine that recognizes the right of a patient to be fully informed of the risks, benefits, and alternatives to treatment before undergoing any such treatment. A long line of legal cases in the twentieth century helped shape the law of informed consent including the concept that treating a patient without consent is a violation of the patient's bodily integrity for which a physician can be liable for assault and battery. The responsibility of informed consent typically falls squarely on the shoulders of the physician because he or she has the necessary training, education, and expertise to understand what information should be provided to the patient to enable them to give informed consent. In the context of the acute abdomen in the pregnant patient, extra consideration should be given by the healthcare provider to informed consent because with most treatments and procedures there are risks, benefits, and alternatives which may impact both the mother and fetus, and often times those conflict with each other. For instance, a medication that is indicated for the mother may involve severe risks to the unborn fetus. Likewise, treatment that could improve the condition of the fetus might compromise the health of the mother.

Elements

There are three main elements of informed consent which should be considered when discussing treatment with a patient: (1) threshold elements, (2) information elements, and (3) decision and authorization.

Elements of Informed Consent

Threshold Elements

- Capacity
- Voluntariness

Information Elements

- Disclosure
- Recommendation
- Understanding

Consent

- Decision
- Authorization

Threshold Elements (Capacity and Voluntariness)

Threshold elements of informed consent take into account whether a patient has the ability to comprehend the treatment being discussed and whether the patient is giving consent voluntarily. The first threshold element to consider is whether the patient has capacity to give consent. Capacity refers to an individual's actual ability to understand or form an intention with regard to some act such as consenting to treatment. The provider needs to evaluate if the patient has an adequate level of attention during the informed consent discussion, whether their judgment is sufficiently intact, and whether they are able to comprehend relevant instructions. The age of the patient, her cognitive capabilities, and her mental status are examples of factors which might prevent her from being able to give informed consent. If a patient lacks capacity to understand the information provided about the proposed treatment, then she is not capable of giving informed consent. Physicians regularly make determinations of capacity. When a patient lacks capacity, informed consent must be obtained from next of kin, a guardian, or some other person who can consent on the patient's behalf.

Sample State Statute

Who May Give Consent

Missouri Revised Statutes, Chapter 431
General Provisions as to Contracts
Section 431.061. August 28, 2016

431.061. Consent to surgical or medical treatment, who may give, when.

1. In addition to such other persons as may be so authorized and empowered, any one of the following persons if otherwise competent to contract, is authorized and empowered to consent, either orally or otherwise, to any surgical, medical, or other treatment or procedures, including immunizations, not prohibited by law:
   (1) Any adult 18 years of age or older for himself;
   (2) Any parent for his minor child in his legal custody;
   (3) Any minor who has been lawfully married and any minor parent or legal custodian of a child for himself, his child and any child in his legal custody;
   (4) Any minor for himself in case of:
      (a) Pregnancy, but excluding abortions;
      (b) Venereal disease;
      (c) Drug or substance abuse including those referred to in chapter 195;
   (5) Any adult standing in loco parentis, whether serving formally or not, for his minor charge in case of emergency as defined in section 431.063;

(continued)

(6) Any guardian of the person for his ward;
(7) Any relative caregiver of a minor child as provided for under section 431.058

2. The provisions of sections 431.061 and 431.063 shall be liberally construed, and all relationships set forth in subsection 1 of this section shall include the adoptive and step-relationship as well as the natural relationship and the relationship by the half-blood as well as by the whole blood.
3. A consent by one person so authorized and empowered shall be sufficient notwithstanding that there are other persons so authorized and empowered or that such other persons shall refuse or decline to consent or shall protest against the proposed surgical, medical, or other treatment or procedures.
4. Any person acting in good faith and not having been put on notice to the contrary shall be justified in relying on the representations of any person purporting to give such consent, including, but not limited to, his identity, his age, his marital status, and his relationship to any other person for whom the consent is purportedly given.

(L. 1971 H.B. 73 § 1, A.L. 1977 S.B. 48, A.L. 2014 S.B. 532)

It is important to recognize that capacity can be a moving target because it can vary over time and with different circumstances. A patient who has current capacity to consent to a procedure today may be disoriented later in the evening, and thus not able to partake in a different informed consent discussion. Likewise, a patient with a behavioral health disorder may not have capacity to consent to something as complex and serious as surgery, but still be able to consent to having an IV started, because they have the cognitive abilities to understand the latter.

Capacity is sometimes confused with the concept of competence, and the terms are often used interchangeably, but they are not interchangeable from a legal perspective. They each have unique definitions. Competence refers to one's legal status as a decision-maker. Competence is a vague and ambiguous term because it is a broad concept that encompasses many different legal issues and contexts. In general, competence refers to some minimal cognitive or behavioral ability, trait, or required capability.

Competence in the civil context is commonly raised in two situations, legal age of majority, and mental disability. With some exceptions the age of majority is 18 and persons of this age are presumed to be competent. Incapacity secondary to mental disability may be slightly more nuanced depending on the context. In the discussion of consent to medical treatment, competency to consent might be questioned if the person is mentally ill, under the influence of drugs or alcohol, has a brain injury, or suffers from some other medical condition which causes mental disability such as Alzheimer's disease. The question of competency and determination of incompetency can only be judicially determined. A person is presumed competent unless adjudicated incompetent. There is no established set of criteria, nor a single test, for

determining a person's competence. Rather, a judge weighs the evidence presented at a hearing which typically includes evaluations of decisional capacity by professionals such as physicians, psychologists, and social workers. The fact that a patient may be deemed incompetent or has been appointed a guardian does not meant they lack capacity to participate meaningfully in certain treatment decisions, or that their wishes should be ignored. To the degree that they are able to participate, there is a moral obligation to allow them to do so.

Capacity and competence do not always coincide. Minors are incompetent to make most healthcare decisions, yet as a matter of public policy they may have decisional capacity in certain circumstances such as pregnancy, sexually transmitted infections, and drug or substance abuse. To encourage minors to seek treatment under those circumstances, most states have granted minors, via minor treatment statutes, the ability to make certain healthcare decisions. Similarly, certain minors who are emancipated or married are considered mature minors who are recognized as competent decision-makers and may consent to treatment on their own behalf, or for their children (see above Sample State Statute: Who May Give Consent).

Voluntariness requires freedom of choice and freedom from controlling influence by others. Undue pressure from family members, clinicians, religious groups, ethnic custom, or others may invalidate a consent. Physicians need to preserve patient voluntariness.

Information Elements (Disclosure, Recommendation, and Understanding)

Information elements of informed consent include disclosure, recommendation, and understanding. Disclosure refers to the key pieces of information that must be made known to the patient and understood by the patient. These include the nature of the therapy, purpose, risks and consequences, benefits, probability of success, feasible alternatives, and prognosis with no therapy.

Informed Consent Disclosure

- Nature of the therapy
- Purpose
- Risks and consequences
- Benefits
- Probability of success
- Feasible alternatives
- Prognosis with no therapy

Once that information is disclosed, a recommendation is made by the physician based on his or her expertise. Recommendations are often meaningful to the patient because without one, the patient may feel lost or overwhelmed. However, the final decision obviously rests with the patient. It is the physician's responsibility to make sure the patient understands what has been discussed and to avoid confusing medical jargon. Asking a patient to describe in their own words their understanding of

the proposed treatment is a helpful way to verify comprehension, as opposed to asking close-ended questions, such as "Do you understand?"

Consent (Decision and Authorization)

Most patients follow a recommended treatment plan, but ultimately it is their right to choose how to proceed. If they decide to undergo the treatment, they must provide authorization of their consent. If they decide not to undergo treatment, although uncommon in pregnant patients, their right to refuse treatment is still a common law right guaranteed by the 14th Amendment. Regardless of the patient's decision, it is important for the physician to document the informed consent discussion so that the record reflects the patient made a well-informed decision. Sometimes refusal to treat involves an end of life issue. There is further discussion of this issue in section "Persistent Vegetative State and End of Life Medical Matters" where the Self Determination Act is addressed.

Exceptions to Informed Consent

There are five situations in which informed consent is not required: emergencies, therapeutic privilege, patient knowingly yields right to informed consent, incompetency, and national/state waivers (in the case of the military).

Informed Consent Exceptions

1. *Emergencies*
   In an emergency the patient may be unable to give consent or will incur greater harm if time is taken to explain medical interventions.
2. *Therapeutic Privilege*
   The withholding of information by the physician based on the judgment that disclosure would be harmful to the patient.
3. *Patient knowingly yields right to informed consent*
   When patients voluntarily and purposefully give up their rights to disclosure and autonomous decision-making
4. *Incompetency*
   In the context of medical decisions "incompetency" is a legal term to describe the condition of a person lacking legal capacity to make certain decisions concerning his/her medical care. Legal incompetency must be determined by a court in a legal proceeding.
5. *National/State Waivers (military)*
   Where a service member is required to undergo physical, psychiatric, or other types of medical care to determine fitness for duty

In an emergency, the patient may be unable to give consent or will incur greater harm if time is taken to explain medical interventions. The most common example is an unconscious or incapacitated patient who comes to the emergency

department as a result of a motor vehicle accident or a shooting. Often the providers are faced with needing to perform life-saving measures or are faced with tremendous blood loss and do not have time to obtain informed consent for treatment. Under these circumstances, the consent of the patient is presumed and it is not necessary to obtain consent to treat the patient. Therapeutic privilege is the withholding of information by the physician based on his or her judgment that disclosure would be harmful to the patient. While it should only be invoked on rare occasions, an example would be not immediately telling a suicidal patient that she has lost her baby for fear that it would provoke a suicidal act on her part. A patient knowingly yielding their right to informed consent is when they voluntarily and purposefully give up their rights to disclosure and autonomous decision-making. This could arise in the context of a medical research study where the patient has agreed they will not be told whether they are receiving a placebo or the actual study drug.

Incompetence, discussed earlier, is an exception to informed consent and it is a legal term to describe where a person lacks *legal* capacity to make certain decisions concerning his or her medical care. Legal incompetency must be determined by a court in a legal proceeding. Unlike capacity, it is not a medical judgment. Before a provider should decide that informed consent is not necessary due to incompetency, they should have documentation from a court which has made that legal determination. Typically when a patient has been declared legally incompetent they have been appointed a legal guardian from whom informed consent must be obtained when treating the patient. The final exception to informed consent is in the context of military service where a service member can be required to undergo physical, psychiatric, or other types of medical care to determine fitness for duty, or required to have certain vaccinations.

Immunity and Good Samaritan Law

The five exceptions to informed consent discussed above protect a healthcare provider against an allegation that treatment was provided without informed consent. Somewhat similar to the emergency exception for informed consent, but extended to liability for negligence, most states grant immunity to healthcare professionals under what is typically referred to as Good Samaritan laws. These statutes vary from state to state, but they typically protect providers responding to an emergency situation from liability if they did so voluntarily and without expectation of pay. The public policy behind these statutes is to encourage trained medical providers to respond to the scene of an emergency and offer aid to people suffering from serious bodily injury or life-threatening situations.

Sample State Statute

Good Samaritan Law

Missouri Revised Statutes, Chapter 537
Torts and Actions for Damages
Section 537.037. August 28, 2016
537.037. Emergency care, no civil liability, exceptions (Good Samaritan law).

1. Any physician or surgeon, registered professional nurse or licensed practical nurse licensed to practice in this state under the provisions of chapter 334 or 335, or licensed to practice under the equivalent laws of any other state and any person licensed as a mobile emergency medical technician under the provisions of chapter 190, may:
   (1) In good faith render emergency care or assistance, without compensation, at the scene of an emergency or accident, and shall not be liable for any civil damages for acts or omissions other than damages occasioned by gross negligence or by willful or wanton acts or omissions by such person in rendering such emergency care.
   (2) In good faith render emergency care or assistance, without compensation, to any minor involved in an accident, or in competitive sports, or other emergency at the scene of an accident, without first obtaining the consent of the parent or guardian of the minor, and shall not be liable for any civil damages other than damages occasioned by gross negligence or by willful or wanton acts or omissions by such person in rendering the emergency care.
2. Any other person who has been trained to provide first aid in a standard recognized training program may, without compensation, render emergency care or assistance to the level for which he or she has been trained, at the scene of an emergency or accident, and shall not be liable for civil damages for acts or omissions other than damages occasioned by gross negligence or by willful or wanton acts or omissions by such person in rendering such emergency care.
3. Any mental health professional, as defined in section 632.005, or qualified counselor, as defined in section 631.005, or any practicing medical, osteopathic, or chiropractic physician, or certified nurse practitioner, or physicians' assistant may in good faith render suicide prevention interventions at the scene of a threatened suicide and shall not be liable for any civil damages for acts or omissions other than damages occasioned by gross negligence or by willful or wanton acts or omissions by such person in rendering such suicide prevention interventions.
4. Any other person may, without compensation, render suicide prevention interventions at the scene of a threatened suicide and shall not be liable for civil damages for acts or omissions other than damages occasioned by gross negligence or by willful or wanton acts or omissions by such person in rendering such suicide prevention interventions.

(L. 1979 H.B. 445 § 1, A.L. 1983 1st Ex. Sess. H.B. 8, A.L. 1986 H.B. 860, A.L. 2005 H.B. 462 & 463, A.L. 2008 S.B. 1081)

EMTALA

The Emergency Medical Treatment and Active Labor Act (EMTALA) was enacted in 1986 to ensure that all patients in a medical crisis were appropriately treated. It was created to address the problem of hospital emergency departments turning away patients who could not pay [16]. The fact that it specifically covers patients in active labor makes it particularly relevant to the subject of this textbook. If a pregnant patient cannot reach her doctor and presents to the emergency department with abdominal pain, or other abdominal issues, the healthcare provider should have a thorough understanding of how to comply with the Act and the ramifications of failing to do so. To comply with EMTALA, a hospital must follow three basic requirements [17]:

1. Screen patients to determine whether a medical emergency exists
2. Stabilize patients with medical emergencies
3. Restrict transfer of nonstabilized patients to two circumstances, described in more detail below

As for requirement 1, the emergency department must provide a medical screening exam to any patient who requests treatment, regardless of ability to pay, in order to determine whether a medical emergency exists. An emergency medical condition is considered to be the presence of acute symptoms of such severity that the absence of immediate medical attention could reasonably be expected to result in placing an individual's health in serious jeopardy, serious impairment to bodily functions or serious dysfunction of any bodily organ or part. The medical screening exam should be comparable to an exam performed on another patient who presents with the same or similar symptoms. With respect to a pregnant woman who is having contractions, an emergency medical condition is one in which there is inadequate time for safe transfer to another hospital before delivery, or one in which transfer may pose a threat to the health or safety of the woman or unborn child.

As for requirement 2, if the patient has an emergency medical condition, the hospital must provide treatment until the patient is stabilized, then transfer the patient to a medical facility that is better able to provide the necessary treatment. The transferring hospital must try to minimize the risk of transfer, obtain the patient's written consent for transfer, provide a signed certificate of transfer, assure that the transfer takes place with qualified personnel and equipment, and send copies of medical records related to the emergency condition to the receiving hospital. The receiving hospital is obligated to have available space and qualified personnel to treat the patient, agree to accept the transfer, and provide appropriate medical treatment. Regional referral centers and hospitals with specialized capabilities cannot refuse to accept an appropriate transfer it they have the capacity.

As for requirement 3, nonstabilized patients may be transferred only if the patient (or someone acting on the patient's behalf) requests a transfer in writing after being informed of the risks involved and the hospital's duty to treat under EMTALA, or a physician certifies that the medical benefits expected from transfer outweigh the risks involved in the transfer.

Triaging abdominal pain in pregnancy can be difficult. The healthcare provider should carefully discern whether the abdominal pain is attributable to labor or another abdominal condition. Failure to make a timely and accurate diagnosis can delay treatment and may lead to an increased risk of adverse events. A real life example illustrates this point: a pregnant patient presented to the Emergency Department with abdominal pain and inability to void. The ED nurse evaluated the patient and contacted the obstetrician by phone, who ordered observation for several hours. After 2 h of observation the nurse discharged the patient. Four hours later the patient returned with worsening abdominal pain and vaginal bleeding. An ultrasound confirmed an intrauterine fetal demise secondary to placental abruption. Setting aside professional liability issues, the patient was allowed to proceed with a claim for an EMTALA violation because of the lack of compliance with hospital policy which required a patient in active labor to be examined by an obstetrician or other physician before discharge [18].

There are two courses of action for violations of EMTALA: private civil suits against the hospital (but not the physician) and a Health and Human Services (HHS) penalty which fines the hospital, the physician, or both. HHS may fine and penalize a physician who fails to respond to an emergency while on call, fails to perform a screening exam, fails to inform emergency patients of the risks and benefits of transfer, or signs a transfer certification when he or she can reasonably be expected to know that the risks outweigh the benefits of the transfer.

An Overview of EMTALA Fines and Penalties for EMTALA Violations [19]
Fines and penalties for violations of the EMTALA statute are as follows:

- Hospitals may be fined $50,000 per violation ($25,000 for hospitals with <100 beds).
- Physicians may be fined $50,000 per violation.
- The hospital or physician's Medicare provider agreement may be terminated.
- The hospital may be sued by the patient in civil court for an EMTALA violation.
- A receiving hospital can bring suit against a transferring hospital for its EMTALA violation.
- More than one violation can result from a single patient encounter.

Healthcare Fraud and Abuse

There are many state and federal laws which govern physician practices and which are enforced by government entities including the Centers for Medicaid and Medicare Services, the Office of Inspector General, the Department of Justice

and the Department of Health and Human Services. The five main areas of fraud and abuse include the False Claims Act (FCA), the Anti-Kickback Statute, the Physician Self-Referral Act (Stark), and the Exclusion Statute and the Civil Monetary Penalty Law [20]. For purposes of this chapter, the focus will be only on the FCA in order to stress the importance of handling coding and billing properly in order to avoid liability.

As alluded to earlier in this chapter, auto-coding and record cloning sometimes causes inflated upper level coding and additional payment. The FCA permits recovery of funds from anyone who knowingly presents or causes to be presented a fraudulent claim for payment to the government. To establish FCA liability, it must be proven that a defendant knowingly submitted or caused to be submitted a false claim for reimbursement of services. The claim need not be entirely fraudulent in order to violate the FCA. Rather, the FCA prohibits use of any false statement or document in support of a claim for government funds. Apart from traditional claims, liability under the FCA also attaches to anyone who acts improperly to avoid having to pay money to the government (known as "reverse" false claims).

Common examples of healthcare fraud include [21]:

1. Billing for services not rendered
2. Falsifying a patient's diagnosis to justify tests, surgeries, or other procedures
3. Misrepresenting procedures performed to obtain payment for noncovered services
4. Billing for a more costly service than the one performed (upcoding services)
5. Billing for more expensive equipment that was delivered to patient (upcoding medical supplies)
6. Billing each stage of a procedure as if it were a separate procedure (unbundling)
7. Billing for services not medically necessary
8. Accepting kickbacks for patient referrals
9. Waiving patient copays or deductibles
10. Overbilling the insurance carrier or benefit plan

Financial recovery against a defendant under the FCA can be devastating, with penalties of $5500–11,000 per claim plus three times the government's damages. In the context of Medicare billing, the potential exists for a catastrophic judgment based on the number of claims at issue. Individuals may be held responsible if found to have acted willfully, recklessly, or with deliberate ignorance in making or causing the submission of false claims. Those responsible may even face criminal charges in extreme cases. The very potential for imposition of individual liability and/or criminal sanctions allows the government to aggressively and effectively leverage settlements when armed with FCA allegations. Further, liability under the FCA is allowable for violations of the Stark Law and the Anti-kickback Statute.

Persistent Vegetative State and End of Life Medical Matters

Patient Self-Determination Act, DPOA Issues, Advance Directives, PVS, Brain Damage

The incidence of encountering end of life medical and legal issues is low in the context of pregnant women, but awareness of possible issues is important, nevertheless. The Patient Self-Determination Act (PSDA) of 1990 encourages all people to make choices now about the types of and extent of medical care they want to accept or refuse should they become unable to make those decisions due to illness or incapacitation. Compliance with this federal law is mandatory. All healthcare agencies (hospitals, long-term care facilities, and home health agencies) receiving Medicare and Medicaid reimbursement are required to recognize living wills, advanced directives, and durable powers of healthcare.

The PSDA does not create new rights but affirms the common law right of self-determination as guaranteed by the due process clause of the 14th Amendment. Healthcare agencies must ask the patient whether they have an advance directive, and if they do not, must provide information about it if requested. This written notification of the patient's right to refuse or consent to medical treatment is an important vehicle to improving the healthcare decision-making process. Complex issues such as irreversible maternal brain injury during pregnancy, persistent vegetative state (PVS), and brain death in contemporary healthcare practice can be navigated more successfully with advance consideration. The literature documents several cases of maternal brain death in pregnancy as well as cases of PVS associated with irreversible brain injury [22]. Feldman et al. described a case of a pregnant mother who sustained irreversible brain damage. The family chose to maintain the pregnancy via aggressive life support of the mother. After a lengthy hospital course, a viable infant was delivered by cesarean section followed by successful organ harvesting from the mother [22]. A protocol for managing such patients was created by Feldman et al. Fig. 14.1 is an adaptation of that protocol.

These are examples of rare but tragic and complex cases a provider may confront when caring for the pregnant patient. Prior to current medical technology, fetuses in utero historically died with the mother. Now women who have experienced a CVA or other brain injury leave the provider to deal with issues of self-determination vis-à-vis the fetus in utero.

Conclusion

This chapter has highlighted a variety of medico-legal issues the healthcare provider may encounter, but it is by no means comprehensive. The legal issue typically most worrisome to the practitioner is medical negligence. To protect oneself from liability, the practitioner must stay abreast of the standard of care and strive to provide the best care possible. Complete, accurate documentation which supports the rationale for the care provided, and is entered in the medical record in a timely manner, will

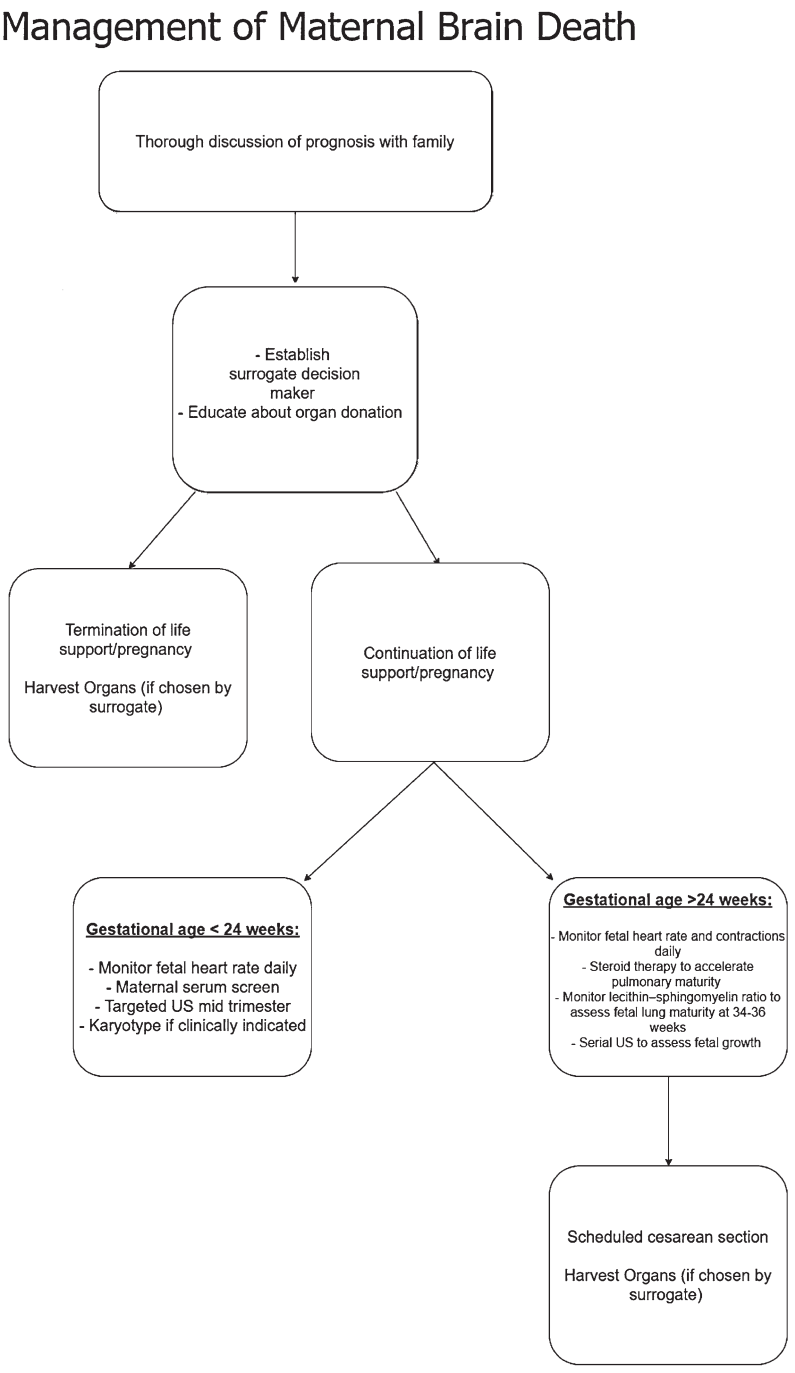

Fig. 14.1 Algorithm for management of maternal brain death [22]

go a long way in protecting against liability. Likewise, ensuring that informed consent discussions cover all necessary components, including risks, benefits, and alternatives; and are thoroughly documented in the medical record, will help establish that the patient understood and voluntarily made a well-informed treatment choice.

Familiarity with regulatory issues such as EMTALA and HIPAA, as well as end of life matters, is essential for the provider in today's complex healthcare environment to avoid legal and ethical pitfalls. Not every legal issue can be anticipated in the healthcare arena, but the practitioner armed with basic legal knowledge will navigate the medico-legal waters more confidently and successfully.

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