Approach to acute abdominal pain in pregnant and postpartum women

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INTRODUCTION

The approach to acute abdominal/pelvic pain in pregnancy is similar to that in the nonpregnant state, with some additional challenges. The initial goal is to identify patients who have a serious or even life-threatening etiology for their symptoms and require urgent intervention. Additional issues in pregnant women include consideration of the effects of physiologic changes related to pregnancy, causes of acute abdominal/pelvic pain that may be more common due to the pregnant state or related to obstetric complications, and the effect of the disorder on the fetus. Indicated diagnostic imaging and interventions should be performed since delay in diagnosis and treatment can increase maternal and fetal/newborn morbidity and mortality.

This topic will review issues specific to the diagnostic evaluation and management of acute abdominal/pelvic pain in pregnant and postpartum women. The approach to acute abdominal/pelvic pain in other populations is discussed separately:

- (See "Evaluation of the adult with abdominal pain".)
- (See "Causes of abdominal pain in adults".)
- (See "Evaluation of acute pelvic pain in women".)

GENERAL APPROACH

The goal in the evaluation of patients with abdominal/pelvic pain is to quickly identify those who have a serious or even life-threatening etiology for their symptoms and require urgent intervention. Signs and symptoms that suggest a possible serious disease process include vaginal bleeding, new onset hypertension, hypotension, moderate or severe pain, vomiting, fever, and history of recent trauma.

We generally assess for pregnancy-related causes of pain first since these disorders are more likely to impact both mother and fetus. Vaginal bleeding and hypertension are key signs of a serious pregnancy-related cause of abdominal pain but may be absent. A simple approach to differential diagnosis of serious

pregnancy-related causes of abdominal pain is provided in the algorithm (algorithm 1). (See 'Acute abdominal pain related to pregnancy or the reproductive tract' below.)

Hypotension suggests severe hemorrhage; in the absence of vaginal bleeding, the patient should be evaluated for rupture of an intraabdominal blood vessel or vascular organ (eg, perforated ulcer, splenic rupture). (See 'Medical-surgical causes of acute abdominal pain' below.)

Patients who have experienced trauma should have a full trauma work-up (see "Initial evaluation and management of blunt abdominal trauma in adults" and "Initial management of trauma in adults"), with attention to pregnancy-related considerations. (See "Initial evaluation and management of pregnant women with major trauma".)

Critical care ultrasonography (CCUS) is most commonly used in the emergency department and is an important diagnostic tool. It may include bedside application of ultrasonography (eg, point-of-care ultrasonography [POCUS]). Protocols that describe the use of CCUS in critically ill patients who present with shock or trauma include rapid ultrasound in shock (RUSH), abdominal and cardiac evaluation with sonography in shock (ACES), focused assessment with sonography for trauma (FAST), and focused cardiac ultrasound (FOCUS). (See "Indications for bedside ultrasonography in the critically-ill adult patient".)

PHYSIOLOGIC CHANGES OF PREGNANCY THAT IMPACT DIFFERENTIAL DIAGNOSIS

Pregnancy complicates the differential diagnosis of abdominal/pelvic pain because physiologic changes associated with pregnancy can mimic clinical features of medical/surgical disorders associated with abdominal/pelvic pain, thus creating diagnostic uncertainty. For example:

- Early in pregnancy, stretching of the round ligament is a normal benign process that may be associated with mild pain (see 'Round ligament' below). In the second half of pregnancy, especially in the third trimester, mild abdominal/pelvic discomfort may be related to normal fetal position or movement, normal intermittent uterine contractions (Braxton-Hicks uterine contractions [ie, contractions not associated with labor/cervical changes]), or normal uterine enlargement.

  In contrast, pain that is moderate or severe, associated with other symptoms (eg, nausea, vomiting, vaginal bleeding, headache, fever), or confined to the upper abdomen suggests a disease process. The presence of peritoneal signs (rebound tenderness, abdominal guarding) is never normal in pregnancy [1]. These patients require prompt maternal-fetal evaluation.

- Nausea and vomiting is a common feature of early pregnancy, and usually abates by 20 weeks of gestation (see "Clinical features and evaluation of nausea and vomiting of pregnancy"). Nausea and vomiting is not a normal manifestation of pregnancy when it occurs with abdominal/pelvic pain, fever, diarrhea, headache, or localized abdominal/pelvic findings on physical examination. Nausea and vomiting in the second half of pregnancy should be considered abnormal and requires further evaluation. (See "Approach to the adult with nausea and vomiting".)

- The uterus becomes an abdominal organ, enlarging beyond the pelvis by 12 weeks of gestation. This enlargement may make it difficult to localize pain as it can impede physical examination, affect the

normal location of pelvic and abdominal organs, and mask or delay peritoneal signs (rebound, guarding) [1]. The normal laxity of the abdominal wall in pregnancy may also diminish peritoneal signs.

- The enlarged uterus may compress the urinary tract, leading to usually mild hydroureter and hydronephrosis [2] and thus mimic some signs of nephrolithiasis. (See "Maternal adaptations to pregnancy: Renal and urinary tract physiology" and "Acute kidney injury in pregnancy".)

- The enlarged uterus may cause aortocaval compression, resulting in lightheadedness or syncope when the pregnant woman is in a supine position [3]. This physiologic change resolves with a change in position (left lateral is best), but symptoms may be falsely attributed to internal bleeding from an acute disease process (eg, ruptured liver or spleen). (See "Maternal adaptations to pregnancy: Cardiovascular and hemodynamic changes", section on 'Postural hypotensive syndrome'.)

- The high maternal progesterone level during pregnancy decreases lower esophageal sphincter tone, small bowel and colonic motility, gallbladder emptying, and ureteral tone [4]. These physiologic changes are also important in the pathogenesis and diagnosis of conditions such as gastroesophageal reflux, constipation, cholelithiasis, and nephrolithiasis, all of which may be associated with abdominal pain. (See "Maternal adaptations to pregnancy: Gastrointestinal tract".)

- Physiologic changes in hematologic parameters may mimic infection and occult hemorrhage, making diagnosis of these disorders more difficult:

  - White cell counts increase to a normal range of 10,000 to 14,000 cells/mm^3 during pregnancy [5]; in labor, the white cell count may be as high as 20,000 to 30,000 cells/mm^3, returning to normal prepregnancy levels at approximately one week postpartum [6]. Bandemia is not a normal variant of pregnancy, so its presence suggests infection until proven otherwise.

  - A larger increase in plasma volume than in red cell volume results in physiologic anemia. The modest decrease in hemoglobin concentration (normal hemoglobin in pregnancy is ≥10.5 to 11.0 g/dL) coupled with the normal modest increase in heart rate (by 10 to 15 beats per minute in pregnancy) can be mistaken for signs of mild hemorrhage. (See "Maternal adaptations to pregnancy: Hematologic changes".)

- The range of normal for multiple other laboratory values may be altered in pregnancy (table 1). (See "Normal reference ranges for laboratory values in pregnancy".)

DIAGNOSTIC EVALUATION

An obstetrician should be part of the team when a pregnant patient with abdominal pain is initially evaluated in the emergency department. Attention to detail, serial physical examinations, clinical awareness of both nonobstetric and obstetric causes of abdominal pain, and systematic evaluation help avoid misdiagnosis and subsequent complications.

History and physical examination — In addition to the usual diagnostic evaluation of adults with abdominal pain (see "Evaluation of the adult with abdominal pain"), pregnant women should be asked about their past and current obstetric history, as pregnancy complications may manifest as abdominal/pelvic pain (eg, preeclampsia may be associated with placental abruption or hepatic bleeding, previous cesarean delivery

may be associated with uterine rupture) and complications often recur in subsequent pregnancies. They should also be asked whether they have any vaginal bleeding or leaking of fluid. Bleeding in the first half of pregnancy may be related to miscarriage or ectopic pregnancy. Placental abruption and labor are common causes of abdominal/pelvic pain in the second half of pregnancy and often accompanied by vaginal bleeding and rupture of the fetal membranes. Rupture of membranes alone, however, is painless. (See "Overview of the etiology and evaluation of vaginal bleeding in pregnant women" and "Preterm prelabor rupture of membranes: Clinical manifestations and diagnosis".)

The uterine examination should evaluate size (which correlates with gestational age), tone, tenderness, and, in the second half of pregnancy, frequency of contractions. The normal uterus is nontender and soft, like any other relaxed muscle. A rigid or tender uterus in the second half of pregnancy suggests placental abruption, intrauterine infection, uterine rupture, or possibly labor. (See 'Second half of pregnancy' below.)

Cervical dilation/effacement and whether the fetal membranes are intact should be assessed. Obstetric and nonobstetric disorders may cause uterine contractions, which may result in cervical change (ie, labor). Rupture of membranes often leads to initiation of labor and may be associated with intrauterine infection or placental abruption. These entities are described in more detail below. (See 'Labor' below and 'Intra-amniotic infection' below and 'Placental abruption' below.)

The fetal heart rate should be documented. Continuous fetal heart rate monitoring is usually appropriate in pregnancies that have reached a gestational age with a reasonable chance of extrauterine survival (≥22 weeks of gestation). An abnormal fetal heart rate may be the direct consequence of a pregnancy-related cause of abdominal/pelvic pain (eg, placental abruption) or it may be an indirect consequence of maternal compromise (eg, hypotension, infection). In either case, fetal resuscitation is usually indicated, and urgent delivery may be appropriate. (See "Nonstress test and contraction stress test" and "Management of intrapartum category I, II, and III fetal heart rate tracings".)

Laboratory — Laboratory tests can help narrow the differential diagnosis. In general, we suggest the following, unless a specific diagnosis is strongly suspected:

- Complete blood count with differential
- Urinalysis
- Liver and pancreatic function tests (aminotransferases, bilirubin, amylase, lipase)

Women with hemodynamic instability should have blood sent for coagulation studies and type and crossmatch. Electrolytes and renal function tests can be useful in women who are vomiting or anorectic. In the presence of fever or unstable vital signs possibly related to sepsis, blood and urine cultures are performed and may be helpful subsequently to confirm suspected infection and guide choice of antibiotic therapy. (See "Evaluation of the adult with abdominal pain".)

Imaging — Diagnostic imaging should be performed as medically indicated since delay in diagnosis and treatment can increase maternal and fetal morbidity and mortality [7,8]. Ultrasound is typically the first-line modality for diagnostic imaging of the abdomen/pelvis in pregnant women since it is widely available, portable, nonionizing, and its diagnostic performance is often adequate. (See "Diagnostic imaging in pregnant and nursing women".)

When ultrasound findings are equivocal or uncertain, the choice of the second-line modality depends on the differential diagnosis and should consider availability, diagnostic performance, and fetal radiation exposure. When indicated, use of magnetic resonance imaging (MRI) is preferable to computed tomography (CT) because it avoids ionizing radiation and, for diagnosis of many disorders, performs as well as or better than CT [9-11]. However, prompt diagnosis should not be delayed if MRI is not readily accessible. It is important to note that gadolinium crosses the placenta and may have potential harmful fetal effects. Therefore, the use of gadolinium generally should be avoided, but there may be some occasional clinical scenarios where the potential benefits are thought to outweigh the potential risks. (See "Diagnostic imaging in pregnant and nursing women", section on 'Magnetic resonance imaging'.)

Ionizing radiation — Concerns about the possible fetal effects of ionizing radiation should not prevent performance of medically indicated diagnostic procedures during pregnancy using the best available modality for the clinical situation. A delay in diagnosis can increase the risk of an adverse maternal and/or fetal outcome.

When procedures requiring ionizing radiation are necessary (eg, trauma, bowel obstruction), radiologists should be familiar with various techniques beyond shielding the abdomen that can be employed to minimize the radiation dose. Almost all diagnostic radiological procedures are associated with exposures that are below the threshold for inducing congenital malformations, growth restriction, or neurodevelopmental delay. Whether there is a small increase in risk of carcinogenesis is controversial.

Chest and abdominal radiographs are commonly used in evaluation of adults with abdominal pain. The estimated fetal absorption per chest radiograph is <0.01 mGy (<0.001 rad); this dose is well below doses that have been associated with any short- or long-term adverse effects [12]. The estimated fetal absorption for abdominal radiographs is 1 to 4.2 mGy (0.1 to 0.42 rad), which is also below doses that have been associated with short- or long-term adverse effects. (See "Diagnostic imaging in pregnant and nursing women", section on 'Fetal effects from ionizing radiation'.)

Laparoscopy — Laparoscopy is sometimes indicated in the evaluation of acute abdominal/pelvic pain, especially when the diagnosis is not clear after less invasive evaluations and the differential diagnoses include potentially life-threatening or organ-threatening disorders. It is usually performed in the first or second trimester, but is usually technically possible even in the early third trimester. Based on retrospective evaluation and survey data, laparoscopic surgery for evaluation of abdominal/pelvic pain in pregnancy appears to be as safe as laparotomy. (See "Laparoscopic surgery in pregnancy".)

When surgery is planned, the appropriate services (Obstetrics, General Surgery, Anesthesia, Pediatrics) should be consulted. Management of pregnant women undergoing surgery may require modifications to the technique used in nonpregnant women. (See "Management of the pregnant patient undergoing nonobstetric surgery".)

ACUTE ABDOMINAL PAIN RELATED TO PREGNANCY OR THE REPRODUCTIVE TRACT

First half of pregnancy

Life-threatening causes

Ectopic pregnancy — Ectopic pregnancies usually occur in the fallopian tube but sometimes within the cervical canal, a cesarean delivery scar, or other extrauterine sites. Rarely, an ectopic pregnancy occurs concurrently with an intrauterine pregnancy; these heterotopic pregnancies can be difficult to diagnose. A pregnancy conceived via assisted reproductive technology (eg, in vitro fertilization [IVF]) is a strong risk factor. (See "Abdominal pregnancy, cesarean scar pregnancy, and heterotopic pregnancy".)

Clinical manifestations are usually related to free blood in the peritoneal cavity due to extrauterine pregnancy rupture or bleeding, and vary depending upon the location. Abdominal pain is a common symptom of all types of extrauterine pregnancy; vaginal bleeding, nausea, and vomiting may also occur. Blood in the peritoneal cavity can be identified by ultrasound examination of the pelvis and abdomen or culdocentesis (rarely performed). Patients may present with tachycardia, hypotension, low grade fever, and a mild elevation in the white cell count.

The diagnosis of ectopic pregnancy is usually based upon results from a combination of ultrasound examination and human chorionic gonadotropin (hCG) hormone testing in the early first trimester. Rarely, ectopic pregnancies progress to the second or third trimester; these pregnancies are typically attached to abdominal viscera (uterine serosa, adnexa, parametrium, liver, spleen, bowel, omentum).

All pregnant patients who present with lower abdominal pain with or without vaginal bleeding should undergo ultrasound examination to determine the location of the pregnancy, unless an intrauterine location has already been documented. (See "Ectopic pregnancy: Clinical manifestations and diagnosis".)

Common causes

Round ligament — Early in pregnancy, unilateral mild pelvic pain related to "stretching" of one of the round ligaments is a common benign process. Pain is more common on the right, and may be bilateral. Vaginal bleeding is not present. Round ligament pain is a clinical diagnosis of exclusion; there are no positive laboratory or imaging findings. (See "Clinical manifestations and diagnosis of early pregnancy", section on 'Pelvic discomfort'.)

Miscarriage — Miscarriage is defined as the loss of a pregnancy before 20 weeks of gestation. Signs and symptoms include mild to moderate midline crampy pelvic pain and mild to moderate vaginal bleeding.

Speculum and pelvic examinations are the first step in the diagnostic evaluation. If no products of conception are identified grossly in the cervix or vagina, then ultrasonography and serial quantitative serum hCG hormone levels are the most useful follow-up tests of women suspected of carrying a potential failed pregnancy. The sonographic signs of a nonviable pregnancy vary with gestational age. (See "Spontaneous abortion: Risk factors, etiology, clinical manifestations, and diagnostic evaluation".)

Second half of pregnancy

Life-threatening causes

Placental abruption — Acute placental abruption (ie, decidual hemorrhage leading to the premature separation of the placenta prior to delivery) classically presents with vaginal bleeding, abdominal and/or back pain, uterine tenderness, uterine rigidity, and uterine contractions; the fetal heart rate pattern may be abnormal. If significant placental separation develops, maternal disseminated intravascular coagulation and/or fetal death commonly occur. A retroplacental or subchorionic clot is the classic ultrasound finding of

placental abruption but is not always present. Diagnosis is based on clinical findings, and delivery is usually indicated. (See "Placental abruption: Pathophysiology, clinical features, diagnosis, and consequences" and "Placental abruption: Management".)

Pregnancy-related liver disease — Pregnancy-related liver diseases can cause epigastric or right upper quadrant abdominal pain. These disorders (preeclampsia with severe features, HELLP syndrome, and acute fatty liver of pregnancy) have overlapping features and can be difficult to distinguish (table 2).

Preeclampsia — Preeclampsia is a syndrome characterized by the new onset of hypertension and usually proteinuria after 20 weeks of gestation in a previously normotensive woman; right upper quadrant or epigastric pain is a sign of liver involvement and signifies the severe spectrum of the disease. The pain may be caused by stretching of Glisson's capsule due periportal or subcapsular bleeding or, rarely, hepatic rupture. (See 'Hepatic rupture' below.)

The diagnosis is based on characteristic symptoms, findings on physical examination, and laboratory results (table 3A-B). (See "Preeclampsia: Clinical features and diagnosis" and "Preeclampsia: Management and prognosis".)

HELLP syndrome — Hemolysis with a microangiopathic blood smear, Elevated Liver enzymes, and a Low Platelet count are the findings in HELLP syndrome. The most common clinical presentation is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum. As with preeclampsia, the pain may be caused by stretching of Glisson's capsule due periportal or subcapsular bleeding or, rarely, hepatic rupture. It may not be possible to distinguish HELLP from preeclampsia with severe features, and they may be different manifestations of the same disease. (See 'Hepatic rupture' below.)

Many women with HELLP also have nausea, vomiting, and malaise, which may be mistaken for a nonspecific viral illness or viral hepatitis, particularly if the serum aspartate aminotransferase and lactate dehydrogenase are markedly elevated (table 4). Hypertension (defined as blood pressure ≥140/90 mmHg) and proteinuria are present in approximately 85 percent of cases, but it is important to remember that either or both may be absent in women with HELLP syndrome. (See "HELLP syndrome".)

Acute fatty liver — Acute fatty liver occurs in the second half of pregnancy, usually in the third trimester. The most frequent initial symptoms are nausea or vomiting (approximately 75 percent of patients), abdominal pain (particularly epigastric, 50 percent), anorexia, and jaundice. Approximately one-half of patients have signs of preeclampsia at presentation or at some time during the course of illness. As discussed above, nausea and vomiting during the second half of pregnancy should be considered abnormal, and this requires further evaluation.

The diagnosis of acute fatty liver of pregnancy is usually made clinically based upon the setting, presentation, and compatible laboratory and imaging results. Laboratory test findings may show elevated aminotransferases, elevated bilirubin, thrombocytopenia, prolonged prothrombin time, low glucose levels, increased uric acid levels, increased creatinine levels, and elevated white cell count. Imaging tests of the liver are primarily used to exclude other diagnoses, such as a hepatic infarct or hematoma, although some authors have reported finding fat on ultrasound, CT, or MRI. Hepatic rupture is rare. (See "Acute fatty liver of pregnancy".)

Uterine rupture — Uterine rupture can be a catastrophic event. Signs and symptoms include nonreassuring fetal heart rate tracing or fetal death, uterine tenderness, abdominal pain, peritoneal irritation, vaginal bleeding, shock, and loss of fetal station.

Most uterine ruptures occur in laboring women with a prior cesarean delivery or prior transmyometrial uterine surgery (eg, myomectomy). The possibility of rupture should always be excluded in such women who have abdominal pain. (See "Uterine rupture: After previous cesarean delivery".)

Rupture of the unscarred uterus during labor is rare; risk factors include grand multiparity, dystocia (malpresentation, macrosomia), obstetrical procedures (breech extraction, uterine instrumentation, cephalic version), and use of uterotonic drugs. (See "Uterine rupture: Unscarred uterus".)

Spontaneous rupture in the absence of labor may occur in women with a scarred uterus, but usually results from sharp or blunt abdominal trauma. Spontaneous rupture may also be related to a cornual pregnancy, pregnancy in a rudimentary uterine horn, or an interstitial pregnancy. (See "Initial evaluation and management of pregnant women with major trauma", section on 'Uterine rupture or penetrating injury'.)

Common causes

Labor — Labor should always be considered in the differential diagnosis of abdominal pain in pregnant women, especially when symptoms are increasing over time It is a clinical diagnosis defined by uterine contractions of increasing frequency, intensity, and duration that cause cervical dilation and/or effacement over time. The presence of light vaginal bleeding and/or rupture of membranes increases diagnostic certainty in women with minimal cervical dilation or effacement. By definition, labor is preterm at 20 to <37 weeks of gestation and term at ≥37 weeks of gestation. (See "Preterm labor: Clinical findings, diagnostic evaluation, and initial treatment", section on 'Diagnosis'.)

Intra-amniotic infection — Signs and symptoms of intra-amniotic infection include fever, abdominal pain, uterine tenderness, leukocytosis, maternal and fetal tachycardia, and uterine contractions. It is most common in the setting of preterm or term rupture of the fetal membranes, with or without labor. (See "Intra-amniotic infection (clinical chorioamnionitis or triple I)".)

Fetal position or movement — Mild abdominal/pelvic discomfort may be related to fetal position or movement. Low fetal station at term may result in pelvic discomfort, while in breech presentation, the fetal head may cause mild discomfort in an upper quadrant. Upper quadrant kicking at term may cause transient intermittent upper quadrant discomfort.

Discomfort from fetal position/movement can usually be diagnosed by history and abdominal and pelvic examination. Ultrasound can be used to confirm fetal position and correlate symptoms with observed fetal behavior.

Uncommon causes

Uterine incarceration — Typically, patients with uterine incarceration present at 14 to 16 weeks of gestation with symptoms related to pressure on the anatomic structures adjacent to the entrapped enlarging uterus. The most common symptoms are pain and progressive difficulty voiding. The pain may be abdominal, suprapubic, or in the back, or may be limited to pelvic discomfort or a feeling of pelvic fullness. Urinary

symptoms include frequency, dysuria, sensation of incomplete emptying, voiding small volumes due to overflow incontinence, and, often, urinary retention [13,14].

The diagnosis is based on characteristic findings on physical and ultrasound examination after the first trimester: severe anterior displacement of the cervix and the uterus filling the posterior pelvis below the sacral promontory (figure 1). (See "Incarcerated gravid uterus".)

Anytime in pregnancy

Common causes

Fibroid degeneration or torsion — The majority of fibroids remain asymptomatic in pregnancy [15-17]. Degeneration may occur, and is more common with leiomyomas >5 cm in diameter. Most patients have only localized pain, although mild leukocytosis, fever, peritoneal signs, and nausea and vomiting can occur. Pedunculated fibroids are at risk of torsion; symptoms are similar to those with degeneration.

Fibroids are readily identified on ultrasound examination. Pain after ballottement by the abdominal ultrasound probe directly over the fibroid supports the diagnosis. (See "Pregnancy in women with uterine leiomyomas (fibroids)", section on 'Symptoms'.)

Bleeding ovarian cyst — Rupture of an ovarian cyst into the peritoneal cavity or bleeding into an ovarian cyst may be associated with the sudden onset of unilateral lower abdominal pain. The pain often begins during strenuous physical activity, such as exercise or sexual intercourse. Rarely, bleeding is sufficiently severe to cause hemodynamic instability.

Ultrasound is the first-line imaging study for identification and characterization of the ovarian neoplasm and to look for fluid in the cul-de-sac. (See "Evaluation and management of ruptured ovarian cyst".)

Constipation — Constipation is common in pregnancy and may cause considerable abdominal discomfort. It is due to a combination of factors, including the effects of the hormonal changes of pregnancy on the gastrointestinal tract, mechanical effects of the enlarging uterus, reduced physical activity, intake of vitamins with iron or iron supplements, and changes in diet [18]. (See "Maternal adaptations to pregnancy: Gastrointestinal tract" and "Maternal adaptations to pregnancy: Gastrointestinal tract", section on 'Bloating and constipation'.)

Uncommon causes

Ovarian torsion — Ovarian torsion typically presents with lateralized lower abdominal pain, frequently accompanied by nausea, vomiting, low-grade fever, and/or leukocytosis [19]. It occurs in all three trimesters, but is most common in the first trimester and can occur postpartum. Risk factors include the presence of an ovarian cyst or mass and induction of ovulation, which can cause enlarged multicystic ovaries [19,20].

A presumptive diagnosis of torsion can be made with reasonable confidence in women with acute pelvic pain and an adnexal mass with the characteristic sonographic appearance (including Doppler studies) of torsion and after exclusion of other conditions. A definitive diagnosis requires direct visualization of a rotated ovary at the time of surgery. Treatment can consist of untwisting of the ovary and ovarian conservation, but this will depend on the appearance of the ovary and surrounding tissue. A salpingo-oophorectomy may be indicated if necrotic, gelatinous, or dead tissue is identified. In one study, 7 of 41 pregnant women who underwent

untwisting of the ovary had recurrent torsion in the same pregnancy [19]. (See "Ovarian and fallopian tube torsion".)

Fallopian tube torsion — The presentation of fallopian tube torsion is similar to ovarian torsion. Torsion is often associated with fallopian tube pathology (hydatid cysts of Morgagni, hydrosalpinx, and pyosalpinx). It commonly occurs on the right side, accompanied by nausea, vomiting, and lower abdominal pain. Ultrasound may help to identify a cystic structure in the pelvis, but differentiation between a paratubal and ovarian cyst is difficult. Diagnosis is made at the time of surgery in most cases and can be managed through the laparoscope by experienced surgeons [21]. (See "Ovarian and fallopian tube torsion".)

Uterine torsion — Uterine torsion is rare, but has been described in all trimesters as well as in nonpregnant women. It can be defined as rotation greater than 45 degrees around the longitudinal axis of the uterus [22]. Most patients have potential risk factors, such as fibroids, müllerian anomalies, fetal malpresentation, pelvic adhesions, and abdominal or ligamentous laxity.

According to literature reviews, rotation is 180 degrees in most cases, but can be up to 360 degrees, and the uterus is usually in dextrorotation [23-25]. Clinical manifestations vary depending on the degree of torsion: Abdominal pain, nausea and vomiting, obstructed labor, intestinal or urinary complaints, uterine hypertonus, vaginal bleeding, fetal bradycardia, and maternal shock have been reported.

Ultrasonography can lead to a correct diagnosis before delivery if a change in the previously determined placental site is noted (eg, from anterior to posterior) or the ovarian vessels are observed to pass in front of the lower uterine segment [24,26]. However, in almost all cases, the signs and symptoms of torsion lead to emergency cesarean delivery resulting in the correct diagnosis.

If derotation of the uterus is not possible, the fetus can be delivered through a transverse incision in the lower posterior uterine segment [22,27]. Fetal mortality and maternal death have been reported in some cases of uterine torsion [25].

Pelvic inflammatory disease — Pelvic inflammatory disease (PID) is rare during pregnancy because the cervical mucous plug and decidua form a barrier that protects the uterus from ascending bacteria. Other diagnoses should be considered before PID in pregnant women with fever and lower abdominal pain. (See "Pelvic inflammatory disease: Clinical manifestations and diagnosis".)

MEDICAL-SURGICAL CAUSES OF ACUTE ABDOMINAL PAIN

An extensive list of causes of abdominal pain is provided in the tables (table 5A-B and figure 2). The location of the pain can be helpful in differential diagnosis, but is not pathognomonic, especially during pregnancy since uterine enlargement can distort normal anatomy. The most common potentially serious nonobstetric causes of acute abdomen pain in pregnancy are acute appendicitis, gallbladder-related disease, and small-bowel obstruction [28].

Upper abdominal pain

Life-threatening causes

Bowel obstruction — The risk of bowel obstruction during pregnancy increases as the uterus enlarges into the upper abdomen with advancing gestation. Adhesions and volvulus are the most common

causes of the obstruction; intussusception is less common, and hernias are rare but should be suspected in those patients with a history of gastric bypass surgery who present with abdominal pain [29]. Patients with a history of gastric bypass who present with upper abdominal pain should be promptly evaluated by the surgical service. (See "Fertility and pregnancy after bariatric surgery", section on 'Bowel obstruction'.)

Volvulus is more common during pregnancy than in the nonpregnant state [30]. (See "Cecal volvulus" and "Sigmoid volvulus".)

Clinical manifestations of bowel obstruction include crampy abdominal pain with vomiting and obstipation. Although nausea and vomiting is common and often a normal symptom of the first half of pregnancy, new onset later in pregnancy or coexistent abdominal pain or peritoneal signs are not normal and require evaluation. Other potential findings inconsistent with nausea and vomiting of pregnancy include abdominal distention, fever, and leukocytosis.

Diagnosis and treatment are similar to that in nonpregnant individuals. Ultrasound may show dilated loops of bowel with air-fluid levels; flat and upright radiographs are more useful for looking for typical findings of obstruction and progressive bowel dilation over time (see 'Ionizing radiation' above). Magnetic resonance imaging (MRI) helps to characterize the site and degree of obstruction. Aggressive intervention is warranted because delay in treatment increases maternal and fetal morbidity and mortality. (See "Epidemiology, clinical features, and diagnosis of mechanical small bowel obstruction in adults" and "Management of small bowel obstruction in adults".)

Perforated ulcer — Peptic ulcer disease is uncommon in pregnancy [31]. Symptoms include nausea, vomiting, and epigastric pain, which is often worse at night and postprandially. In contrast, gastroesophageal reflux disease is common in pregnancy and characterized by both regurgitation and pain, which is worse postprandially and with recumbency.

Ulcer perforation should be suspected in patients with a history of peptic ulcer symptoms who develop the sudden onset of severe, diffuse abdominal pain. The characteristics of the pain and associated symptoms and physical findings (eg, tachycardia, low temperature, peritoneal signs) evolve over the first 12 hours after perforation. (See "Peptic ulcer disease: Clinical manifestations and diagnosis".)

Rapid diagnosis is essential, since the prognosis is excellent within the first 6 hours but deteriorates with more than a 12-hour delay. Perforation is largely a clinical diagnosis with the history and physical examination providing essential clues. If imaging is required, plain abdominal radiographs are typically obtained first to detect diagnostic free air, although approximately 10 to 20 percent of patients with a perforated duodenal ulcer will not have free air. (See 'Ionizing radiation' above.)

Visceral artery aneurysm — Rupture of a visceral artery aneurysm (typically splenic artery aneurysm) is rare, but it can occur during pregnancy, usually in the third trimester, and is typically a catastrophic event [32,33]. However, 20 to 25 percent of patients have an initial small, contained rupture that occurs hours before hemorrhage with circulatory collapse [32]. Presenting symptoms include diffuse abdominal pain centered in the midline or left upper quadrant and radiating to the shoulder, anorexia, nausea, vomiting, syncope, and diarrhea or constipation. In stable women, a curvilinear or signet-ring shaped calcification on an abdominal radiograph is strongly suggestive of splenic artery aneurysm [33]. Treatment is recommended for all symptomatic visceral artery aneurysms in pregnant women. (See "Overview of visceral artery aneurysm and pseudoaneurysm" and "Treatment of visceral artery aneurysm and pseudoaneurysm".)

Hepatic rupture — In pregnant women, hepatic rupture is rare and most likely associated with HELLP syndrome, trauma, or preeclampsia with severe features (see 'Pregnancy-related liver disease' above). Other causes are extremely rare (eg, neoplasm, peliosis hepatis).

If rupture is suspected, ultrasound examination may show intra- or extra-hepatic bleeding, but hepatic complications are best characterized by MRI or computed tomography (CT). (See "HELLP syndrome", section on 'Hepatic hematoma and rupture'.)

Common causes

Gastroesophageal reflux — Gastroesophageal reflux disease is more common during pregnancy. The most common symptoms are heartburn, regurgitation, and dysphagia; other symptoms include chest pain, water brash, globus sensation, odynophagia, and nausea. A presumptive diagnosis can be based on clinical symptoms. Indications for additional evaluation and treatment are reviewed separately. (See "Clinical manifestations and diagnosis of gastroesophageal reflux in adults" and "Medical management of gastroesophageal reflux disease in adults", section on 'Pregnancy and lactation'.)

Gallbladder disease — Pregnancy predisposes patients to formation of gallstones. The presentation of gallstone disease during pregnancy is not significantly different from the nonpregnant state. Affected patients typically complain of deep and gnawing pain that is occasionally sharp, colicky, and severe. The pain is localized in the right upper quadrant or epigastrium. There is often a history of fatty food ingestion one hour or more before onset of pain. As the gallbladder relaxes, the stones often fall back from the cystic duct. As a result, the attack reaches a crescendo over a number of hours and then resolves completely.

Acute cholecystitis refers to a syndrome of right upper quadrant pain that is steady and severe, fever, tachycardia, and leukocytosis associated with gallbladder inflammation, which is usually related to gallstone disease. Murphy's sign is variably positive (a positive Murphy's sign refers to pain resulting from palpating the area of the gallbladder fossa just beneath the liver edge while the patient is asked to inspire deeply. Patients may also have an associated inspiratory arrest).

Ultrasonography is the best method for making the diagnosis of cholelithiasis and differentiating this diagnosis from acute cholecystitis and chronic cholecystitis, when used along with history, physical examination, and laboratory findings. The white cell count and alkaline phosphatase level are normally elevated in pregnancy, which reduces the diagnostic usefulness of these laboratory tests (see 'Physiologic changes of pregnancy that impact differential diagnosis' above). Significant elevations of the transaminases and alkaline phosphatase or direct bilirubin should raise the possibility of a common bile duct stone, cholangitis, or the Mirizzi syndrome. (See "Gallstones in pregnancy" and "Acute calculous cholecystitis: Clinical features and diagnosis" and "Mirizzi syndrome".)

Pneumonia — Pneumonia involving the lower lobes of the lung is a common cause of abdominal pain syndromes, presumably related to diaphragmatic irritation, and may be confused with acute cholecystitis or, rarely, an acute abdomen. Abdominal pain is occasionally the sole presenting complaint in a patient with lower lobe pneumonia. Common symptoms of pneumonia include cough, fever, pleuritic chest pain, dyspnea, and sputum production. (See "Diagnostic approach to community-acquired pneumonia in adults".)

The presence of an infiltrate on plain chest radiograph is considered the gold standard for diagnosing pneumonia when clinical and microbiologic features are supportive. The estimated fetal absorption per chest

radiograph is <0.01 mGy (<0.001 rad); this dose is well below doses that have been associated with any short- or long-term adverse effects [12]. (See "Treatment of respiratory infections in pregnant women", section on 'Pneumonia' and 'Ionizing radiation' above.)

Uncommon causes

Acute hepatitis — Pregnancy generally does not affect the course of hepatitis A, B, or C, whereas women with hepatitis E in the third trimester are predisposed to severe clinical disease. Cytomegalovirus, Epstein-Barr virus, and adenoviruses can also cause hepatitis in association with systemic infection. Constitutional symptoms of hepatitis include anorexia, nausea, jaundice, and right upper quadrant discomfort. The diagnosis is based on characteristic laboratory findings. (See "Intercurrent hepatobiliary disease during pregnancy" and "Approach to liver disease occurring during pregnancy".)

Pancreatic disease — Acute pancreatitis is a rare complication of pregnancy [34,35]; most cases are related to gallstone disease. Almost all patients have acute and persistent upper abdominal pain, which may radiate to the back, may be relieved with leaning forward, and may be accompanied by fever and postprandial nausea and vomiting.

The range of normal serum amylase and lipase levels are similar in healthy pregnant and nonpregnant women; significantly elevated values should be considered pathologic (table 1) [36-39]. Ultrasound can be used to look for choledocholithiasis and pseudocyst formation. If further imaging is needed, MRI may be helpful. (See "Clinical manifestations and diagnosis of acute pancreatitis" and "Endoscopic retrograde cholangiopancreatography (ERCP) in pregnancy", section on 'Acute biliary pancreatitis'.)

Rupture of a solid pseudopapillary neoplasm of the pancreas, characterized by peritoneal signs, hypotension, and back pain, has been reported as an unusual cause of acute abdomen in pregnancy [40]. (See "Pancreatic cystic neoplasms: Clinical manifestations, diagnosis, and management".)

Rectus sheath hematoma — Rectus sheath hematoma is a rare cause of acute upper abdominal pain in pregnancy [41]. Risk factors for this disorder include female gender, coagulation disorders, anticoagulant use, trauma, abdominal straining (coughing, exercising, vomiting), degenerative muscular disease, prior abdominal surgery, obesity, and pregnancy.

Classic findings include abdominal pain and an abdominal mass that remains unchanged with contraction of the rectus muscles. Periumbilical and/or flank ecchymosis may be present, and hypotension can occur with severe bleeding.

Although ultrasound is typically the first-line imaging study (sensitivity 85 to 96 percent), CT is 100 percent sensitive in the diagnosis when the hematoma is less than 5 days duration. In addition to anemia, laboratory evaluation may show elevated transaminases as a result of trauma to skeletal muscle. (See "Rectus sheath hematoma".)

Adrenal hemorrhage — Adrenal hemorrhage in pregnancy is rare, presenting with nonspecific symptoms, most commonly abdominal pain and hypotension. A high index of suspicion is needed for diagnosis, and MRI is the most sensitive and specific imaging modality. Conservative management with fluid resuscitation and correction of coagulopathies is necessary. Surgery is indicated for continued clinical deterioration despite aggressive resuscitative efforts, and adrenal insufficiency should be addressed in order to prevent circulatory collapse [42].

Hiatal hernia — The most common symptoms of hiatal hernia are epigastric or substernal pain, postprandial fullness, substernal fullness, nausea, and retching. The pain can be severe if the hernia incarcerates. The diagnosis is often made on the basis of characteristic clinical symptoms and findings on chest radiograph (see 'Ionizing radiation' above). Bariatric surgery increases the risk of hiatal hernia. (See "Hiatus hernia".)

Wandering spleen syndrome — The wandering spleen syndrome is a rare cause of acute abdominal pain where the spleen migrates from its normal site to another location in the abdomen because of laxity or maldevelopment of the supporting ligaments. It is usually seen in younger adolescents and children, although it can occur in adults. Patients typically present with acute left upper quadrant pain associated with an abdominal mass. Ultrasound can help make the diagnosis [43]. (See "Causes of abdominal pain in adults", section on 'Less common causes'.)

Pain in the lower abdomen

Common causes

Acute appendicitis — Appendicitis is the most common cause of the acute surgical abdomen during pregnancy [44]. The most common symptom of appendicitis (ie, right lower quadrant pain) occurs maximally within a few centimeters of McBurney's point (1.5 to 2 inches from the anterior superior iliac spine (ASIS) on a straight line from the ASIS to the umbilicus) in the vast majority of pregnant women, regardless of the stage of pregnancy.

The clinical diagnosis should be strongly suspected in pregnant women with classic findings: abdominal pain that migrates to the right lower quadrant, right lower quadrant tenderness, nausea/vomiting, fever, and leukocytosis with left shift. However, pregnant women are less likely to have a classic presentation of appendicitis than nonpregnant women, especially in late pregnancy. The location of the appendix migrates a few centimeters cephalad with the enlarging uterus, so in the third trimester, pain may localize to the mid or even the upper right side of the abdomen, and tenderness at that point may be less prominent than in nonpregnant women.

Graded compression ultrasonography is the first-line imaging modality. The primary goal of imaging is to reduce delays in surgical intervention due to diagnostic uncertainty. A secondary goal is to reduce, but not eliminate, the negative appendectomy rate. However, the diagnosis should not be excluded if the appendix appears normal, unless sonographic findings suggest a likely alternative diagnosis (eg, ovarian torsion, nephrolithiasis). (See "Acute appendicitis in pregnancy".)

Nephrolithiasis — Affected patients usually present in the second or third trimester (approximately 20 percent in the first trimester) with acute flank pain (90 percent), which often radiates to the groin or lower abdomen; hematuria is present in 75 to 95 percent, one-third of whom have gross hematuria and 40 percent of whom have pyuria. Fever is present if there is an accompanying upper urinary tract infection.

When diagnostic ultrasound is performed, physiological hydronephrosis of pregnancy must be distinguished from pathological hydronephrosis from obstruction. Transvaginal ultrasonography should be performed in women in whom transabdominal ultrasonography is not informative, and can help detect distal ureteral stones. Further options, when needed, include MRI urography or low-dose CT. (See "Nephrolithiasis during pregnancy".)

Uncommon causes

Inflammatory bowel disease — The pain of inflammatory bowel disease is crampy and associated with changes in bowel movements (loose, bloody, mucousy). Pain ranges from mild to severe and positively correlates with other bowel symptoms. Fever and weight loss occur in severe disease.

The course of inflammatory bowel disease during pregnancy appears to be determined, in part, by the activity of the disease at conception. The initial diagnosis is complicated in pregnancy and based on endoscopic findings or imaging studies in a patient with a compatible clinical history. (See "Fertility, pregnancy, and nursing in inflammatory bowel disease".)

Diverticulitis — Most cases of diverticulitis occur after age 45. However, diverticulitis in pregnant women has been described in case reports; several of these cases involved Meckel's diverticulum [45-51]. Imaging modalities used in the diagnosis of appendicitis (ultrasonography, MRI, CT) may be helpful, but a high degree of clinical suspicion and surgical intervention is usually necessary to make the diagnosis [45,51,52]. (See "Clinical manifestations and diagnosis of acute diverticulitis in adults".)

Diffuse abdominal pain or pain in variable locations

Life-threatening causes

Trauma — Trauma is estimated to complicate approximately 1 in 12 pregnancies [53] and can lead to maternal and/or fetal death. The initial evaluation of the pregnant trauma patient should focus on establishing maternal cardiopulmonary stability. Any treatment required to save the mother's life or treat her critical status should be undertaken, regardless of her pregnancy, including any diagnostic imaging deemed necessary. Obstetric providers (if available) should be notified of the patient as soon as possible upon presentation, or while the patient is en route, so that they can aid in the management and evaluation. (See "Initial evaluation and management of pregnant women with major trauma", section on 'Initial evaluation and management of major trauma'.)

Abdominal pain is a common consequence of blunt or penetrating abdominal trauma. The evaluation is similar to that in nonpregnant patients. (See "Initial evaluation and management of blunt abdominal trauma in adults" and "Initial evaluation and management of abdominal stab wounds in adults" and "Initial evaluation and management of abdominal gunshot wounds in adults".)

Once catastrophic trauma has been excluded, the obstetric clinician can determine whether the patient has any obstetric complications (eg, placental abruption, uterine rupture, fetomaternal hemorrhage, preterm labor, prelabor rupture of membranes). The majority of women who develop adverse obstetric outcomes have symptoms such as contractions, vaginal bleeding, or abdominal pain upon initial presentation, but some may have minimal symptoms. (See "Initial evaluation and management of pregnant women with major trauma", section on 'Pregnancy evaluation and management after initial maternal stabilization'.)

Spontaneous hemoperitoneum — Spontaneous hemoperitoneum (spontaneous intraperitoneal hemorrhage) in pregnancy is a rare life-threatening disorder; fewer than 50 cases have been reported in the past two decades [54-56]. The patients presented with sudden onset of abdominal pain in the second half of pregnancy, often with hypovolemic shock and/or abnormal fetal heart rate. Exploratory laparotomy revealed 500 to 4000 mL of blood in the abdomen, usually from bleeding superficial veins/varicosities on the posterior

surface of the uterus or the parametrium. Thus, imaging by abdominal ultrasound or MRI, if possible, may show free peritoneal fluid.

Risk factors include nulliparity and history of endometriosis. In one series, biopsy of the bleeding site was performed in five cases and endometriosis was identified in all [54]; in another series, 11 out of 11 women had a history of endometriosis [55].

Timely intervention and control of bleeding allowed approximately half of the pregnancies to deliver or continue normally; the remainder ended in stillbirth or neonatal death. There were no maternal deaths. Bleeding can be controlled by suturing and/or the use of hemostatic agents; hysterectomy is rarely required [57].

Recurrence has been reported in the same and in future pregnancies [55].

Aneurysm — Dissection and rupture of arterial aneurysms (eg, splenic, renal, uterine, ovarian, aorta) have also been described, mostly in case reports, and appear to be related to the physiologic and hemodynamic changes of pregnancy [58-64]. Women with Marfan syndrome, Ehlers Danlos syndrome, or Turner syndrome are particularly at risk.

Patients present with sudden-onset abdominal pain, free peritoneal fluid, sudden hemodynamic collapse, and, often, failure to correctly identify the cause prior to exploratory laparotomy [58]. Visceral artery aneurysm (typically splenic artery)can also occur in women without connective tissue disease and has a strong association with pregnancy. (See 'Visceral artery aneurysm' above.)

Mesenteric venous thrombosis — Mesenteric venous thrombosis can lead to bowel edema and, if arterial inflow becomes impaired, bowel infarction. The clinical presentation is characterized by insidious onset of poorly localized abdominal pain, which may be accompanied by nausea, vomiting, and abdominal distention [65]. It has been described in pregnancy [66,67]. (See "Overview of intestinal ischemia in adults" and "Mesenteric venous thrombosis in adults".)

Common causes

Gastroenteritis — Acute gastroenteritis is defined as diarrheal disease (three or more times per day or at least 200 g of stool per day) of rapid onset that lasts less than two weeks and may be accompanied by nausea, vomiting, fever, or abdominal pain. Severe abdominal pain is uncommon and identifies patients may need hospitalization or evaluation for other causes. (See "Acute viral gastroenteritis in adults".)

Severe abdominal pain suggestive of placental abruption has been reported in association with maternal enterovirus infection [68,69]. Other types of gastroenteritis and mesenteric adenitis also may cause an acute abdomen. (See "Causes of abdominal pain in adults".)

Sickle cell crisis — In women with sickle cell disease, anemia and vasoocclusive or acute painful episodes occur more often in pregnancy and are the most common maternal complications associated with pregnancy, occurring in over 50 percent of pregnant women with the disease.

Vasoocclusive crisis may be difficult to distinguish from other causes of acute abdomen. Right upper quadrant symptoms are common in the setting of hepatic involvement. Approximately 50 percent of episodes are accompanied by objective clinical signs such as fever, swelling, tenderness, tachypnea, hypertension,

nausea, and vomiting. (See "Overview of the clinical manifestations of sickle cell disease" and "Pregnancy in women with sickle cell disease" and "Hepatic manifestations of sickle cell disease".)

Hereditary angioedema — One-third of women with hereditary angioedema experience exacerbation of symptoms during pregnancy. The disease is characterized clinically by recurrent episodes of angioedema, which most commonly affect the skin, upper airway, or bowel. Bowel edema manifests as varying degrees of gastrointestinal colic, nausea, vomiting, and/or diarrhea. Hives and pruritus are not present.

Ultrasonography is useful for evaluation of gastrointestinal attacks of these patients. The most common early finding is bowel wall edema, although this may resolve rapidly. Ascites may be the only finding during later stages of the attack. (See "Hereditary angioedema: Epidemiology, clinical manifestations, exacerbating factors, and prognosis" and "Hereditary angioedema: Pathogenesis and diagnosis".)

Uncommon causes

Iliopsoas abscess — An abscess of the psoas muscle is a rare cause of abdominal pain in pregnancy or postpartum and has only been described in case reports [70-72]. Patients usually present with vague findings including back pain, difficulty with ambulation, weight loss, and malaise. Diagnosis requires a high clinical suspicion in a patient with a history of intravenous drug use. Physical examination findings may include fever, costovertebral angle tenderness, lower back tenderness, or a mass in the groin. CT or MRI may help to diagnose the abscess and guide treatment. (See "Psoas abscess".)

Cutaneous nerve entrapment — Anterior cutaneous nerve entrapment syndrome typically causes chronic abdominal wall pain. On physical examination, the patient is able to point with one finger to the area of maximal tenderness and may display the "hover sign," referring to patients who guard the affected area from the examiner's hands. (See "Causes of abdominal pain in adults".)

Abdominal wall hernia — Abdominal wall hernias may present with pain, bulging, or both. If severe, there may be signs of bowel obstruction. These hernias develop as a result of prior surgery (incisional) or spontaneously (umbilical, epigastric, Spigelian, or lumbar hernias). Presentation depends on the type and location of the hernia. (See "Overview of abdominal wall hernias in adults".)

Spontaneous rupture of the urinary tract — Spontaneous rupture of the urinary tract in pregnancy is extremely rare with only case reports in the literature [73]. Clinical presentation is similar to ureteric colic or pyelonephritis: sudden onset flank pain, most commonly right sided, with radiation to the lower abdomen or groin. In severe cases, the patient may present with an acute abdomen due to a retroperitoneal hematoma or urinoma if there is associated renal parenchymal involvement [74]. A high clinical suspicion and imaging (contrast enhanced computerized tomography scan) can aid in diagnosis. A delay in diagnosis can lead to abscess formation and possible nephrectomy.

CAUSES OF POSTPARTUM ACUTE ABDOMINAL PAIN

Any of the medical-surgical causes of abdominal pain discussed above can occur in the postpartum woman as well (table 6).

Life-threatening causes

Necrotizing fasciitis — Unexplained pain, which increases rapidly over time, may be the first manifestation of necrotizing fasciitis. Erythema may be present diffusely or locally, but in some patients, excruciating pain in the absence of any cutaneous findings is the only clue to the infection. In addition to pain and skin findings, fever, malaise, myalgias, diarrhea, and anorexia may also be present during the first 24 hours. The development of anesthesia may precede the appearance of skin necrosis and provide a clue that the process is necrotizing fasciitis rather than cellulitis.

It is important to consider this diagnosis in the setting of fever, toxicity, soft tissue involvement with severe pain (out of proportion to skin findings in some cases), crepitus, rapid progression of clinical manifestations, and elevated serum creatine kinase level. Blood cultures should be obtained, but the diagnosis is established surgically. (See "Necrotizing soft tissue infections" and "Surgical management of necrotizing soft tissue infections".)

Abdominal compartment syndrome — Abdominal compartment syndrome should be considered when severe abdominal pain with abdominal distension occurs in women with unusually severe abdominal pain postcesarean delivery. The syndrome is lethal if not diagnosed early. Findings noted on CT imaging are bowel wall thickening, elevated diaphragm, and collapse of the inferior vena cava along with mucosal hyperenhancement and hemoperitoneum [75]. Definitive diagnosis of abdominal compartment syndrome requires measurement of the intra-abdominal pressure, which should be performed with a low threshold for diagnosis. (See "Abdominal compartment syndrome in adults".)

Group A streptococcal infection — Group A streptococcal (GAS) infection is an uncommon but frequently life-threatening infection [76-79]. A broad spectrum of GAS postpartum infections can develop rapidly, ranging from mild endomyometritis (with absence of tachycardia and leukocytosis) to fulminant endomyonecrosis and death. The presentation varies slightly depending on the length of time since delivery. In one series of patients who developed the disease within two days of delivery, clinical findings included abdominal pain (58 percent), purulent vaginal discharge (38 percent), and uterine tenderness (31 percent) [78]. Gastrointestinal symptoms (diarrhea, nausea, vomiting) occurred in 31 percent of cases. Systemic symptoms included fever (73 percent), chills (35 percent), and hypotension (35 percent). Leukocytosis and tachycardia were not frequent findings.

Marked leukocytosis, hypotension, and tachycardia are signs of developing streptococcal toxic shock syndrome and are associated with higher mortality. However, leukopenia or a marked bandemia (greater than 10 percent) in the absence of a leukocytosis may be seen. Other signs and symptoms include an influenza-like syndrome (fever, chills, myalgia, nausea, vomiting, diarrhea), renal impairment, coagulopathy, hepatic dysfunction, adult respiratory distress syndrome, soft tissue necrosis, and generalized erythematous rash that may desquamate [80].

A pelvic examination should be performed; vaginal discharge and/or infection at the site of an episiotomy may be detected via direct observation (or with a speculum to visualize the entire vagina and cervix). (See "Pregnancy-related group A streptococcal infection".)

Common causes

Uterine involution — Midline, intermittent, lower abdominal and back pain are common normal symptoms postpartum and believed to be due to hypertonic uterine contractions. Typically, the pain is exacerbated by breastfeeding and is worse in multiparas than primiparas [81,82]. The pain usually resolves

by the end of the first postpartum week. (See "Overview of the postpartum period: Physiology, complications, and maternal care", section on 'Afterpains'.)

Urinary retention — Vaginal birth (especially forceps-assisted), epidural anesthesia [83], and cesarean delivery have been associated with postpartum urinary retention in non-catheterized patients. Patients may complain of suprapubic and abdominal pain and display varying degrees of bladder emptying. On examination, the fundal height may extend well above the umbilicus due to the excessively enlarged bladder. (See "Overview of the postpartum period: Physiology, complications, and maternal care", section on 'Voiding difficulty and urinary retention'.)

Endometritis — The diagnosis of postpartum endometritis is largely based upon clinical criteria of fever and uterine tenderness occurring in a postpartum woman. Other signs and symptoms that support the diagnosis include malodorous lochia, chills, and lower abdominal pain. The uterus may be soft and subinvoluted, which can lead to excessive uterine bleeding. Sepsis is an unusual presentation. Most cases develop after cesarean delivery and within the first week after birth, but 15 percent present between one and six weeks postpartum. (See "Postpartum endometritis".)

Incisional complications — Complications related to an incision for cesarean delivery (hematomas, seromas, infection, dehiscence) are a common cause of postoperative abdominal wall pain. The diagnosis is based on characteristic findings on physical examination, with ultrasound of the abdominal wall in cases of diagnostic uncertainty. (See "Cesarean delivery: Postoperative issues", section on 'Wound complications'.)

Uncommon causes

Ovarian vein thrombophlebitis — Women with ovarian vein thrombophlebitis (OVT) usually present within one week after delivery. They appear clinically ill; symptoms may include fever and abdominal, flank, or back pain on the side of the affected vein. The right ovarian vein is more commonly involved than the left (80 versus 6 percent); bilateral involvement occurs in 14 percent of cases. Pelvic tenderness may reflect OVT or an alternative diagnosis such as endometritis. Nausea, ileus, and other gastrointestinal symptoms may occur, but are usually mild, which may be helpful in distinguishing right-sided OVT from appendicitis, pyelonephritis, or other processes. Although much less common, other pelvic vessels may develop thrombosis [84].

Women with deep septic pelvic thrombophlebitis usually present with fever in the early postpartum period (usually within three to five days), although the onset may be delayed to up to three weeks following delivery. Patients usually do not appear clinically ill; fever or chills may be the only symptoms. Abdominal or pelvic tenderness is notably absent, which helps to distinguish this disorder from OVT.

Imaging should be obtained to evaluate the pelvic vessels and for other potential processes. CT is the preferred diagnostic modality but MR is acceptable; ultrasonography is not very useful. (See "Septic pelvic thrombophlebitis".)

Clostridioides (formerly Clostridium) difficile — *C. difficile*-associated diarrhea with colitis is uncommon but may be increasing in postpartum women [85,86]. Mild manifestations of the disease include watery diarrhea (≥3 loose stools in 24 hours) with lower abdominal pain and cramping, low grade fever, and leukocytosis. However, severe or fulminant colitis can also occur. The symptoms generally occur in the setting of recent antibiotic administration.

The diagnosis of *C. difficile* infection is established via a positive stool test for *C. difficile* toxin(s) or *C. difficile* toxin gene. (See "Clostridioides (formerly Clostridium) difficile infection in adults: Clinical manifestations and diagnosis".)

Hemorrhage — Intra-abdominal or retroperitoneal hemorrhage may be associated with abdominal pain, but more commonly manifests as hemodynamic instability (tachycardia, hypotension, or shock). Hemorrhage may be related to injury to a blood vessel at cesarean or vaginal delivery or unrecognized uterine rupture during delivery. (See "Overview of postpartum hemorrhage" and "Management of hematomas incurred as a result of obstetrical delivery".)

Acute colonic pseudoobstruction (Ogilvie's syndrome) — Some degree of postoperative ileus is a normal physiologic response to abdominal surgery that generally resolves without serious sequelae. (See "Postoperative ileus".)

Acute colonic pseudoobstruction is a rare life-threatening form of ileus characterized by massive dilation of the colon in the absence of mechanical obstruction. It is more likely to occur after cesarean than vaginal delivery [87]. The diagnosis can be made only after excluding toxic megacolon or mechanical obstruction. (See "Acute colonic pseudo-obstruction (Ogilvie's syndrome)".)

In a systematic review of 65 cases of postpartum Ogilvie's syndrome reported between 2002 and 2016, the types and frequencies of symptoms were: abdominal distension (89 percent), abdominal pain (60 percent), vomiting (27 percent), fever (25 percent), constipation (16 percent), nausea (13 percent), and diarrhea (7 percent) [87]. Patients presented from 6 hours to 8 days after delivery. Six patients had cecal diameters >12 cm, and all of these patients perforated; 19 patients had cecal diameters of 9 to 12 cm, and 21 percent perforated; 17 patients had cecal diameters <9 cm, and 18 percent perforated.

Pregnancy-related liver disease — Hepatic manifestations of severe preeclampsia, HELLP syndrome, and acute fatty liver may develop or be first recognized postpartum. (See 'Pregnancy-related liver disease' above.)

Pubic symphysis separation — Clinical manifestations of pubic symphysis separation include suprapubic pain, tenderness, swelling, and edema with pain radiating to the legs, hips, or back. The pain often increases with weight bearing, especially with walking and climbing stairs. Turning in bed, lifting, or getting up from a chair may also cause pain. Some women report waking up during the night because of pain.

The diagnosis is based on characteristic symptoms and physical examination: pain evoked by bilateral pressure on the trochanters or by hip flexion with the legs in extension. Rarely, a palpable groove at the level of the symphysis may be detected by internal or external examination. (See "Maternal adaptations to pregnancy: Musculoskeletal changes and pain", section on 'Pelvic girdle pain'.)

Foreign body — After cesarean delivery, the possibility of a retained instrument or gauze sponge should be considered in patients with symptoms such as nonspecific abdominal pain, fever, nausea, and vomiting. However, the presentation may also be years after the surgery. The diagnosis is made radiographically.

Unrecognized visceral injury — An unrecognized injury to the genitourinary or gastrointestinal system that occurred during a cesarean delivery or postpartum sterilization procedure could lead to postpartum peritonitis, bowel obstruction, or bowel ischemia.

Intra-abdominal or pelvic abscess — Pelvic abscess in women is usually a complication of pelvic inflammatory disease, but can also follow pelvic surgery or be related to an intra-abdominal inflammatory or septic process. (See "Epidemiology, clinical manifestations, and diagnosis of tubo-ovarian abscess".)

Myocardial infarction — Myocardial infarction (MI) is rare in women of childbearing age, although the risk is increased in the third trimester and the early postpartum period. Risk factors include the traditional coronary heart disease risk factors, particularly maternal age over 35 years, diabetes mellitus, hypertension, smoking, thrombophilia, postpartum hemorrhage, and postpartum infection.

Patients often complain of the development (over the course of minutes) of chest discomfort that is felt in the anterior chest or epigastric area and often with radiation to the shoulders, arms, jaws, or back. Shortness of breath and nausea may also be present.

In a review of 103 cases from 1995 to 2005, coronary artery morphology was evaluated in 96 by arteriography or autopsy [88]. Coronary atherosclerosis with or without intracoronary thrombus was present in only 40 percent. The remaining cases consisted of coronary artery dissection (27 percent), thrombus in a normal coronary artery (8 percent), spasm (2 percent), emboli (2 percent), and normal coronary arteries (13 percent). Atherosclerosis is more common with antepartum MI, while coronary dissection is more common peripartum and postpartum [88-92].

The diagnosis of acute MI is mostly guided by the same principles as in the general population, including ischemic symptoms, electrocardiogram changes, and elevations in cardiac biomarkers. (See "Acute myocardial infarction and pregnancy".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Acute abdomen (belly pain) (The Basics)")

SUMMARY AND RECOMMENDATIONS

- When evaluating pregnant women with abdominal pain, the clinician needs to consider the normal physiologic/anatomic alterations associated with pregnancy since they affect interpretation of signs and symptoms and laboratory results. (See 'Physiologic changes of pregnancy that impact differential diagnosis' above.)

- In addition to the usual diagnostic evaluation of adults with abdominal pain (see "Evaluation of the adult with abdominal pain"), key points in evaluation of pregnant women include assessment of gestational age and fetal heart rate, past and current obstetrical history, vaginal bleeding, amniotic fluid leakage, and cervical and uterine status. (See 'Diagnostic evaluation' above.)

- The goal of the evaluation is to quickly identify those who have a serious or even life-threatening etiology for their symptoms and require urgent intervention. Signs and symptoms that suggest a possible serious disease process include vaginal bleeding, new onset hypertension, hypotension, moderate or severe pain, vomiting, fever and history of recent trauma. (See 'General approach' above.)

- Prompt consultation with an obstetrician should be sought when a pregnant patient with abdominal pain is evaluated in the emergency department. We generally assess for pregnancy-related causes of pain first since these disorders are more likely to impact both mother and fetus. Vaginal bleeding and hypertension are key signs of a potentially serious pregnancy-related cause of abdominal pain, but may be absent. A basic initial approach to differential diagnosis of serious pregnancy-related causes of abdominal pain is provided in the algorithm (algorithm 1). (See 'General approach' above.)

- Although abdominal discomfort, nausea, vomiting, and constipation can be a normal part of pregnancy, peritoneal signs (rebound tenderness, abdominal guarding) are never normal in pregnant women. Nausea and vomiting are not normal manifestations of advanced pregnancy (after 20 weeks) and, when they occur with abdominal pain, fever, diarrhea, headache, or localized abdominal findings, require a thorough evaluation. (See 'Physiologic changes of pregnancy that impact differential diagnosis' above.)

- Requisite diagnostic imaging and interventions should be performed as indicated since delay in diagnosis and treatment can increase maternal and fetal/newborn morbidity and mortality. Abdominal and pelvic ultrasound examinations are the most useful tests for evaluation of abdominal pain in pregnant women. These examinations are safe for the fetus and perform well for making and excluding most diagnoses associated with abdominal pain. When indicated, chest and abdominal plain films result in very low fetal absorption of ionizing radiation, and below doses that have been associated with short- or long-term adverse effects. Magnetic resonance imaging does not involve ionizing radiation and thus is preferable to computed tomography, which exposes the fetus to higher doses of ionizing radiation than plain films. (See 'Imaging' above.)

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REFERENCES

1. Parangi S, Levine D, Henry A, et al. Surgical gastrointestinal disorders during pregnancy. Am J Surg 2007; 193:223.

2. Cormier CM, Canzoneri BJ, Lewis DF, et al. Urolithiasis in pregnancy: Current diagnosis, treatment, and pregnancy complications. Obstet Gynecol Surv 2006; 61:733.

3. Stone K. Acute abdominal emergencies associated with pregnancy. Clin Obstet Gynecol 2002; 45:553.

4. Ryan JP, Pellecchia D. Effect of ovarian hormone pretreatment on gallbladder motility in vitro. Life Sci 1982; 31:1445.

5. Lurie S, Rahamim E, Piper I, et al. Total and differential leukocyte counts percentiles in normal pregnancy. Eur J Obstet Gynecol Reprod Biol 2008; 136:16.

6. Acker DB, Johnson MP, Sachs BP, Friedman EA. The leukocyte count in labor. Am J Obstet Gynecol 1985; 153:737.

7. Kilpatrick CC, Monga M. Approach to the acute abdomen in pregnancy. Obstet Gynecol Clin North Am 2007; 34:389.

8. Kilpatrick CC, Orejuela FJ. Management of the acute abdomen in pregnancy: a review. Curr Opin Obstet Gynecol 2008; 20:534.

9. Baron KT, Arleo EK, Robinson C, Sanelli PC. Comparing the diagnostic performance of MRI versus CT in the evaluation of acute nontraumatic abdominal pain during pregnancy. Emerg Radiol 2012; 19:519.

10. Spalluto LB, Woodfield CA, DeBenedectis CM, Lazarus E. MR imaging evaluation of abdominal pain during pregnancy: appendicitis and other nonobstetric causes. Radiographics 2012; 32:317.

11. Beddy P, Keogan MT, Sala E, Griffin N. Magnetic resonance imaging for the evaluation of acute abdominal pain in pregnancy. Semin Ultrasound CT MR 2010; 31:433.

12. Groen RS, Bae JY, Lim KJ. Fear of the unknown: ionizing radiation exposure during pregnancy. Am J Obstet Gynecol 2012; 206:456.

13. Shnaekel KL, Wendel MP, Rabie NZ, Magann EF. Incarceration of the Gravid Uterus. Obstet Gynecol Surv 2016; 71:613.

14. Newell SD, Crofts JF, Grant SR. The incarcerated gravid uterus: complications and lessons learned. Obstet Gynecol 2014; 123:423.

15. Strobelt N, Ghidini A, Cavallone M, et al. Natural history of uterine leiomyomas in pregnancy. J Ultrasound Med 1994; 13:399.

16. Aharoni A, Reiter A, Golan D, et al. Patterns of growth of uterine leiomyomas during pregnancy. A prospective longitudinal study. Br J Obstet Gynaecol 1988; 95:510.

17. Neiger R, Sonek JD, Croom CS, Ventolini G. Pregnancy-related changes in the size of uterine leiomyomas. J Reprod Med 2006; 51:671.

18. Cullen G, O'Donoghue D. Constipation and pregnancy. Best Pract Res Clin Gastroenterol 2007; 21:807.

19. Hasson J, Tsafrir Z, Azem F, et al. Comparison of adnexal torsion between pregnant and nonpregnant women. Am J Obstet Gynecol 2010; 202:536.e1.

20. Smorgick N, Pansky M, Feingold M, et al. The clinical characteristics and sonographic findings of maternal ovarian torsion in pregnancy. Fertil Steril 2009; 92:1983.

21. Chohan L, Ramirez MM, Wray CJ, Kilpatrick CC. Laparoscopic management of fallopian tube torsion at 35 weeks of gestation: case report. J Minim Invasive Gynecol 2011; 18:390.

22. De Ioris A, Pezzuto C, Nardelli GB, Modena AB. Caesarean delivery through deliberate posterior hysterotomy in irreducible uterine torsion: case report. Acta Biomed 2010; 81:141.

23. Cook KE, Jenkins SM. Pathologic uterine torsion associated with placental abruption, maternal shock, and intrauterine fetal demise. Am J Obstet Gynecol 2005; 192:2082.

24. Guié P, Adjobi R, N'guessan E, et al. Uterine torsion with maternal death: our experience and literature review. Clin Exp Obstet Gynecol 2005; 32:245.

25. Fatih FF, Gowri V, Rao K. Uterine torsion in second trimester of pregnancy followed by a successful-term pregnancy. BMJ Case Rep 2012; 2012.

26. Salani R, Theiler RN, Lindsay M. Uterine torsion and fetal bradycardia associated with external cephalic version. Obstet Gynecol 2006; 108:820.

27. Albayrak M, Benian A, Ozdemir I, et al. Deliberate posterior low transverse incision at cesarean section of a gravid uterus in 180 degrees of torsion: a case report. J Reprod Med 2011; 56:181.

28. Skubic JJ, Salim A. Emergency general surgery in pregnancy. Trauma Surg Acute Care Open 2017; 2:e000125.

29. Kakarla N, Dailey C, Marino T, et al. Pregnancy after gastric bypass surgery and internal hernia formation. Obstet Gynecol 2005; 105:1195.

30. Chase DM, Sparks DA, Dawood MY, Perry E. Cecal volvulus in a multiple-gestation pregnancy. Obstet Gynecol 2009; 114:475.

31. Essilfie P, Hussain M, Bolaji I. Perforated duodenal ulcer in pregnancy-a rare cause of acute abdominal pain in pregnancy: a case report and literature review. Case Rep Obstet Gynecol 2011; 2011:263016.

32. Selo-Ojeme DO, Welch CC. Review: spontaneous rupture of splenic artery aneurysm in pregnancy. Eur J Obstet Gynecol Reprod Biol 2003; 109:124.

33. Sadat U, Dar O, Walsh S, Varty K. Splenic artery aneurysms in pregnancy--a systematic review. Int J Surg 2008; 6:261.

34. Ramin KD, Ramin SM, Richey SD, Cunningham FG. Acute pancreatitis in pregnancy. Am J Obstet Gynecol 1995; 173:187.

35. Papadakis EP, Sarigianni M, Mikhailidis DP, et al. Acute pancreatitis in pregnancy: an overview. Eur J Obstet Gynecol Reprod Biol 2011; 159:261.

36. Karsenti D, Bacq Y, Bréchot JF, et al. Serum amylase and lipase activities in normal pregnancy: a prospective case-control study. Am J Gastroenterol 2001; 96:697.

37. Ordorica SA, Frieden FJ, Marks F, et al. Pancreatic enzyme activity in pregnancy. J Reprod Med 1991; 36:359.

38. Kaiser R, Berk JE, Fridhandler L. Serum amylase changes during pregnancy. Am J Obstet Gynecol 1975; 122:283.

39. Xydas NP, May JH, Henson MC. Maternal serum amylase and lipase profiles in pregnancy: determinations in both once-sampled and multisampled patient cohorts. South Med J 1996; 89:199.

40. Huang SC, Wu TH, Chen CC, Chen TC. Spontaneous rupture of solid pseudopapillary neoplasm of the pancreas during pregnancy. Obstet Gynecol 2013; 121:486.

41. Tolcher MC, Nitsche JF, Arendt KW, Rose CH. Spontaneous rectus sheath hematoma pregnancy: case report and review of the literature. Obstet Gynecol Surv 2010; 65:517.

42. Bockorny B, Posteraro A, Bilgrami S. Bilateral spontaneous adrenal hemorrhage during pregnancy. Obstet Gynecol 2012; 120:377.

43. Karmazyn B, Steinberg R, Gayer G, et al. Wandering spleen--the challenge of ultrasound diagnosis: report of 7 cases. J Clin Ultrasound 2005; 33:433.

44. Tamir IL, Bongard FS, Klein SR. Acute appendicitis in the pregnant patient. Am J Surg 1990; 160:571.

45. Huerta S, Barleben A, Peck MA, Gordon IL. Meckel's diverticulitis: a rare etiology of an acute abdomen during pregnancy. Curr Surg 2006; 63:290.

46. Ragu N, Tichoux C, Bouyabrine H, et al. [Complicated diverticulitis during pregnancy]. J Radiol 2004; 85:1950.

47. Bodner J, Windisch J, Bale R, et al. Perforated right colonic diverticulitis complicating pregnancy at 37 weeks' gestation. Int J Colorectal Dis 2005; 20:381.

48. Chanrachakul B, Tangtrakul S, Herabutya Y, et al. Meckel's diverticulitis: an uncommon complication during pregnancy. BJOG 2001; 108:1199.

49. Sherer DM, Frager D, Eliakim R. An unusual case of diverticulitis complicating pregnancy at 33 weeks' gestation. Am J Perinatol 2001; 18:107.

50. Pelosi MA 3rd, Pelosi MA, Villalona E. Right-sided colonic diverticulitis mimicking acute cholecystitis in pregnancy: case report and laparoscopic treatment. Surg Laparosc Endosc 1999; 9:63.

51. Wong YS, Liu SY, Ng SS, et al. Giant Meckel's diverticulitis: a rare condition complicating pregnancy. Am J Surg 2010; 200:184.

52. Longo SA, Moore RC, Canzoneri BJ, Robichaux A. Gastrointestinal Conditions during Pregnancy. Clin Colon Rectal Surg 2010; 23:80.

53. Mendez-Figueroa H, Dahlke JD, Vrees RA, Rouse DJ. Trauma in pregnancy: an updated systematic review. Am J Obstet Gynecol 2013; 209:1.

54. Brosens IA, Fusi L, Brosens JJ. Endometriosis is a risk factor for spontaneous hemoperitoneum during pregnancy. Fertil Steril 2009; 92:1243.

55. Lier M, Malik RF, van Waesberghe J, et al. Spontaneous haemoperitoneum in pregnancy and endometriosis: a case series. BJOG 2017; 124:306.

56. Hamadeh S, Addas B, Hamadeh N, Rahman J. Spontaneous intraperitoneal hemorrhage in the third trimester of pregnancy: Clinical suspicion made the difference. J Obstet Gynaecol Res 2018; 44:161.

57. Van den Bosch T. Spontaneous haemoperitoneum in pregnancy (SHiP): take-home messages. BJOG 2017; 124:313.

58. Bloom SL, Uppot R, Roberts DJ. Case records of the Massachusetts General Hospital. Case 32-2010. A pregnant woman with abdominal pain and fluid in the peritoneal cavity. N Engl J Med 2010; 363:1657.

59. Fiori O, Prugnolles H, Darai E, et al. Spontaneous uterine artery rupture during pregnancy in a woman with sickle cell disease: a case report. J Reprod Med 2007; 52:657.

60. Swaegers MC, Hauspy JJ, Buytaert PM, De Maeseneer MG. Spontaneous rupture of the uterine artery in pregnancy. Eur J Obstet Gynecol Reprod Biol 1997; 75:145.

61. Practice Committee of American Society For Reproductive Medicine. Increased maternal cardiovascular mortality associated with pregnancy in women with Turner syndrome. Fertil Steril 2012; 97:282.

62. la Chapelle CF, Schutte JM, Schuitemaker NW, et al. Maternal mortality attributable to vascular dissection and rupture in the Netherlands: a nationwide confidential enquiry. BJOG 2012; 119:86.

63. Chao LW, Chen CH. Spontaneous rupture of an ovarian artery aneurysm: case report and review of the literature. Gynecol Obstet Invest 2009; 68:104.

64. Sakaguchi I, Ohba T, Ikeda O, et al. Embolization for post-partum rupture of ovarian artery aneurysm: case report and review. J Obstet Gynaecol Res 2015; 41:623.

65. Woodfield CA, Lazarus E, Chen KC, Mayo-Smith WW. Abdominal pain in pregnancy: diagnoses and imaging unique to pregnancy--review. AJR Am J Roentgenol 2010; 194:WS14.

66. Atakan Al R, Borekci B, Ozturk G, et al. Acute mesenteric venous thrombosis due to protein S deficiency in a pregnant woman. J Obstet Gynaecol Res 2009; 35:804.

67. Engelhardt TC, Kerstein MD. Pregnancy and mesenteric venous thrombosis. South Med J 1989; 82:1441.

68. Johansson ME, Holmström S, Abebe A, et al. Intrauterine fetal death due to echovirus 11. Scand J Infect Dis 1992; 24:381.

69. Modlin JF. Fatal echovirus 11 disease in premature neonates. Pediatrics 1980; 66:775.

70. Nelson DB, Manders DB, Shivvers SA. Primary iliopsoas abscess and pregnancy. Obstet Gynecol 2010; 116 Suppl 2:479.

71. Young OM, Werner E, Sfakianaki AK. Primary psoas muscle abscess after an uncomplicated spontaneous vaginal delivery. Obstet Gynecol 2010; 116 Suppl 2:477.

72. Delke I. Psoas abscess in obstetrics: uncommon condition with common presentations. Obstet Gynecol 2010; 116 Suppl 2:473.

73. Satoh S, Okuma A, Fujita Y, et al. Spontaneous rupture of the renal pelvis during pregnancy: a case report and review of the literature. Am J Perinatol 2002; 19:189.

74. Narasimhulu DM, Egbert NM, Matthew S. Intrapartum Spontaneous Ureteral Rupture. Obstet Gynecol 2015; 126:610.

75. Patel A, Lall CG, Jennings SG, Sandrasegaran K. Abdominal compartment syndrome. AJR Am J Roentgenol 2007; 189:1037.

76. Anteby EY, Yagel S, Hanoch J, et al. Puerperal and intrapartum group A streptococcal infection. Infect Dis Obstet Gynecol 1999; 7:276.

77. de Moya MA, del Carmen MG, Allain RM, et al. Case records of the Massachusetts General Hospital. Case 33-2009. A 35-year-old woman with fever, abdominal pain, and hypotension after cesarean section. N Engl J Med 2009; 361:1689.

78. Hamilton SM, Stevens DL, Bryant AE. Pregnancy-related group a streptococcal infections: temporal relationships between bacterial acquisition, infection onset, clinical findings, and outcome. Clin Infect Dis 2013; 57:870.

79. Gustafson LW, Blaakær J, Helmig RB. Group A streptococci infection. A systematic clinical review exemplified by cases from an obstetric department. Eur J Obstet Gynecol Reprod Biol 2017; 215:33.

80. Defining the group A streptococcal toxic shock syndrome. Rationale and consensus definition. The Working Group on Severe Streptococcal Infections. JAMA 1993; 269:390.

81. Murray A, Holdcroft A. Incidence and intensity of postpartum lower abdominal pain. BMJ 1989; 298:1619.

82. Holdcroft A, Snidvongs S, Cason A, et al. Pain and uterine contractions during breast feeding in the immediate post-partum period increase with parity. Pain 2003; 104:589.

83. Yip SK, Sahota D, Pang MW, Day L. Postpartum urinary retention. Obstet Gynecol 2005; 106:602.

84. Ducarme G, Lidove O, Leduey A, et al. Postpartum thrombosis of the superior mesenteric artery after vaginal delivery. Obstet Gynecol 2008; 111:535.

85. Garey KW, Jiang ZD, Yadav Y, et al. Peripartum Clostridium difficile infection: case series and review of the literature. Am J Obstet Gynecol 2008; 199:332.

86. Rouphael NG, O'Donnell JA, Bhatnagar J, et al. Clostridium difficile-associated diarrhea: an emerging threat to pregnant women. Am J Obstet Gynecol 2008; 198:635.e1.

87. Jayaram P, Mohan M, Lindow S, Konje J. Postpartum Acute Colonic Pseudo-Obstruction (Ogilvie's Syndrome): A systematic review of case reports and case series. Eur J Obstet Gynecol Reprod Biol 2017; 214:145.

88. Roth A, Elkayam U. Acute myocardial infarction associated with pregnancy. J Am Coll Cardiol 2008; 52:171.

89. Koul AK, Hollander G, Moskovits N, et al. Coronary artery dissection during pregnancy and the postpartum period: two case reports and review of literature. Catheter Cardiovasc Interv 2001; 52:88.

90. Petitti DB, Sidney S, Quesenberry CP Jr, Bernstein A. Incidence of stroke and myocardial infarction in women of reproductive age. Stroke 1997; 28:280.

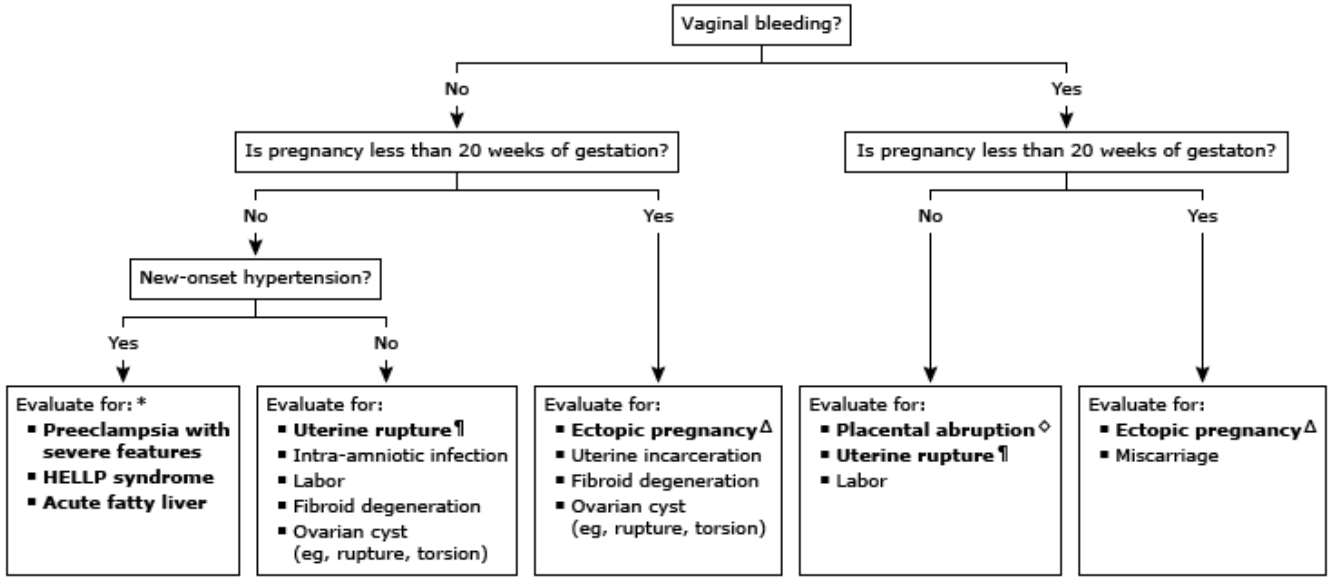
91. Mather PJ, Hansen CL, Goldman B, et al. Postpartum multivessel coronary dissection. J Heart Lung Transplant 1994; 13:533.

92. Pabla JS, John L, McCrea WA. Spontaneous coronary artery dissection as a cause of sudden cardiac death in the peripartum period. BMJ Case Rep 2010; 2010.

Topic 4807 Version 43.0

GRAPHICS

Initial basic approach to the differential diagnosis of obstetrical and gynecological causes of acute abdominal pain in pregnant women



The goal in the evaluation of pregnant patients with abdominal/pelvic pain is to quickly identify those who have a serious or even life-threatening etiology for their symptoms and require urgent intervention. Two key signs of a potentially serious obstetric etiology of abdominal pain are vaginal bleeding and hypertension.

This algorithm presents a basic approach to the differential diagnosis of obstetrical and gynecological causes of acute abdominal pain in pregnant women. Nonobstetrical-gynecological causes of abdominal pain are not included, but remain in the differential diagnosis. These disorders are reviewed in the UpToDate topic on approach to acute abdominal pain in pregnant and postpartum women.

Disorders in bold font can be life-threatening. It should be noted that some of these disorders, such as uterine rupture and uterine incarceration, are rare. Also note that some life-threatening disorders, such as uterine rupture and ectopic pregnancy, may or may not be associated with vaginal bleeding.

* Pregnancy-related liver diseases can cause epigastric or right upper quadrant abdominal pain. These disorders (preeclampsia with severe features, HELLP syndrome, and acute fatty liver of pregnancy) have overlapping features and can be difficult to distinguish.

- Preeclampsia is characterized by the new onset of hypertension and usually proteinuria after 20 weeks of gestation in a previously normotensive woman; right upper quadrant or epigastric pain is a sign of liver involvement and signifies the severe spectrum of the disease. The pain may be caused by stretching of Glisson's capsule due periportal or subcapsular bleeding or, rarely, hepatic rupture.
- Hemolysis with a microangiopathic blood smear, elevated liver chemistries, and a low platelet count are the findings in HELLP syndrome. The most common clinical presentation is abdominal pain and tenderness in the midepigastrium, in the right upper quadrant, or below the sternum. As with preeclampsia, the pain may be caused by stretching of Glisson's capsule due to periportal or subcapsular bleeding or, rarely, hepatic rupture. It may not be possible to distinguish HELLP from preeclampsia with severe features, and they may be different manifestations of the same disease.
- Acute fatty liver occurs in the second half of pregnancy, usually in the third trimester. The most frequent initial symptoms are nausea or vomiting, abdominal pain (particularly epigastric), anorexia, and jaundice. About one-half of patients have signs of preeclampsia at presentation or at some time during the course of illness. The diagnosis is usually made clinically based upon the setting, presentation, and compatible laboratory and imaging results. Laboratory tests may show elevated aminotransferases, elevated bilirubin, thrombocytopenia, prolonged prothrombin time, low glucose levels, increased uric acid levels, increased creatinine levels, and elevated white cell count. Imaging tests of the liver are primarily used to exclude other diagnoses, such as a hepatic infarct or hematoma.

¶ Uterine rupture can be a catastrophic event. Signs and symptoms include nonreassuring fetal heart rate tracing or fetal death, uterine tenderness, peritoneal irritation, loss of fetal station, shock (due to intra-abdominal bleeding), and sometimes vaginal bleeding (which is generally modest). The possibility of rupture should always be excluded in women with a previous cesarean delivery and abdominal pain. Most uterine ruptures occur in laboring women with a prior cesarean delivery or prior transmyometrial uterine surgery (eg, myomectomy). Spontaneous rupture in the absence of labor may occur in women with a scarred uterus, but usually results from sharp or blunt abdominal trauma. Spontaneous rupture may also be related to a cornual pregnancy, pregnancy in a rudimentary uterine horn, or an interstitial pregnancy.

Δ Ectopic pregnancies usually occur in the fallopian tube, but sometimes occur within the cervical canal or a cesarean delivery scar. Rarely, an ectopic pregnancy occurs concurrently with an intrauterine pregnancy. A pregnancy conceived via assisted

reproductive technology (eg, in vitro fertilization) is a strong risk factor. Abdominal pain is a common symptom of all types of extrauterine pregnancy; vaginal bleeding, nausea, and vomiting sometimes occur but may be absent. Patients may present with tachycardia and hypotension due to intraabdominal bleeding. They may also have a low-grade temperature and a mild elevation in the white cell count. The diagnosis of ectopic pregnancy is usually based upon results from ultrasound examination and human chorionic gonadotropin hormone testing.

◇ Acute abruption classically presents with vaginal bleeding, abdominal and/or back pain, uterine tenderness, uterine rigidity, and uterine contractions; the fetal heart rate pattern may be abnormal. If significant placental separation develops, maternal disseminated intravascular coagulation and/or fetal death commonly occur. A retroplacental or subchorionic clot is the classic ultrasound finding of placental abruption, but is not always present. Diagnosis is based on clinical findings, and delivery is usually indicated.

Graphic 112276 Version 1.0

Normal reference ranges in pregnant women

	Nonpregnant woman*	First trimester	Second trimester	Third trimester	References
Hematology					
Erythropoietin¶ (units/L)	4 to 27	12 to 25	8 to 67	14 to 222	1-3
Ferritin¶ (ng/mL)	10 to 150Δ	6 to 130	2 to 230	0 to 116	1-8
Folate, red blood cell (ng/mL)	150 to 450	137 to 589	94 to 828	109 to 663	6, 9, 10
Folate, serum (ng/mL)	5.4 to 18.0	2.6 to 15.0	0.8 to 24.0	1.4 to 20.7	1, 6, 9-13
Haptoglobin (mg/mL)	25 to 250	130 ± 43	115 ± 50	135 ± 65	93
Hemoglobin¶ (g/dL)	12 to 15.8Δ	11.6 to 13.9	9.7 to 14.8	9.5 to 15.0	2, 3, 6, 7, 13
Hematocrit¶ (percent)	35.4 to 44.4	31.0 to 41.0	30.0 to 39.0	28.0 to 40.0	1, 2, 5, 6, 13-15
Iron, total binding capacity¶ (mcg/dL)	251 to 406	278 to 403	Not reported	359 to 609	7
Iron, serum¶ (mcg/dL)	41 to 141	72 to 143	44 to 178	30 to 193	2, 7
Mean corpuscular hemoglobin (pg/cell)	27 to 32	30 to 32	30 to 33	29 to 32	5
Mean corpuscular volume (xm^3)	79 to 93	81 to 96	82 to 97	81 to 99	5, 6, 13, 14
Platelet ($x10^9$/L)	165 to 415	174 to 391	155 to 409	146 to 429	5, 6, 14, 16, 17
Mean platelet volume (mcm^3)	6.4 to 11.0	7.7 to 10.3	7.8 to 10.2	8.2 to 10.4	5
Red blood cell count ($x10^6/mm^3$)	4.00 to 5.20Δ	3.42 to 4.55	2.81 to 4.49	2.71 to 4.43	5, 6, 13, 14
Red cell distribution width (percent)	<14.5	12.5 to 14.1	13.4 to 13.6	12.7 to 15.3	5
White blood cell count ($x10^3/mm^3$)	3.5 to 9.1	5.7 to 13.6	5.6 to 14.8	5.9 to 16.9	5, 6, 13, 14, 18
Neutrophils ($x10^3/mm^3$)	1.4 to 4.6	3.6 to 10.1	3.8 to 12.3	3.9 to 13.1	5, 14, 16, 18
Lymphocytes ($x10^3/mm^3$)	0.7 to 4.6	1.1 to 3.6	0.9 to 3.9	1.0 to 3.6	5, 14, 16, 18
Monocytes ($x10^3/mm^3$)	0.1 to 0.7	0.1 to 1.1	0.1 to 1.1	0.1 to 1.4	5, 14, 18
Eosinophils ($x10^3/mm^3$)	0 to 0.6	0 to 0.6	0 to 0.6	0 to 0.6	14, 18
Basophils ($x10^3/mm^3$)	0 to 0.2	0 to 0.1	0 to 0.1	0 to 0.1	14, 18
Transferrin (mg/dL)	200 to 400	254 to 344	220 to 441	288 to 530	4, 5
Transferrin, saturation without iron (percent)	22 to 46¶	Not reported	10 to 44	5 to 37	3
Transferrin, saturation with iron (percent)	22 to 46¶	Not reported	18 to 92	9 to 98	3
Coagulation					
Antithrombin, functional (percent)	70 to 130	89 to 114	78 to 126	82 to 116	17, 19, 20
D-dimer (mcg/mL)	0.22 to 0.74	0.05 to 0.95	0.32 to 1.29	0.13 to 1.7	17, 20-24, 87

Factor V (percent)	50 to 150	75 to 95	72 to 96	60 to 88	25
Factor VII (percent)	50 to 150	100 to 146	95 to 153	149 to 211	17
Factor VIII (percent)	50 to 150	90 to 210	97 to 312	143 to 353	17, 25
Factor IX (percent)	50 to 150	103 to 172	154 to 217	164 to 235	17
Factor XI (percent)	50 to 150	80 to 127	82 to 144	65 to 123	17
Factor XII (percent)	50 to 150	78 to 124	90 to 151	129 to 194	17
Fibrinogen (mg/dL)	211 to 496	244 to 510	291 to 538	301 to 696	5, 17, 20, 21, 23, 24, 87
Homocysteine (mmol/L)	4.4 to 10.8	3.34 to 11	2.0 to 26.9	3.2 to 21.4	6, 9, 10-12
International Normalized Ratio	0.9 to 1.04◇	0.86 to 1.08	0.83 to 1.02	0.80 to 1.09	19, 24
Partial thromboplastin time, activated (seconds)	26.3 to 39.4	23.0 to 38.9	22.9 to 38.1	22.6 to 35.0	5, 17, 19, 24
Plasminogen activator inhibitor-1 (PAI-1) antigen (pg/mL)	17.3 ± 5.7	17.7 ± 1.9	Not reported	66.4 ± 4.9	87
Plasminogen activator inhibitor-1 (PAI-1) activity (arbitrary units)	9.3 ± 1.9	9.0 ± 0.8	Not reported	31.4 ± 3.0	87
Prothrombin time (seconds)	12.7 to 15.4	9.7 to 13.5	9.5 to 13.4	9.6 to 12.9	5, 17, 24
Protein C, functional (percent)	70 to 130	78 to 121	83 to 133	67 to 135	19, 25, 26
Protein S, total (percent)	70 to 140	39 to 105	27 to 101	33 to 101	17, 25, 26
Protein S, free (percent)	70 to 140	34 to 133	19 to 113	20 to 65	25, 26
Protein S, functional activity (percent)	65 to 140	57 to 95	42 to 68	16 to 42	25
Tissue plasminogen activator (ng/mL)	1.6 to 13§	1.8 to 6.0	2.36 to 6.6	3.34 to 9.20	17, 19, 87
Tissue plasminogen activator inhibitor-1 (ng/mL)	4 to 43	16 to 33	36 to 55	67 to 92	17
von Willebrand measurements					
von Willebrand factor antigen (percent)	75 to 125	62 to 318	90 to 247	84 to 422	20, 27, 28
ADAMTS-13, von Willebrand cleaving protease	40 to 170¥	40 to 160	22 to 135	38 to 105	20, 28
Blood chemical constituents					
Alanine transaminase (units/L)	7 to 41	3 to 30	2 to 33	2 to 25	4, 5, 8, 29
Albumin (g/dL)	4.1 to 5.3Δ	3.1 to 5.1	2.6 to 4.5	2.3 to 4.2	29-32
Alkaline phosphatase (units/L)	33 to 96	17 to 88	25 to 126	38 to 229	4, 5, 8, 29, 30
Alpha-1 antitrypsin (mg/dL)	100 to 200	225 to 323	273 to 391	327 to 487	5
Alpha-fetoprotein (ng/mL)	—	—	Approximately 130-400	Approximately 130-590	95
Ammonia (microM)	31 ± 3.2	—	—	27.3 ± 1.6	94
Amylase (units/L)	20 to 96	24 to 83	16 to 73	15 to 81	4, 5, 33, 34

Anion gap (mmol/L)	7 to 16	13 to 17	12 to 16	12 to 16	5
Aspartate transaminase (units/L)	12 to 38	3 to 23	3 to 33	4 to 32	4, 5, 8, 29
Bicarbonate (mmol/L)	22 to 30	20 to 24	20 to 24	20 to 24	5
Bilirubin, total (mg/dL)	0.3 to 1.3	0.1 to 0.4	0.1 to 0.8	0.1 to 1.1	4, 29
Bilirubin, unconjugated (mg/dL)	0.2 to 0.9	0.1 to 0.5	0.1 to 0.4	0.1 to 0.5	5, 29
Bilirubin, conjugated (mg/dL)	0.1 to 0.4	0 to 0.1	0 to 0.1	0 to 0.1	29
Bile acids (micromol/L)	0.3 to 4.8‡	0 to 4.9	0 to 9.1	0 to 11.3	29, 35
CA-125 antigen (units/mL)	7.2 to 27.0	2/2 to 268	12 to 25.1	16.8 to 43.8	88, 89, 90
Calcium, ionized (mg/dL)	4.5 to 5.3	4.5 to 5.1	4.4 to 5.0	4.4 to 5.3	5, 31, 36, 37
Calcium, total (mg/dL)	8.7 to 10.2	8.8 to 10.6	8.2 to 9.0	8.2 to 9.7	4, 5, 30, 32, 36-38
Ceruloplasmin (mg/dL)	25 to 63	30 to 49	40 to 53	43 to 78	5, 39
Chloride (mEq/L)	102 to 109	101 to 105	97 to 109	97 to 109	4, 5, 40
Creatinine (mg/dL)	0.5 to 0.9Δ	0.4 to 0.7	0.4 to 0.8	0.4 to 0.9	4, 5, 46
Gamma-glutamyl transpeptidase (units/L)	9 to 58	2 to 23	4 to 22	3 to 26	4, 5, 8, 29
Lactate dehydrogenase (units/L)	115 to 221	78 to 433	80 to 447	82 to 524	4, 5, 32, 8
Lipase (units/L)	3 to 43	21 to 76	26 to 100	41 to 112	33
Magnesium (mg/dL)	1.5 to 2.3	1.6 to 2.2	1.5 to 2.2	1.1 to 2.2	4, 5, 30-32, 36, 38
Osmolality (mOsm/kg H20)	275 to 295	275 to 280	276 to 289	278 to 280	38, 41
Phosphate (mg/dL)	2.5 to 4.3	3.1 to 4.6	2.5 to 4.6	2.8 to 4.6	4, 5, 30, 31, 42
Potassium (mEq/L)	3.5 to 5.0	3.6 to 5.0	3.3 to 5.0	3.3 to 5.1	4, 5, 15, 31, 32, 38, 40
Prealbumin (mg/dL)	17 to 34	15 to 27	20 to 27	14 to 23	5
Protein, total (g/dL)	6.7 to 8.6	6.2 to 7.6	5.7 to 6.9	5.6 to 6.7	5, 31, 32
Sodium (mEq/L)	136 to 146	133 to 148	129 to 148	130 to 148	4, 5, 15, 31, 32, 38, 41
Urea nitrogen (mg/dL)	7 to 20	7 to 12	3 to 13	3 to 11	4, 5, 40
Uric acid (mg/dL)	2.5 to 5.6Δ	2.0 to 4.2	2.4 to 4.9	3.1 to 6.3	4, 5, 41
Metabolic and endocrine tests					
Aldosterone (ng/dL)	2 to 9	6 to 104	9 to 104	15 to 101	43, 44, 45
Angiotensin converting enzyme (units/L)	9 to 67	1 to 38	1 to 36	1 to 39	39, 46
Alpha-fetoprotein (ng/mL)	0 to 8.5	Not reported	50 to 425	50 to 590	84, 86
Cortisol (mcg/dL)	0 to 25	7 to 19	10 to 42	12 to 50	5, 45
Hemoglobin A_{1C} (percent)	4 to 6	4 to 6	4 to 6	4 to 7	36, 47, 48
Parathyroid hormone (pg/mL)	8 to 51	10 to 15	18 to 25	9 to 26	30
Parathyroid hormone-related protein (pmol/L)	<1.3†	0.7 to 0.9	1.8 to 2.2	2.5 to 2.8	30

Renin, plasma activity (ng/mL/hour)	0.3 to 9.0[T]	Not reported	7.5 to 54.0	5.9 to 58.8	40, 44
Thyroid-stimulating hormone (milli-int. units/mL)	0.34 to 4.25	0.60 to 3.40	0.37 to 3.60	0.38 to 4.04	4, 5, 49
[American Thyroid Association recommendation]**		0.1 to 2.5	0.2 to 3.0	0.3 to 3.0	85
Thyroxine-binding globulin (mg/dL)	1.3 to 3.0	1.8 to 3.2	2.8 to 4.0	2.6 to 4.2	5
Thyroxine, free (ng/dL)	0.8 to 1.7	0.8 to 1.2	0.6 to 1.0	0.5 to 0.8	5, 49
Thyroxine, total (mcg/dL)	5.4 to 11.7	6.5 to 10.1	7.5 to 10.3	6.3 to 9.7	5, 32
Triiodothyronine, free (pg/mL)	2.4 to 4.2	4.1 to 4.4	4.0 to 4.2	Not reported	49
Triiodothyronine, total (ng/dL)	77 to 135	97 to 149	117 to 169	123 to 162	5
Vitamins and minerals					
Copper (mcg/dL)	70 to 140	112 to 199	165 to 221	130 to 240	50, 51, 5
Selenium (mcg/L)	63 to 160	116 to 146	75 to 145	71 to 133	5, 50
Vitamin A (retinol) (mcg/dL)	20 to 100	32 to 47	35 to 44	29 to 42	5
Vitamin B12 (pg/mL)	279 to 966	118 to 438	130 to 656	99 to 526	6, 10
Vitamin C (ascorbic acid) (mg/dL)	0.4 to 1.0	Not reported	Not reported	0.9 to 1.3	52
Vitamin D, 1,25-dihydroxy (pg/mL)	25 to 45	20 to 65	72 to 160	60 to 119	30, 36
Vitamin D, 24,25-dihydroxy (ng/mL)	0.5 to 5.0[†]	1.2 to 1.8	1.1 to 1.5	0.7 to 0.9	53
Vitamin D, 25-hydroxy (ng/mL)	14 to 80	18 to 27	10 to 22	10 to 18	30, 53
Vitamin E (α-tocopherol) (mcg/mL)	5 to 18	7 to 13	10 to 16	13 to 23	5
Zinc (mcg/dL)	75 to 120	57 to 88	51 to 80	50 to 77	5, 13, 50
Autoimmune and inflammatory mediators					
C3 complement (mg/dL)	83 to 177	62 to 98	73 to 103	77 to 111	5
C4 complement (mg/dL)	16 to 47	18 to 36	18 to 34	22 to 32	5
C-reactive protein (mg/L)	0.2 to 3.0	Not reported	0.4 to 20.3	0.4 to 8.1	54
Erythrocyte sedimentation rate (mm/hour)	0 to 20[Δ]	4 to 57	7 to 47	13 to 70	55
Immunoglobulin A (mg/dL)	70 to 350	95 to 243	99 to 237	112 to 250	5
Immunoglobulin G (mg/dL)	700 to 1700	981 to 1267	813 to 1131	678 to 990	5
Immunoglobulin M (mg/dL)	50 to 300	78 to 232	74 to 218	85 to 269	5
Sex hormones					
Dehydroepiandrosterone sulfate (mmol/L)	1.3 to 6.8[†]	2.0 to 16.5	0.9 to 7.8	0.8 to 6.5	56
Estradiol (pg/mL)	<20 to	188 to 2497	1278 to 7192	614 to 3460	56, 57

	443[Δ,¶¶]				
Progesterone (ng/mL)	<1 to 20[Δ]	8 to 48		99 to 342	56, 57
Prolactin (ng/mL)	0 to 20	36 to 213	110 to 330	137 to 372	30, 47, 57, 58
Sex hormone binding globulin (nmol/L)	18 to 114[Δ]	39 to 131	214 to 717	216 to 724	56, 59
Testosterone (ng/dL)	6 to 86[Δ]	25.7 to 211.4	34.3 to 242.9	62.9 to 308.6	56
17-hydroxyprogesterone (nmol/L)	0.6 to 10.6[Δ,†]	5.2 to 28.5	5.2 to 28.5	15.5 to 84	56
Lipids					
Cholesterol, total (mg/dL)	<200	141 to 210	176 to 299	219 to 349	5, 60-62
High-density lipoprotein cholesterol (mg/dL)	40 to 60	40 to 78	52 to 87	48 to 87	5, 60-63
Low-density lipoprotein cholesterol (mg/dL)	<100	60 to 153	77 to 184	101 to 224	5, 60-63
Very-low-density lipoprotein cholesterol (mg/dL)	6 to 40[†]	10 to 18	13 to 23	21 to 36	62
Triglycerides (mg/dL)	<150	40 to 159	75 to 382	131 to 453	4, 5, 60-63
Apolipoprotein A-I (mg/dL)	119 to 240	111 to 150	142 to 253	145 to 262	4, 47, 61
Apolipoprotein B (mg/dL)	52 to 163	58 to 81	66 to 188	85 to 238	4, 47, 61
Cardiac function					
Cardiac output (L/minute)	4.8 to 6.8	5.6 to 9.7	5.5 to 9.9	4.8 to 8.7	64, 65, 66, 67, 68
Cardiac index ($L/min/m^2$)	2.6 to 4.2	3.2 to 4.6	3.1 to 4.7	2.5 to 4.4	65, 68
Stroke volume (mL)	79 to 90	77.5 to 107.6	70.3 to 107.6	54 to 99	65, 68, 69
Stroke index (mL/m^2)		46 to 62	39 to 62	30 to 42	65
Systemic vascular resistance ($dyns/cm^5$)	700 to 1600	747 to 1485	692 to 1201	1034 to 1201	65, 67, 70
Echocardiography					
Intraventricular septal dimension (cm)	0.7 to 0.9	0.63 to 0.83	0.65 to 0.85	0.66 to 0.9	68, 69, 70, 91, 92
Posterior ventricular wall dimension (cm)	0.75 to 0.9	0.56 to 0.8	0.59 to 0.9	0.59 to 0.9	68, 69, 70, 91, 92
Left ventricular mass (g)	116 to 143	108 to 167	115 to 150	128 to 162	68, 70, 91, 92
Left ventricular mass index	40 to 78	53 to 79	58 to 82	60 to 88	68, 70, 91, 92
E/A ratio	1.4 to 1.75	1.6	1.4	1.3	68, 70
Left ventricular diastolic diameter (cm)	4.3 to 4.8	4.3 to 4.6	4.4 to 4.9	5.1	69, 70
Left ventricular systolic diameter (cm)	2.8 to 3.1	2.8 to 2.9	2.8 to 3.4	2.8 to 3.3	69, 70
Left vent, fractional shortening (percent)	35 to 36	35 to 37	3.5	35 to 36	69, 70
Left vent ejection	60 to 73	61 to 75	61 to 63	60 to 73	69, 70

fraction (percent)					
Diastolic function					
Mitral E wave (m/second)	0.77 ± 0.11	0.85 ± 0.13	0.84 ± 0.16	0.77 ± 0.15	91, 92
Mitral A wave (m/second)	0.46 ± 0.1	0.5 ± 0.09	0.5 ± 0.1	0.55 ± 0.1	91, 92
Isovolumic relaxation time (m/second)	69 ± 10	50 ± 10	79 ± 18	72 ± 16	91, 92
Cardiac function (blood tests)					
Atrial natriuretic peptide (pg/mL)	Not reported	Not reported	28.1 to 70.1	Not reported	73
B-type natriuretic peptide (pg/mL)	<167 (age- and gender-specific)	18.4	13.5 to 29.5	15.5 to 46	71, 72, 73
Creatine kinase (units/L)	39 to 238$^{\Delta}$	27 to 83	25 to 75	13 to 101	5, 74
Creatine kinase-MB (units/L)	<6$^{\Delta\Delta}$	—	—	1.8 to 2.4	74
N-terminal pro-brain natriuretic peptide (pg/mL)	50 ± 26	60 ± 45	60 ± 40	43 ± 34	96
Troponin I (ng/mL)	0 to 0.08	Not reported	Not reported	0 to 0.064 (intrapartum)	75, 76
Blood gas					
pH	7.38 to 7.42 (arterial)	7.36 to 7.52 (venous)	7.40 to 7.52 (venous)	7.41 to 7.53 (venous) 7.39 to 7.45 (arterial)	31, 77
PO_2 (mmHg)	90 to 100	93 to 100	90 to 98	92 to 107	77, 78
PCO_2 (mmHg)	38 to 42	Not reported	Not reported	25 to 33	77
Bicarbonate (HCO_3^-) (mEq/L)	22 to 26	Not reported	Not reported	16 to 22	77
Renal function tests					
Effective renal plasma flow (mL/minute)	492 to 696$^{\Delta,\dagger}$	696 to 985	612 to 1170	595 to 945	79, 80
Glomerular filtration rate (GFR) (mL/minute)	106 to 132$^{\Delta}$	131 to 166	135 to 170	117 to 182	79, 80, 81
Filtration fraction (percent)	16.9 to 24.7$^{\diamond\diamond}$	14.7 to 21.6	14.3 to 21.9	17.1 to 25.1	79, 80, 81
Osmolarity, urine (mOsm/kg)	500 to 800	326 to 975	278 to 1066	238 to 1034	82
2-4h albumin excretion (mg/24 hours)	<30	5 to 15	4 to 18	3 to 22	82, 83
24-h calcium excretion (mmol/24 hours)	<7.5†	1.6 to 5.2	0.3 to 6.9	0.8 to 4.2	15
24-h creatinine clearance (mL/minute)	91 to 130	69 to 140	55 to 136	50 to 166	15, 80
24-h creatinine excretion (mmol/24 hours)	8.8 to 14†	10.6 to 11.6	10.3 to 11.5	10.2 to 11.4	82
24-h potassium excretion (mmol/24 hours)	25 to 100†	17 to 33	10 to 38	11 to 35	15
24-h protein excretion	<150	19 to 141	47 to 186	46 to 185	83

(mg/24 hours)					
24-h sodium excretion (mmol/24 hours)	100 to 260 †	53 to 215	34 to 213	37 to 149	15, 41

* Unless otherwise specified, all normal reference values are from the seventeenth edition of *Harrison's Principles of Internal Medicine*[84].

¶ Range includes references with and without iron supplementation.

Δ Normal reference range is specific range for females.

◇ Reference values are from Cerneca et al: Coagulation and fibrinolysis changes in normal pregnancy increased levels of procoagulants and reduced levels of inhibitors during pregnancy induce a hypercoagulable state, combined with a reactive fibrinolysis[19].

§ References values are from Cerneca et al and Choi et al: Tissue plasminogen activator levels change with plasma fibrinogen concentrations during pregnancy[17,19].

¥ Reference values are from Mannuci et al: Changes in health and disease of the metalloprotease that cleaves von Willebrand factor[28].

‡ Reference values are from Bacq Y et al: Liver function tests in normal pregnancy: a prospective study of 102 pregnant women and 102 matched controls[29].

† Reference values are from the fifteenth edition of *Harrison's Principles of Internal Medicine*[85].

** The American Thyroid Association recommends these TSH ranges if individual laboratories do not determine their own trimester-specific reference ranges.

¶¶ Range is for premenopausal females and varies by menstrual cycle phase.

ΔΔ Reference values are from Leiserowitz GS et al: Creatine kinase and its MB isoenzyme in the third trimester and the peripartum period[74].

◇◇ Reference values are from Dunlop W: Serial changes in renal haemodynamics during normal human pregnancy[79].

References:

1. *Beguin Y, Lipscei G, Thourmsin H, et al: Blunted erythropoietin production and decreased erythropoiesis in early pregnancy. Blood 78(1):89, 1991.*
2. *Bianco I, Mastropietro F, D'Aseri C, et al: Serum levels of erythropoietin and soluble transferrin receptor during pregnancy in non-β-thalassemic and β-thalassemic women. Haematologica 85:902, 2000 [PMID: 10980626].*
3. *Milman N, Graudal N, Nielsen OJ: Serum erythropoietin during normal pregnancy: Relationship to hemoglobin and iron status markers and impact of iron supplementation in a longitudinal, placebo-controlled study on 118 women. Int J Hematol 66:159, 1997 [PMID: 9277046].*
4. *Larsson A, Palm M, Hansson L-O, et al: Reference values for clinical chemistry tests during normal pregnancy. BJOG 115:874, 2008 [PMID: 18485166].*
5. *Lockitch G: Handbook of Diagnostic Biochemistry and Hematology in Normal Pregnancy. Boca Raton, FL, CRC Press, 1993.*
6. *Milman N, Bergholt T, Byg KE, et al: Reference intervals for haematological variables during normal pregnancy and postpartum in 434 healthy Danish women. Eur J Haematol 79:39, 2007 [PMID: 17598837].*
7. *Romslo I, Haram K, Sagen N, et al: Iron requirement in normal pregnancy as assessed by serum ferritin, serum transferring saturation and erythrocyte protoporphyrin determinations. Br J Obstet Gynaecol 90:101, 1983 [PMID: 6824608].*
8. *Van Buul EJA, Steegers EAP, Jongsma HW, et al: Haematological and biochemical profile of uncomplicated pregnancy in nulliparous women; a longitudinal study. Neth J Med 46:73, 1995.*
9. *Milman N, Byg KE, Hvas AM, et al: Erythrocyte folate, plasma folate and plasma homocysteine during normal pregnancy and postpartum: A longitudinal study comprising 404 Danish women. Eur J Haematol 76:200, 2006 [PMID: 16412135].*
10. *Walker MC, Smith GN, Perkins SL, et al: Changes in homocysteine levels during normal pregnancy. Am J Obstet Gynecol 180:660, 1999 [PMID: 10076144].*
11. *López-Quesada E, Vilaseca MA, Lailla JM: Plasma total homocysteine in uncomplicated pregnancy and in preeclampsia. Eur J Obstet Gynecol Reprod Biol 108:45, 2003 [PMID: 19899161].*
12. *Özerol E, Özerol I, Gökdeniz R, et al: Effect of smoking on serum concentrations of total homocysteine, folate, vitamin B12, and nitric oxide in pregnancy: A preliminary study. Fetal Diagn Ther 19:145, 2004.*
13. *Qvist I, Abdulla M, Jägerstad M, et al: Iron, zinc and folate status during pregnancy and two months after delivery. Acta Obstet Gynecol Scand 65:15, 1986 [PMID: 3716775].*
14. *Balloch AJ, Cauchi MN: Reference ranges for haematology parameters in pregnancy derived from patient populations. Clin Lab Haemat 15:7, 1993 [PMID: 8472501].*
15. *Singh HJ, Mohammad NH, Nila A: Serum calcium and parathormone during normal pregnancy in Malay women. J Matern Fetal Med 8:95, 1999 [PMID: 10338062].*
16. *AzizKarim S, Khurshid M, Rizvi JH, et al: Platelets and leucocyte counts in pregnancy. J Pak Med Assoc 42:86, 1992.*
17. *Choi JW, Pai SH: Tissue plasminogen activator levels change with plasma fibrinogen concentrations during pregnancy. Ann Hematol 81:611, 2002 [PMID: 12454697].*

18. *Belo L, Santos-Silva A, Rocha S, et al: Fluctuations in C-reactive protein concentration and neutrophil activation during normal human pregnancy. Eur J Obstet Gynecol Reprod Biol 123:46, 2005 [PMID: 16260340].*
19. *Cerneca F, Ricci G, Simeone R, et al: Coagulation and fibrinolysis changes in normal pregnancy increased levels of procoagulants and reduced levels of inhibitors during pregnancy induce a hypercoagulable state, combined with a reactive fibrinolysis. Eur J Obstet Gynecol Reprod Biol 73:31, 1997 [PMID: 9175686].*
20. *Lattuada A, Rossi E, Calzarossa C, et al: Mild to moderate reduction of a von Willebrand factor cleaving protease (ADAMTS-13) in pregnant women with HELLP microangiopathic syndrome. Haematologica 88(9):1029, 2003.*
21. *Francalanci I, Comeglio P, Liotta AA, et al: D-Dimer concentrations during normal pregnancy, as measured by ELISA. Thromb Res 78:399, 1995 [PMID: 7660356].*
22. *Kline JA, Williams GW, Hernandez-Nino J: D-Dimer concentrations in normal pregnancy: New diagnostic thresholds are needed. Clin Chem 51:825, 2005 [PMID: 15764641].*
23. *Morse M: Establishing a normal range for D-dimer levels through pregnancy to aid in the diagnosis of pulmonary embolism and deep vein thrombosis. J Thromb Haemost 2:1202, 2004 [PMID: 15219216].*
24. *Liu XH, Jiang YM, Shi H, et al: Prospective, sequential, longitudinal study of coagulation changes during pregnancy in Chinese women. Int J Gynaecol Obstet 105(3):240, 2009.*
25. *Lefkowitz JB, Clarke SH, Barbour LA: Comparison of protein S functional and antigenic assays in normal pregnancy. Am J Obstet Gynecol 175:657, 1996 [PMID: 8828430].*
26. *Faught W, Garner P, Jones G, et al: Changes in protein C and protein S levels in normal pregnancy. Am J Obstet Gynecol 172:147, 1995 [PMID: 7847526].*
27. *Wickström K, Edelstam G, Löwbeer CH, et al: Reference intervals for plasma levels of fibronectin, von Willebrand factor, free protein S and antithrombin during third-trimester pregnancy. Scand J Clin Lab Invest 64:31, 2004 [PMID: 13035697].*
28. *Mannucci PM, Canciani MT, Forza I, et al: Changes in health and disease of the metalloprotease that cleaves von Willebrand factor. Blood 98(9):2730, 2001.*
29. *Bacq Y, Zarka O, Bréchot JF, et al: Liver function tests in normal pregnancy: A prospective study of 102 pregnant women and 102 matched controls. Hepatology 23:1030, 1996 [PMID: 8621129].*
30. *Ardawi MSM, Nasrat HAN, BA'Aqueel HS: Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: A longitudinal study. Eur J Endocrinol 137:402, 1997 [PMID: 9368509].*
31. *Handwerker SM, Altura BT, Altura BM: Serum ionized magnesium and other electrolytes in the antenatal period of human pregnancy. J Am Coll Nutr 15:36, 1996 [PMID: 8632112].*
32. *Hytten FE, Lind T: Diagnostic Indices in Pregnancy. Summit, NJ, CIBA-GEIGY Corporation, 1975.*
33. *Karsenti D, Bacq Y, Bréchot JF, et al: Serum amylase and lipase activities in normal pregnancy: A prospective case-control study. Am J Gastroenterol 96:697, 2001 [PMID: 11280536].*
34. *Strickland DM, Hauth JC, Widish J, et al: Amylase and isoamylase activities in serum of pregnant women. Obstet Gynecol 63:389, 1984 [PMID: 6199704].*
35. *Carter J: Serum bile acids in normal pregnancy. BJOG 98:540, 1991 [PMID: 1873244].*
36. *Mimouni F, Tsang RC, Hertzbert VS, et al: Parathyroid hormone and calcitriol changes in normal and insulin-dependent diabetic pregnancies. Obstet Gynecol 74:49, 1989 [PMID: 2733941].*
37. *Pitkin RM, Gebhardt MP: Serum calcium concentrations in human pregnancy. Am J Obstet Gynecol 127:775, 1977 [PMID: 848531].*
38. *Shakhmatova EI, Osipova NA, Natochin YV: Changes in osmolality and blood serum ion concentrations in pregnancy. Hum Physiol 26:92, 2000.*
39. *Louro MO, Cocho JA, Tutor JC: Assessment of copper status in pregnancy by means of determining the specific oxidase activity of ceruloplasmin. Clin Chim Acta 312:123, 2001 [PMID: 11580917].*
40. *Dux S, Yaron A, Carmel A, et al: Renin, aldosterone, and serum-converting enzyme activity during normal and hypertensive pregnancy. Gynecol Obstet Invest 17:252, 1984 [PMID: 6329926].*
41. *Davison JB, Vallotton MB, Lindheimer MD: Plasma osmolality and urinary concentration and dilution during and after pregnancy: Evidence that lateral recumbency inhibits maximal urinary concentrating ability. BJOG 88:472, 1981 [PMID: 7236550].*
42. *Kato T, Seki K, Matsui H, et al: Monomeric calcitonin in pregnant women and in cord blood. Obstet Gynecol 92:241, 1998 [PMID: 9699759].*
43. *Elsheikh A, Creatsas G, Mastorakos G, et al: The renin-aldosterone system during normal and hypertensive pregnancy. Arch Gynecol Obstet 264:182, 2001 [PMID: 11205704].*
44. *Kim EH, Lim JH, Kim YH, et al: The relationship between aldosterone to renin ratio and RI value of the uterine artery in the preeclamptic patient vs. normal pregnancy. Yonsei Med J 49(1):138, 2008.*
45. *Suri D, Moran J, Hibbard JU, et al: Assessment of adrenal reserve in pregnancy: Defining the normal response to the adrenocorticotropin stimulation test. J Clin Endocrinol Metab 91:3866, 2006 [PMID: 16895954].*
46. *Parente JV, Franco JG, Greene LJ, et al: Angiotensin-converting enzyme: Serum levels during normal pregnancy. Am J Obstet Gynecol 135:586, 1979 [PMID: 228554].*
47. *Montelongo A, Lasunción MA, Pallardo LF, et al: Longitudinal study of plasma lipoproteins and hormones during pregnancy in normal and diabetic women. Diabetes 41:1651, 1992 [PMID: 1446807].*
48. *Radder JK, Van Roosmalen J: HbAIC in healthy, pregnant women. Neth J Med 63:256, 2005 [PMID: 16093576].*
49. *Price A, Obel O, Cresswell J, et al: Comparison of thyroid function in pregnant and non-pregnant Asian and western Caucasian women. Clin Chim Acta 208:91, 2001.*

50. *Álvarez SI, Castañón SG, Ruata MLC, et al: Updating of normal levels of copper, zinc and selenium in serum of pregnant women. J Trace Elem Med Biol 21(S1):49, 2007.*
51. *Ilhan N, Ilhan N, Simsek M: The changes of trace elements, malondialdehyde levels and superoxide dismutase activities in pregnancy with or without preeclampsia. Clin Biochem 35:393, 2002 [PMID: 12270770].*
52. *Sharma SC, Sabra A, Molloy A, et al: Comparison of blood levels of histamine and total ascorbic acid in pre-eclampsia with normal pregnancy. Hum Nutr Clin Nutr 38C:3, 1984.*
53. *Reiter EO, Braunstein GD, Vargas A, et al: Changes in 25-hydroxyvitamin D and 24,25-dihydroxyvitamin D during pregnancy. Am J Obstet Gynecol 135:227, 1979 [PMID: 474676].*
54. *Hwang HS, Kwon JY, Kim MA, et al: Maternal serum highly sensitive C-reactive protein in normal pregnancy and pre-eclampsia. Int J Gynecol Obstet 98:105, 2007 [PMID: 17588579].*
55. *van den Broek NR, Letsky EA: Pregnancy and the erythrocyte sedimentation rate. Br J Obstet Gynaecol 108:1164, 2001.*
56. *O'Leary P, Boyne P, Flett P, et al: Longitudinal assessment of changes in reproductive hormones during normal pregnancy. Clin Chem 35(5):667, 1991.*
57. *Carranza-Lira S, Hernández F, Sánchez M, et al: Prolactin secretion in molar and normal pregnancy. Int J Gynaecol Obstet 60:137, 1998 [PMID: 9509951].*
58. *Larrea F, Méndez I, Parra A: Serum pattern of different molecular forms of prolactin during normal human pregnancy. Hum Reprod 8:1617, 1993 [PMID: 8300816].*
59. *Acromite MT, Mantzoros CS, Leach RE, et al: Androgens in preeclampsia. Am J Obstet Gynecol 180:60, 1999 [PMID: 9914579].*
60. *Belo L, Caslake M, Gaffney D, et al: Changes in LDL size and HDL concentration in normal and preeclamptic pregnancies. Atherosclerosis 162:425, 2002 [PMID: 11996963].*
61. *Desoye G, Schweditsch MO, Pfeiffer KP, et al: Correlation of hormones with lipid and lipoprotein levels during normal pregnancy and postpartum. J Clin Endocrinol Metab 64:704, 1987 [PMID: 3546352].*
62. *Jimenez DM, Pocovi M, Ramon-Cajal J, et al: Longitudinal study of plasma lipids and lipoprotein cholesterol in normal pregnancy and puerperium. Gynecol Obstet Invest 25:158, 1988 [PMID: 3391425].*
63. *Piechota W, Staszewski A: Reference ranges of lipids and apolipoproteins in pregnancy. Eur J Obstet Gynecol Reprod Biol 45:27, 1992 [PMID: 1618359].*
64. *Rang S, van Montfrans GA, Wolf H. Serial hemodynamic measurement in normal pregnancy, preeclampsia, and intrauterine growth restriction. Am J Obstet Gynecol. 198(5):519.e1-9, 2008 PMID: 18279824.*
65. *Moertl MG, Ulrich D, Pickel K, et al: Changes in haemodynamic and autonomous nervous system parameters measured non-invasively throughout normal pregnancy. Eur J Obstet Gynecol Reprod Biol. 144 Suppl 1:S179-83. 2009 PMID: 19285779.*
66. *Pandey Ak, Das A, Srinivas C, et al: Maternal myocardial performances in various stages of pregnancy and post-partum. Research Jour of Cardiology 3(1):9-16, 2010.*
67. *Lees M. Central circulatory responses in normotensive and hypertensive pregnancy. Postgrad Med J. 55(643): 311–314, 1979. PMCID: PMC2425449.*
68. *Poppas A, Shroff SG, Korcarz CE, et al: Serial assessment of the cardiovascular system in normal pregnancy: Role of arterial compliance and pulsatile arterial load. Circulation 95:2407-2415, 1997.*
69. *Katz R, Karliner JS, Resnik R: Effects of a natural volume overload state (pregnancy) on left ventricular performance in normal human subjects. Circulation 58: 434-441, 1978.*
70. *Mesa A, Jessurun C, Hernandez A, et al: Left ventricular diastolic function in normal human pregnancy. Circulation 99:511-517, 1999.*
71. *Resnik JL, Hong C, Resnik R, et al: Evaluation of B-type natriuetic peptide (BNP) levels in normal and preeclamptic women. Am J Obstet Gynecol 193:450-458, 2005.*
72. *Hamid RR, Larsson A, Pernow J, et al: Assessment of left ventricular structure and function in preeclampsia by echocardiography and cardiovascular biomarkers. J Hypertens 27L2257-2264, 2009.*
73. *Borghi CB, Esposti DD, Immordino V, et al: Relationship of systemic hemodynamics, left ventricular structure and function, and plasma natriuretic peptide concentrations during pregnancy complicated by preeclampsia. Am J Obstet Gynecol 183:140, 2000 [PMID: 10920322].*
74. *Leiserowitz GS, Evans AT, Samuels SJ, et al: Creatine kinase and its MB isoenzyme in the third trimester and the peripartum period. J Reprod Med 37:910, 1992 [PMID: 1460608].*
75. *Koscica KL, Bebbington M, Bernstein PS: Are maternal serum troponin I levels affected by vaginal or cesarean delivery? Am J Perinatol 21(1):31, 2004.*
76. *Shivvers SA, Wians FH, Keffer JH, et al: Maternal cardiac troponin I levels during labor and delivery. Am J Obstet Gynecol 180:122, 1999 [PMID: 9914590].*
77. *Fadel HE, Northrop G, Misenhimer HR, et al: Acid-base determinations in amniotic fluid and blood of normal late pregnancy. Obstet Gynecol 53:99, 1979 [PMID: 32503].*
78. *Spiropoulos K, Prodromaki E, Tsapanos V: Effect of body position on PaO2 and PaCO2 during pregnancy. Gynecol Obstet Invest 58:22, 2004 [PMID: 15028865].*
79. *Dunlop W: Serial changes in renal haemodynamics during normal human pregnancy. Br J Obstet Gynaecol 88:1, 1981 [PMID: 7459285].*
80. *Ezimokhai M, Davison JM, Philips PR, et al: Non-postural serial changes in renal function during the third trimester of normal human pregnancy. Br J Obstet Gynaecol 88:465, 1981 [PMID: 7236549].*

81. *Moran P, Baylis PH, Lindheimer, et al: Glomerular ultrafiltration in normal and preeclamptic pregnancy. J Am Soc Nephrol 14:648, 2003 [PMID: 12595500].*
82. *Risberg A, Larsson A, Olsson K, et al: Relationship between urinary albumin and albumin/creatinine ratio during normal pregnancy and pre-eclampsia. Scand J Clin Lab Invest 64:17, 2004 [PMID: 15025425].*
83. *Higby K, Suiter CR, Phelps JY, et al: Normal values of urinary albumin and total protein excretion during pregnancy. Am J Obstet Gynecol 171:984, 1994 [PMID: 7943114].*
84. *Kratz A, Pesce MA, Basner RC, Einstein AJ. Appendix: Laboratory values of clinical importance. In: Longo DL, Fauci AS, Kasper DL, et al (Eds). Harrison's Principles of Internal Medicine, 18th ed, McGraw-Hill, New York 2012. Appendix 1, p A-1.*
85. *Stagnaro-Green A, Abalovich M, Alexander E, et al. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and postpartum. Thyroid 2011; 21:1081.*
86. *Leek AE, Ruoss CF, Kitau MJ, Chard T. Magernal plasma alphafetoprotein levels in the second half of normal pregnancy: Relationship to fetal weight, and maternal age and parity. BJOG 1975; 82:669.*
87. *Hale SA, Sobel B, Benvenuto A, et al. Coagulation and fibrinolytic system protein profiles in women with normal pregnancies and pregnancies complicated by hypertension. Pregnancy Hypertens 2012; 2:152.*
88. *Spitzer M, Kaushal N, Benjamin F. Maternal CA-125 levels in pregnancy and the puerperium. J Reprod Med 1998; 43:387.*
89. *Aslam N, Ong C, Woelfer B, et al. Serum CA-125 at 11-14 weeks of gestation in women with morphologically normal ovaries. BJOG 2000; 107:689.*
90. *Jacobs IJ, Fay TN, Stabile I, et al. The distribution of CA 125 in the reproductive tract of pregnant and non-pregnant women. Br J Obstet Gynaecol 1988; 95:1190.*
91. *Savu O, Jurcuţ R, Giuşcă S, et al. Morphological and functional adaptation of the maternal heart during pregnancy. Circ Cardiovasc Imaging 2012; 5:289.*
92. *Vitarelli A, Capotosto L. Role of echocardiography in the assessment and management of adult congenital heart disease in pregnancy. Int J Cardiovasc Imaging 2011; 27:843.*
93. *Haram K, Augensen K, Elsayed S. Serum protein pattern in normal pregnancy with special reference to acute-phase reactants. BJOG 1983; 90:139.*
94. *Jozwik M, Jozwik M, Pierzycki K, et al. Maternal and fetal blood ammonia concentrations in normal term human pregnancies. Biol Neonate 2005; 87:38.*
95. *Leek AE, Ruoss CF, Kitau MG, et al. Maternal plasma alphafetoprotein levels in the second half of normal pregnancy: relationship to fetal weight and maternal age and parity. BJOG 1975; 82:669.*
96. *Burlingame J, Hyeong JA, Tang WHW. Changes in cardiovascular biomarkers throughout pregnancy and the remote postpartum period. Am J Obstet Gynecol 2013; 208:S97.*

Graphic 81137 Version 45.0

Clinical characteristics of liver diseases in pregnancy

Disease	Symptoms	New onset hypertension	Gestational age at diagnosis	Laboratory findings	
				Aminotransferase levels	Other findings
Hyperemesis gravidarum	Persistent vomiting accompanied by weight loss exceeding 5% of pre-pregnancy body weight and ketonuria unrelated to other causes.	No	Onset in the first trimester. Often continues into the early second trimester, but usually resolves by 20 weeks of gestation.	Abnormal liver chemistries occur in approximately 50% of patients who are hospitalized because of the disease. Alanine aminotransferase (ALT) is typically elevated to a greater degree than aspartate aminotransferase (AST). Values for both are typically only mildly elevated.	▪ Bilirubin usually normal. Rarely exceeds 4 mg/dL.
HELLP syndrome (Hemolysis, Elevated Liver chemistries, and Low Platelets)	Most common symptom is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum. Many patients also have nausea, vomiting, and malaise. Headache, visual changes, and jaundice may occur but are uncommon. Liver rupture is rare.	Yes, in 85% of cases	Onset in the second half of pregnancy, usually in the third trimester. First recognition of disease may be postpartum, usually within 48 hours of delivery.	AST >2 times upper limit of normal for local laboratory (usually >70 international units/L). Marked elevations in the setting of hepatic infarction.	▪ Platelets <100,000/mm^3. ▪ LDH >600 international units/L. ▪ Total bilirubin ≥1.2 mg/dL (20.52 micromol/L). ▪ Random protein:creatinine ratio ≥0.3 mg protein/mg creatinine common. ▪ Elevated uric acid.
Preeclampsia with severe features	New-onset cerebral or visual disturbance (eg, severe headache, photopsia [flashes of light], scotomata [dark areas or gaps in the visual field], altered mental status) and severe, persistent right upper quadrant or epigastric	Yes, in 100% of cases	Onset in the second half of pregnancy, usually in the third trimester. Can also present postpartum, usually within 48 hours of delivery.	Transaminase levels ≥2 times upper limit of normal for a specific laboratory.	▪ Platelets <100,000/mm^3. ▪ Serum creatinine >1.1 mg/dL [97.3 micromol/L] (or twice the baseline value). ▪ Random protein:creatinine ratio ≥0.3 mg protein/mg creatinine common. ▪ Elevated uric acid.

	pain are most common symptoms. Pulmonary edema may occur.				
Intrahepatic cholestasis of pregnancy	Pruritus is the cardinal sign, and ranges from mild to intolerable. It is often generalized, but typically starts and predominates on the palms and soles and is worse at night. Right upper quadrant pain, nausea, poor appetite, sleep deprivation, or steatorrhea may occur.	No	Onset typically in the late second or the third trimester. Transient first trimester symptoms have been linked to ovarian hyperstimulation syndrome.	Serum aminotransferases are elevated in 60% of cases, and usually less than two times the upper limit of normal, but may reach values greater than 1000 international units/L.	▪ Elevated serum bile acid levels. ▪ Total and direct bilirubin concentrations are elevated in 25% of cases; in over 90% of cases, total bilirubin levels rarely exceed 6 mg/dL.
Acute fatty liver of pregnancy	Initial symptoms may be nonspecific (eg nausea, vomiting, abdominal pain, malaise, and/or anorexia), but patients may develop manifestations of acute liver failure including jaundice, encephalopathy, coagulopathy and/or hypoglycemia.	Yes, on occasion	Onset usually in third trimester, but the diagnosis has been made as early as 22 weeks of gestation and as late as four days after delivery.	Modest elevations, up to 500 international units/L.	▪ Elevated WBC count. ▪ Elevated serum creatinine. ▪ Elevated uric acid level. ▪ Elevated ammonia level. ▪ Prolonged PT/PTT. ▪ Decreased platelets. ▪ Decreased glucose. ▪ Decreased antithrombin level. ▪ Decreased fibrinogen.

HELLP syndrome likely represents a form of preeclampsia with severe features.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; WBC: white blood cell.

Graphic 57913 Version 6.0

Criteria for the diagnosis of preeclampsia

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on at least two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient AND the new onset of one or more of the following*:
▪ Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (mg/mg) (30 mg/mmol) in a random urine specimen or dipstick ≥2+ if a quantitative measurement is unavailable
▪ Platelet count <100,000/microL
▪ Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
▪ Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
▪ Pulmonary edema
▪ Cerebral or visual symptoms (eg, new-onset and persistent headaches not accounted for by alternative diagnoses and not responding to usual doses of analgesics ¶; blurred vision, flashing lights or sparks, scotomata)

In a woman with chronic/preexisting hypertension, criteria for superimposed preeclampsia are new onset of proteinuria, significant end-organ dysfunction, or both after 20 weeks of gestation. For women with chronic/preexisting hypertension who have proteinuria prior to or in early pregnancy, superimposed preeclampsia is defined by worsening or resistant hypertension (especially acutely) in the last half of pregnancy or development of signs/symptoms of the severe end of the disease spectrum.

* If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient.
¶ Response to analgesia does not exclude the possibility of preeclampsia.

Adapted from: American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2019; 133:e1-e25.

Graphic 79977 Version 33.0

In a patient with preeclampsia, the presence of one or more of the following indicates a diagnosis of "preeclampsia with severe features"

Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on two occasions at least four hours apart while the patient is on bedrest (antihypertensive therapy may be initiated upon confirmation of severe hypertension, in which case criteria for severe blood pressure elevation can be satisfied without waiting until four hours have elapsed)
Symptoms of central nervous system dysfunction:
New-onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy and not accounted for by alternative diagnoses
Hepatic abnormality:
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥2 times the upper limit of the normal range, or both
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

In contrast to older criteria, the 2013 criteria do not include proteinuria >5 g/24 hours and fetal growth restriction as features of severe disease.

Adapted from: American College of Obstetricians and Gynecologists (ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol 2019; 133:e1-e25.

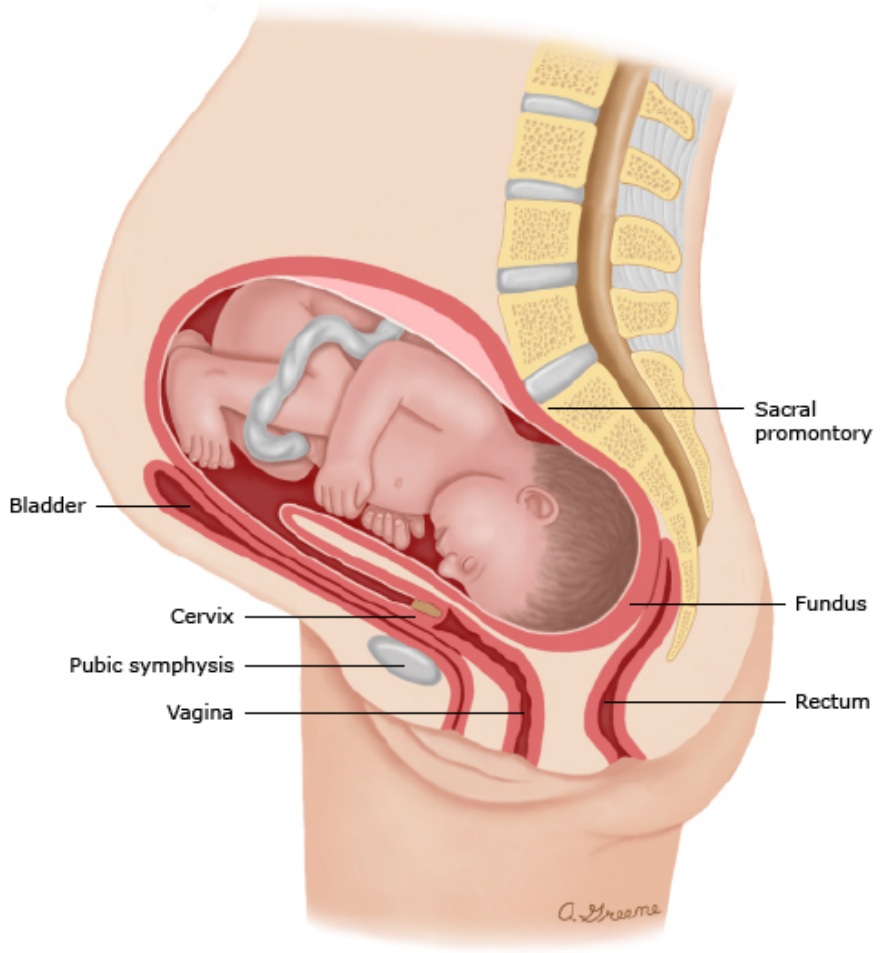
Graphic 76975 Version 20.0

Reported frequency of signs and symptoms of HELLP syndrome

Sign/symptom	Frequency, percent
Proteinuria	86 to 100
Hypertension	82 to 88
Right upper quadrant/epigastric pain	40 to 90
Nausea, vomiting	29 to 84
Headache	33 to 61
Visual changes	10 to 20
Jaundice	5

Graphic 64665 Version 2.0

Incarcerated gravid uterus



The sacculation originating from the anterior lower segment faces the maternal umbilicus, while the uterine fundus remains in the lower posterior pelvis below the sacral promontory (inverted polarity). Concomitantly, both the bladder and the cervix are pulled into the abdominal cavity, towards the umbilicus. The cervix can be stretched to 10 cm in length or more, with the internal os located above the symphysis pubis and occasionally above the bladder.

Graphic 82473 Version 3.0

Causes of abdominal pain by location

Right upper quadrant
Hepatitis
Cholecystitis
Cholangitis
Biliary colic
Pancreatitis
Budd-Chiari syndrome
Pneumonia/empyema pleurisy
Subdiaphragmatic abscess
Right lower quadrant
Appendicitis
Salpingitis
Ectopic pregnancy
Inguinal hernia
Nephrolithiasis
Inflammatory bowel disease
Mesenteric adenitis (yersina)
Epigastric
Peptic ulcer disease
Gastroesophageal reflux disease
Gastritis
Pancreatitis
Myocardial infarction
Pericarditis
Ruptured aortic aneurysm
Periumbilical
Early appendicitis
Gastroenteritis
Bowel obstruction
Ruptured aortic aneurysm

Left upper quadrant
Splenic abscess
Splenic infarct
Gastritis
Gastric ulcer
Pancreatitis
Left lower quadrant
Diverticulitis
Salpingitis
Ectopic pregnancy
Inguinal hernia
Nephrolithiasis
Irritable bowel syndrome
Inflammatory bowel disease
Diffuse
Gastroenteritis
Mesenteric ischemia
Metabolic (eg, DKA, porphyria)
Malaria
Familial Mediterranean fever
Bowel obstruction
Peritonitis
Irritable bowel syndrome

DKA: diabetic ketoacidosis.

Graphic 70233 Version 4.0

Selected extra-abdominal causes of acute abdominal pain

Cardiac
Myocardial ischemia and infarction
Myocarditis
Endocarditis
Heart failure
Thoracic
Pneumonitis
Pleurodynia, Bornholm's disease
Pulmonary embolism and infarction
Pneumothorax
Empyema
Esophagitis
Esophageal spasm
Esophageal rupture (Boerhaave's syndrome)
Neurologic
Radiculitis: spinal cord or peripheral nerve tumors, degenerative arthritis of spine
Abdominal epilepsy
Tabes dorsalis (tertiary syphilis)
Metabolic
Uremia
Diabetes mellitus (ketoacidosis)
Porphyria
Acute adrenal insufficiency
Hyperlipidemia
Hyperparathyroidism

Hematologic
Sickle cell anemia
Hemolytic anemia
Henoch-Schönlein purpura
Acute leukemia
Toxins
Hypersensitivity reactions: insect bites, reptile venoms
Heavy metals and corrosives (eg, lead or iron)
Infections
Herpes zoster
Osteomyelitis
Typhoid fever
Miscellaneous
Muscular contusion, hematoma, or tumor
Narcotic withdrawal
Familial Mediterranean fever
Psychiatric disorders
Heat stroke

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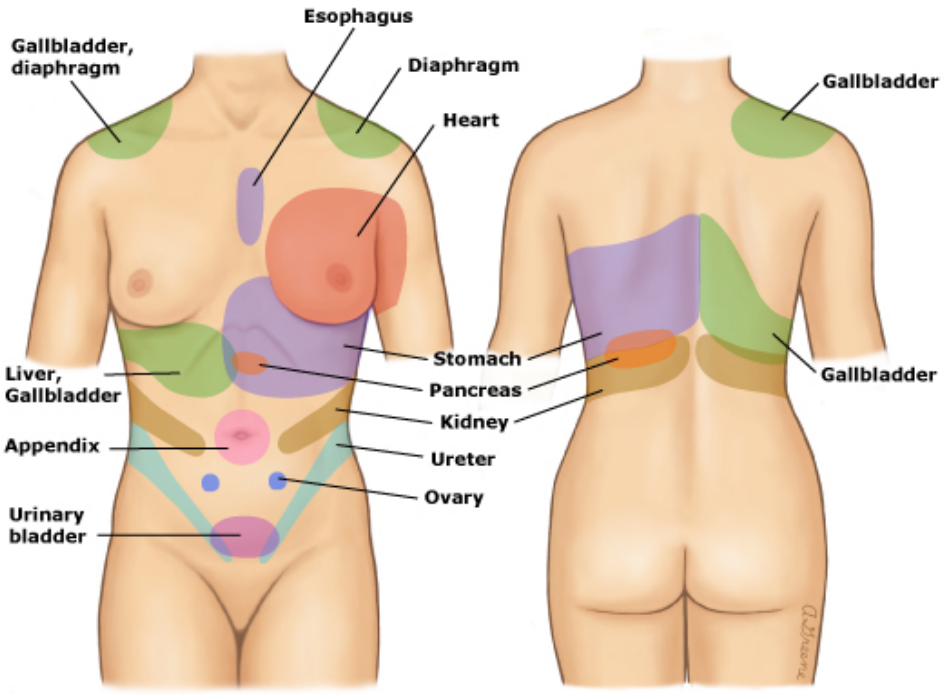
Graphic 60310 Version 7.0

Patterns of referred abdominal pain



Pain from abdominal viscera often (but not always) localizes according to the structure's embryologic origin, with foregut structures (mouth to proximal half of duodenum) presenting with upper abdominal pain, midgut structures (distal half of duodenum to middle of the transverse colon) presenting with periumbilical pain, and hind gut structures (remainder of colon and rectum, pelvic genitourinary organs) presenting with lower abdominal pain. Radiation of pain may provide insight into the diagnosis. As examples, pain from pancreatitis may radiate to the back while pain from gallbladder disease may radiate to the right shoulder or subscapular region.

Graphic 61375 Version 7.0

Differential diagnosis of postpartum abdominal pain

Gastrointestinal disorders
Bowel obstruction
Postoperative ileus
Acute appendicitis
Acute cholecystitis
Acute pancreatitis
Peptic ulceration
Gynecologic disorders
Ovarian torsion
Ovarian cyst hemorrhage
Ovarian vein thrombosis
Uterine fibroid degeneration
Renal disorders
Acute pyelonephritis
Acute urinary retention
Renal colic
Urolithiasis
Bladder rupture
Pregnancy-related disorders
Endometritis
Preeclampsia with liver distension/rupture
Uterine rupture
Acute fatty liver
Breastfeeding can be associated with painful uterine contractions
Cardiovascular disorders
Acute myocardial infarction
Aortic aneurysm
Mesenteric vascular occlusion
Other
Sickle cell disease
Splenic rupture

Graphic 54003 Version 1.0

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