

Williams Obstetrics, 25e

CHAPTER 54: Gastrointestinal Disorders

The diagnosis of acute appendicitis is more difficult than at other times, as the enlarged uterus renders it almost impossible to explore the right iliac region satisfactorily.

—J. Whitridge Williams (1903)

INTRODUCTION

These words summarize that during normal pregnancy, the gastrointestinal tract and its appendages undergo remarkable anatomical, physiological, and functional alterations. These changes, which are discussed in detail in [Chapter 4 \(Gastrointestinal Tract\)](#), can appreciably alter clinical findings normally relied on for diagnosis and treatment of gastrointestinal disorders such as appendicitis. Moreover, as pregnancy progresses, gastrointestinal symptoms become more difficult to assess. Physical findings are often obscured by a large uterus that displaces abdominal organs and can alter the location and intensity of pain and tenderness.

GENERAL CONSIDERATIONS

Diagnostic Techniques

Endoscopy

Fiberoptic endoscopic instruments have revolutionized diagnosis and management of most gastrointestinal conditions, and these are particularly well suited for pregnancy. Endoscopy in pregnancy is associated with a slightly increased risk for preterm birth, but this is likely due to the disease itself ([Ludvigsson, 2017](#)). With endoscopy, the esophagus, stomach, duodenum, and colon can be inspected ([Cappell, 2011](#); [Savas, 2014](#)). The proximal jejunum can also be studied, and the ampulla of Vater cannulated to perform *endoscopic retrograde cholangiopancreatography—ERCP* ([Akakaya, 2014](#); [Fogel, 2014](#)). Preliminary data suggest that postendoscopic pancreatitis following gallstone removal may have a higher incidence in pregnant women ([Inamdar, 2016](#)). Experience in pregnancy with *videocapsule endoscopy* for small-bowel evaluation remains limited ([Storch, 2006](#)).

Upper gastrointestinal endoscopy is used for management as well as diagnosis of several problems. Common bile duct exploration and drainage are used for choledocholithiasis as described in [Chapter 55 \(Pancreatic Disorders\)](#). It is also used for sclerotherapy and for placement of *percutaneous endoscopic gastrostomy (PEG)* tubes. Several concise reviews have been provided ([Cappell, 2011](#); [Fogel, 2014](#); [Gilinsky, 2006](#)).

For visualization of the large bowel, *flexible sigmoidoscopy* can be used safely in pregnant women ([Siddiqui, 2006](#)). *Colonoscopy* is indispensable for viewing the entire colon and distal ileum to aid diagnosis and management of several bowel disorders. Except for the midtrimester, reports of colonoscopy during pregnancy are limited, but most results indicate that it should be performed if indicated ([Cappell, 2010, 2011](#); [De Lima, 2015](#)). Bowel preparation is completed using polyethylene glycol electrolyte or sodium phosphate solutions. With these, serious maternal dehydration that may cause diminished uteroplacental perfusion should be avoided.

Noninvasive Imaging Techniques

The obvious ideal technique for gastrointestinal evaluation during pregnancy is abdominal sonography. Because computed tomography (CT) use is limited in pregnancy due to radiation exposure, magnetic resonance (MR) imaging is now commonly used to evaluate the abdomen and retroperitoneal space ([Khandelwal, 2013](#)). One example is magnetic resonance cholangiopancreatography—MRCP ([Oto, 2009](#)). Another is magnetic resonance enterography—MRE ([Stern, 2014](#)). These and other imaging modalities, and their safe use in pregnancy, are considered in more detail in [Chapter 46](#).

Laparotomy and Laparoscopy

Surgery is lifesaving for certain gastrointestinal conditions— perforative appendicitis being the most common example. Laparoscopic procedures have replaced traditional surgical techniques for many abdominal disorders during pregnancy. These are shown in detail with descriptions of surgical technique in [Chapter 46 \(Perinatal Outcomes\)](#) and in *Cunningham and Gilstrap's Operative Obstetrics, 3rd edition* ([Kho, 2016](#)). Guidelines for diagnosis, treatment, and use of laparoscopy for surgical problems during pregnancy have been provided by the Society of American Gastrointestinal and Endoscopic Surgeons—SAGES ([Pearl, 2017](#)).

Nutritional Support

Specialized nutritional support can be delivered *enterally*, usually via nasogastric tube feedings, or *parenterally* with nutrition given by venous catheter access, either peripherally or centrally.

When possible, enteral alimentation is preferable because it has fewer serious complications ([Bistran, 2012](#); [Stokke, 2015](#)). In obstetrical patients, very few conditions prohibit enteral nutrition as a first effort to prevent catabolism. For extreme cases, such as recalcitrant hyperemesis gravidarum, percutaneous endoscopic gastrostomy with a jejunal port (PEG-J tube) has been described ([Saha, 2009](#)).

The purpose of *parenteral feeding*, or *hyperalimentation*, is to provide nutrition when the intestinal tract must be quiescent. Central venous access is necessary for [total parenteral nutrition](#) because its hyperosmolarity requires rapid dilution in a high-flow vascular system. These solutions provide 24 to 40 kcal/kg/d, principally as a hypertonic glucose solution.

Various conditions may prompt [total parenteral nutrition](#) during pregnancy ([Table 54-1](#)). Not surprisingly, gastrointestinal disorders are the most common indication, and in the many studies cited, feeding duration averaged approximately 33 days.

TABLE 54-1

Some Conditions Treated with Enteral or Parenteral Nutrition During Pregnancy^a

Achalasia
Anorexia nervosa
Appendiceal rupture
Bowel obstruction
Burns
Cholecystitis
Crohn disease
Diabetic gastropathy
Esophageal injury
Hyperemesis gravidarum
Jejunioileal bypass
Malignancies
Ostomy obstruction
Pancreatitis
Preeclampsia syndrome
Short gut syndrome
Stroke
Ulcerative colitis

^aDisorders are listed alphabetically.

Data from [Folk, 2004](#); [Guglielmi, 2006](#); [Manhadevan, 2015](#); [Ogura, 2003](#); [Porter, 2014](#); [Russo-Stieglitz, 1999](#); [Saha, 2009](#); [Spiliopoulos, 2013](#).

Importantly, complications of parenteral nutrition are frequent, and they may be severe (Guglielmi, 2006). An early report of 26 pregnancies described a 50-percent rate of complications, which included pneumothorax, hemothorax, and brachial plexus injury (Russo-Stieglitz, 1999). The most frequent serious complication is catheter sepsis, and Folk (2004) reported a 25-percent incidence in 27 women with hyperemesis gravidarum. Although bacterial sepsis is most common, *Candida* septicemia has been described (Paranyuk, 2006). The Centers for Disease Control and Prevention has updated its detailed guidelines to prevent catheter-related sepsis, and these serve to lessen the dangers of serious infections (O'Grady, 2011). Perinatal complications are uncommon, however, fetal subdural hematoma caused by maternal vitamin K deficiency has been described (Sakai, 2003).

Appreciable morbidity is also associated with long-term use of a *peripherally inserted central catheter* (PICC). Infection is the most common serious long-term complication (Holmgren, 2008; Ogura, 2003). In a series of 84 such catheters inserted in 66 pregnant women, Cape and coworkers (2014) reported a 56-percent complication rate, of which bacteremia was the most frequent. From a review of 48 reports of nonpregnant adults, Turcotte and associates (2006) concluded that peripherally placed catheters provided no advantages compared with centrally placed ones. Still, for short-term nutrition lasting a few weeks, it seems reasonable that PICC placement has a greater benefit-versus-risk ratio (Bistran, 2012).

UPPER GASTROINTESTINAL TRACT DISORDERS

Hyperemesis Gravidarum

Mild to moderate nausea and vomiting are especially common in pregnant women until approximately 16 weeks' gestation (Chap. 9, Caffeine). In a small but significant proportion of these, however, it is severe and unresponsive to simple dietary modification and antiemetics. Severe unrelenting nausea and vomiting—*hyperemesis gravidarum*—is defined variably as being sufficiently severe to produce weight loss, dehydration, ketosis, alkalosis from loss of hydrochloric acid, and hypokalemia. Acidosis develops from partial starvation. In some women, transient hepatic dysfunction develops, and biliary sludge accumulates (Matsubara, 2012). Other causes should be considered because ultimately hyperemesis gravidarum is a diagnosis of exclusion (Benson, 2013).

Study criteria have not been homogeneous, thus reports of population incidences vary. There does, however, appear to be an ethnic or familial predilection (Grjibovski, 2008). In population-based studies from California, Nova Scotia, and Norway, the hospitalization rate for hyperemesis gravidarum was 0.5 to 1 percent (Bailit, 2005; Fell, 2006; Vikanes, 2013). Up to 20 percent of those hospitalized in a previous pregnancy for hyperemesis will again require hospitalization (Dodds, 2006; Trogstad, 2005). In general, obese women are less likely to be hospitalized for this (Cedergren, 2008).

The etiopathogenesis of hyperemesis gravidarum is unknown and is likely multifactorial. It apparently is related to high or rapidly rising serum levels of pregnancy-related hormones. Putative culprits include human chorionic gonadotropin (hCG), estrogen, progesterone, leptin, placental growth hormone, prolactin, thyroxine, and adrenocortical hormones (Verberg, 2005). More recently implicated are other hormones that include ghrelin, leptin, nesfatin-1, and peptide YY (3–36) (Albayrak, 2013; Gungor, 2013).

Superimposed on this hormonal cornucopia are an imposing number of biological and environmental factors. Moreover, in some but not all severe cases, interrelated psychological components play a major role (Christodoulou-Smith, 2011; McCarthy, 2011). Other factors that increase the risk for admission include hyperthyroidism, previous molar pregnancy, diabetes, gastrointestinal illnesses, some restrictive diets, and asthma and other allergic disorders (Fell, 2006; Mullin, 2012). An association of *Helicobacter pylori* infection has been proposed, but evidence is not conclusive (Goldberg, 2007). Chronic marijuana use may cause the similar *cannabinoid hyperemesis syndrome* (Alaniz, 2015; Andrews, 2015). And for unknown reasons—perhaps estrogen-related—a female fetus increases the risk by 1.5-fold (Schiff, 2004; Tan, 2006; Veenendaal, 2011). Finally, some but not all studies have reported an association between hyperemesis gravidarum and preterm labor, placental abruption, and preeclampsia (Bolin, 2013; Vandraas, 2013; Vikanes, 2013).

Complications

Vomiting may be prolonged, frequent, and severe, and a list of potentially fatal complications is given in Table 54-2. Various degrees of acute kidney injury from dehydration are encountered (Nwoko, 2012). An extreme example was a woman we cared for who required 5 days of dialysis when her serum creatinine level rose to 10.7 mg/dL (Hill, 2002). One complication from continuous retching is a Mallory-Weiss tear. Others are pneumothorax, pneumomediastinum, diaphragmatic rupture, and gastroesophageal rupture—*Boerhaave syndrome* (American College of Obstetricians and Gynecologists, 2015; Chen, 2012).

TABLE 54-2

Some Serious and Life-Threatening Complications of Recalcitrant Hyperemesis Gravidarum

Acute kidney injury—may require dialysis
Depression—cause versus effect?
Diaphragmatic rupture
Esophageal rupture—Boerhaave syndrome
Hypoprothrombinemia—vitamin K deficiency
Hyperalimentation complications
Mallory-Weiss tears—bleeding, pneumothorax, pneumomediastinum, pneumopericardium
Rhabdomyolysis
Wernicke encephalopathy—thiamine deficiency

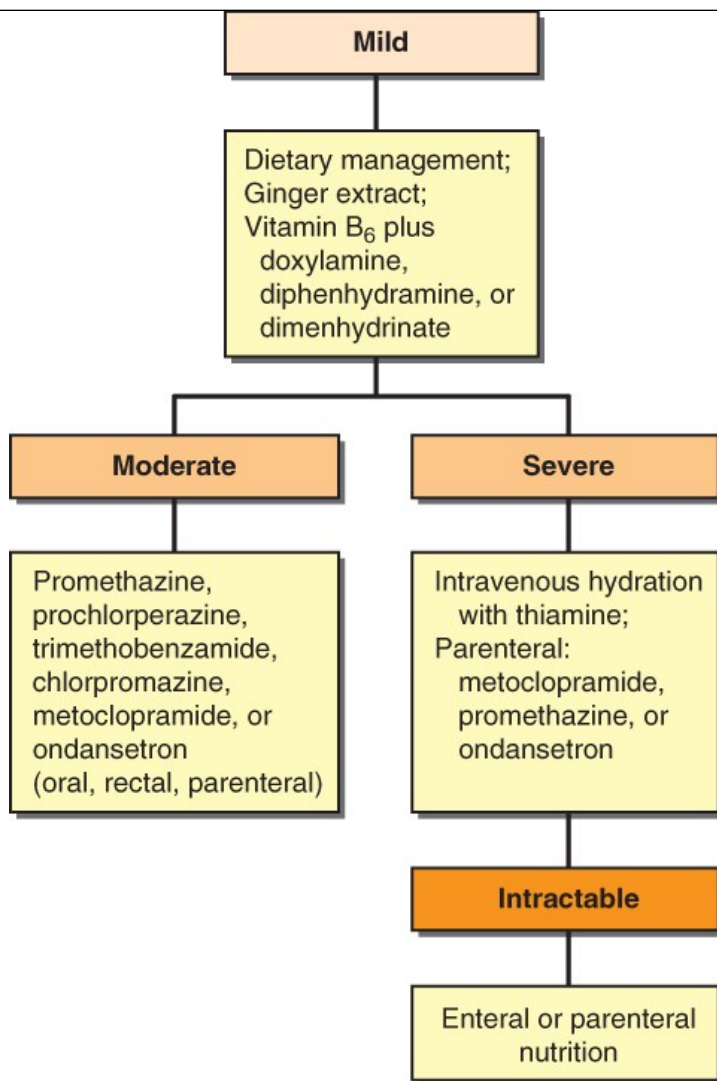
At least two serious vitamin deficiencies have been reported with hyperemesis in pregnancy. One is *Wernicke encephalopathy* from [thiamine](#) deficiency that has been recognized with increasing frequency ([Di Gangi, 2012](#); [Palacios-Marqués, 2012](#)). In two reviews, ocular signs, confusion, and ataxia were common, but only half had this triad ([Chiossi, 2006](#); [Selitsky, 2006](#)). With this encephalopathy, an abnormal electroencephalogram (EEG) may be seen, and usually MR imaging shows findings ([Vaknin, 2006](#); [Zara, 2012](#)). At least three maternal deaths have been described, and long-term sequelae include blindness, convulsions, and coma ([Selitsky, 2006](#)). The second is *vitamin K deficiency* that has been reported to cause maternal coagulopathy and fetal intracranial hemorrhage, as well as vitamin K embryopathy ([Kawamura, 2008](#); [Lane, 2015](#); [Sakai, 2003](#)).

Management

One algorithm for management of nausea and vomiting of pregnancy is shown in [Figure 54-1](#). Most women with mild to moderate symptoms respond as outpatients to any of several first-line antiemetic agents ([Clark, 2014](#); [Matthews, 2014](#)). One that is becoming a mainstay is *Diclegis*—a combination of [doxylamine](#) (10 mg) plus [pyridoxine](#) (10 mg). It has been proven safe and effective ([Briggs, 2015](#); [Koren, 2014](#)). The usual dose is two tablets orally at bedtime. If relief is insufficient, then additional doses, first in the morning, and then in the morning and midafternoon can be added each day to the bedtime dose. At our institution, for cost savings, we prescribe these two agents individually: Unisom ([doxylamine](#)) ½ of a 50-mg tablet plus a 25-mg vitamin B₆ tablet. The same graduated dosing is used but does not exceed three total daily doses.

FIGURE 54-1

Algorithm for outpatient and inpatient management of hyperemesis gravidarum.



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition
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Ondansetron (Zofran) also does not appear to be teratogenic. It was slightly more efficacious than a combination of **doxylamine and pyridoxine** in a randomized trial (Oliveira, 2014; Pasternak, 2013). Its drawbacks include potential maternal effects from prolonged QT-interval and serotonin syndrome (Koren, 2014).

When simple measures fail, intravenous crystalloid solutions are given to correct dehydration, ketonemia, electrolyte deficits, acid-base imbalances, and hypokalemia. No benefits are gained by infusing 5-percent **dextrose** along with crystalloids (Tan, 2013). **Thiamine**, 100 mg, is given to prevent Wernicke encephalopathy (Giugale, 2015; Niebyl, 2010). This is usually diluted in 1 L of the selected crystalloid and infused at the maintenance rate desired for patient hydration.

If vomiting persists after rehydration and failed outpatient management, hospitalization is recommended (American College of Obstetricians and Gynecologists, 2015). Day care has also been shown to be effective in one randomized study (McCarthy, 2014). Intravenous hydration is continued and antiemetics such as **promethazine**, **prochlorperazine**, **chlorpromazine**, or **metoclopramide** are given parenterally (Table 54-3). The bulk of evidence is that treatment with **glucocorticosteroids** is not effective (Yost, 2003). Because of their putative teratogenicity, they are not routinely recommended (American College of Obstetricians and Gynecologists, 2015).

TABLE 54-3

Medications for Gastric Disorders in Pregnancy

Medication (Brand Name)	Usual Dosing	Route(s)
Options for Nausea and Vomiting		
Antihistamine Doxylamine + pyridoxine (Diclegis) ^a	At bedtime; up to 4 times daily	PO
Phenothiazines	Every 6 hr	
Promethazine (Phenergan) ^c	12.5–25 mg	IM, IV, PO, PR
Prochlorperazine (Compazine) ^c	5–10 (25 PR) mg	IM, IV, PO, PR
Serotonin antagonist	Every 8 hr	
Ondansetron (Zofran) ^b	8 mg	IV, PO
Benzamides	Every 6 hr	
Metoclopramide (Reglan) ^b	5–15 mg	IM, IV, PO
Oral Options for Gastroesophageal Reflux (GERD)		
H2 receptor antagonists		
Ranitidine (Zantac) ^b	150 mg twice daily	
Cimetidine (Tagamet) ^b	400 mg 4 times daily for up to 12 wks 800 mg twice daily for up to 12 wks	
Nizatidine (Axiid) ^b	150 mg twice daily	
Famotidine (Pepcid) ^b	20 mg twice daily up to 6 wks	
Proton-pump inhibitors		
Pantoprazole (Protonix) ^b	40 mg daily for up to 8 wks	
Lansoprazole (Prevacid) ^b	15 mg daily for up to 8 wks	
Omeprazole (Prilosec, Zegerid) ^c	20 mg daily for 4–8 wks	
Dexlansoprazole (Dexilant) ^c	30 mg daily for up to 4 wks	

^aFood and Drug Administration category A.

^bFood and Drug Administration category B.

^cFood and Drug Administration category C.

With persistent vomiting after hospitalization, appropriate steps should be taken to exclude possible underlying diseases as a cause of hyperemesis. That said, in one study, endoscopy did not change management in 49 women (Debbly, 2008). Other potential causes of vomiting include gastroenteritis, cholecystitis, pancreatitis, hepatitis, peptic ulcer, and pyelonephritis. In addition, severe preeclampsia and fatty liver are more likely after midpregnancy. And although clinical thyrotoxicosis has been implicated as a cause of hyperemesis, it is more likely that abnormally elevated serum thyroxine levels are a surrogate for higher-than-average serum hCG levels (Sun, 2014). This is discussed further in Chapter 5 (Human Placental Lactogen). In our experiences, serum free thyroxine levels normalize quickly with hydration and emesis treatment.

With treatment, most women will have a salutary response and may be sent home with antiemetic therapy. Their readmission rate is 25 to 35 percent in most prospective studies. If associated psychiatric and social factors contribute to the illness, the woman usually improves remarkably while hospitalized (Swallow, 2004). That said, symptoms may relapse in these women, and some go on to develop *posttraumatic stress syndrome* (Christodoulou-Smith, 2011; McCarthy, 2011). For some women, hyperemesis can be an indication for elective termination (Poursharif, 2007).

In the small percentage of women who continue to have recalcitrant vomiting after intensive therapy, consideration is given for *enteral nutrition* (Upper Gastrointestinal Tract Disorders). Stokke and associates (2015) described successful use of nasojejunal feeding for up to 41 days in 107 such women. Use of sonography to confirm correct placement of the tube has been described (Swartzlander, 2013). Percutaneous endoscopic gastrostomy with a jejunal port has also been reported (Saha, 2009; Schrag, 2007). A randomized trial failed to show any advantages from early enteral feeding (Grooten, 2017).

In our experiences, only a very few women will require *parenteral nutrition* (Yost, 2003). In a study of 599 women, however, Peled and coworkers (2014) reported that 20 percent required central venous access to be established for nutrition.

Gastroesophageal Reflux Disease

Symptomatic reflux is seen in up to 15 percent of nonpregnant individuals (Kahrilas, 2015). The spectrum of sequelae includes esophagitis, stricture, Barrett esophagus, and adenocarcinoma. The main symptom of reflux is heartburn, or *pyrosis*, which is especially common in pregnancy. Its prevalence rose from 26 percent in the first trimester to 36 percent in the second and 51 percent in the third trimesters (Malfertheiner, 2012). The retrosternal burning sensation stems from esophagitis caused by gastroesophageal reflux related to relaxation of the lower esophageal sphincter.

Reflux symptoms usually respond to tobacco and alcohol abstinence, small meals, head of the bed elevation, and avoidance of postprandial recumbency. So-called “trigger” foods are also avoided and usually include fatty foods, tomato-based foods, and coffee. Oral antacids are first-line therapy. If severe symptoms persist, *sucralfate* (Carafate) is given along with a proton-pump inhibitor or an H₂-receptor antagonist (see Table 54-3).

Both classes are generally safe for use in pregnancy (Briggs, 2015; Mahadevan, 2006b). Of these, a 1-g *sucralfate* tablet is taken orally 1 hour before each of the three meals and at bedtime for up to 8 weeks. Antacids are not used within ½ hour before or after *sucralfate* doses. If relief is not attained, then endoscopy should be considered. *Misoprostol* is contraindicated because it stimulates labor (Chap. 26, Methods of Induction and Augmentation).

In nonpregnant patients, surgical fundoplication is performed (Kahrilas, 2015). Although the procedure is not done during pregnancy, Biertho and colleagues (2006) described 25 women who had undergone laparoscopic Nissen fundoplication before pregnancy. Only 20 percent had reflux symptoms during pregnancy.

Hiatal Hernia

The older literature is informative regarding hiatal hernias in pregnancy. Upper gastrointestinal radiographs performed in 195 women in late pregnancy showed that 20 percent of 116 multiparas and 5 percent of 79 nulliparas had a hiatal hernia (Rigler, 1935). Of 10 women studied postpartum, hernia persisted in three at 1 to 18 months.

The relationship of hiatal hernia with reflux esophagitis, and thus symptoms, is not clear. One study demonstrated no relationship between reflux and hernia and showed that the lower esophageal sphincter functioned effectively even when displaced intrathoracically (Cohen, 1971). Nevertheless, during pregnancy, these hiatal hernias may cause vomiting, epigastric pain, and bleeding from ulceration. Schwentner (2011) reported severe herniation requiring surgical repair in a woman with a 12-week gestation. Curran and coworkers (1999) described a 30-week pregnancy complicated by

gastric outlet obstruction from a paraesophageal hernia.

Diaphragmatic Hernia

These are caused by herniations of abdominal contents through either the foramen of Bochdalek or Morgagni. Fortunately, they rarely complicate pregnancy. [Kurznel and associates \(1988\)](#) reviewed the outcomes of 18 pregnant women with such a hernia and who developed acute obstruction. Because the maternal mortality rate was 45 percent, they recommend repair during pregnancy even if a woman is asymptomatic. Herniation has been reported in one pregnant woman from a previous traumatic diaphragmatic defect and in another who had antireflux surgery in early pregnancy ([Brygger, 2013](#); [Flick, 1999](#)). Several case reports also describe spontaneous diaphragmatic rupture from increased intraabdominal pressure during delivery ([Chen, 2012](#); [Sharifah, 2003](#)).

Achalasia

This is a rare motility disorder in which the lower esophageal sphincter does not relax properly with swallowing. There is also nonperistaltic contraction activity of the esophageal muscularis to cause symptoms ([Kahrilas, 2015](#); [Khudyak, 2006](#)). The defect is caused by inflammatory destruction of the myenteric (Auerbach) plexus within smooth muscle of the lower esophagus and its sphincter. Postganglionic cholinergic neurons are unaffected, thus, sphincter stimulation is unopposed. Symptoms are dysphagia, chest pain, and regurgitation. Barium swallow radiography demonstrates *bird beak* or *ace of spades* narrowing at the distal esophagus. Endoscopy is performed to exclude gastric carcinoma, and manometry is confirmatory. If dilatation of the esophagus and medical therapy does not provide relief, myotomy is considered ([Torquati, 2006](#)).

During pregnancy, normal relaxation of the lower esophageal sphincter in women with achalasia theoretically should not occur. Even so, in most women, pregnancy does not seem to worsen achalasia. One report of 20 affected pregnant women found no excessive reflux esophagitis ([Mayberry, 1987](#)). [Khudyak and coworkers \(2006\)](#) reviewed 35 cases and described most women as symptom free, although esophageal dilatation was needed in a few. A maternal death was reported at 24 weeks' gestation associated with perforation of a 14-cm diameter megaesophagus ([Fassina, 1995](#)).

Management of achalasia includes soft diet and anticholinergic drugs. With persistent symptoms, other options include nitrates, calcium-channel antagonists, and botulinum toxin A injected locally ([Hooft, 2015](#); [Kahrilas, 2015](#)). Balloon dilatation of the sphincter may be necessary, and 85 percent of nonpregnant patients respond to this. [Satin \(1992\)](#) and [Fiest \(1993\)](#) and their associates reported successful use of pneumatic dilatation in pregnancy. *One caveat is that esophageal perforation is a serious complication of dilatation.* [Spiliopoulos and colleagues \(2013\)](#) described a 29-week pregnant woman with achalasia treated for 10 weeks with parenteral nutrition. Surgical correction was performed postpartum.

Peptic Ulcer Disease

The lifetime prevalence of acid peptic disorders in women is 10 percent ([Del Valle, 2015](#)). Erosive ulcer disease involves the stomach and duodenum. Gastroduodenal ulcers may be caused by chronic gastritis from *H pylori*, or they develop from nonsteroidal antiinflammatory drug (NSAID) use. Neither is common in pregnancy ([McKenna, 2003](#); [Weyermann, 2003](#)). Acid secretion is also important, and thus underlies the efficacy of antisecretory agents ([Suerbaum, 2002](#)). Gastroprotection during pregnancy probably originates from physiological changes that include reduced gastric acid secretion, decreased motility, and considerably increased mucus secretion ([Hytten, 1991](#)). Despite this, ulcer disease may be underdiagnosed because of frequent treatment for reflux esophagitis ([Mehta, 2010](#)). In the past 50 years at Parkland Hospital, during which time we have cared for more than 500,000 pregnant women, we have encountered very few who had proven ulcer disease. Perforation is rare ([Goel, 2014](#)). Before appropriate therapy was commonplace, [Clark \(1953\)](#) studied 313 pregnancies in 118 women with ulcer disease and noted a clear remission during pregnancy in almost 90 percent. However, benefits were short lived. Symptoms recurred in more than half by 3 months postpartum and in almost all by 2 years.

The mainstay of management is eradication of *H pylori* and prevention of NSAID-induced disease. Antacids are usually self-prescribed, but first-line therapy is with H₂-receptor blockers or proton-pump inhibitors ([Del Valle, 2015](#)). *Sucralfate* is the aluminum salt of sulfated sucrose that inhibits pepsin. It provides a protective coating at the ulcer base. Approximately 10 percent of the aluminum salt is absorbed, and it is considered safe for pregnant women ([Briggs, 2015](#)).

With active ulcers, a search for *H pylori* is undertaken. Diagnostic aids include the urea breath test, serological testing, or endoscopic biopsy. If any of these yield positive results, combination antimicrobial and proton-pump inhibitor therapy is indicated. Several effective oral treatment regimens do not include tetracycline and can be used during pregnancy. These 14-day regimens include amoxicillin, 1000 mg twice daily plus clarithromycin, 250 to 500 mg twice daily, plus metronidazole, 500 mg twice daily given along with the proton-pump inhibitor omeprazole ([Del Valle, 2015](#)).

Upper Gastrointestinal Bleeding

In some women, persistent vomiting is accompanied by worrisome upper gastrointestinal bleeding. Occasionally, a peptic ulceration is the source. However, most of these women have small linear mucosal tears near the gastroesophageal junction—*Mallory-Weiss tears*, described earlier. Bleeding usually responds promptly to conservative measures, including iced-saline irrigations, topical antacids, and intravenously administered H₂-blockers or proton-pump inhibitors. Transfusions may be needed, and if bleeding persists, then endoscopy is usually indicated (O'Mahony, 2007). With sustained retching, the less common, but more serious, esophageal rupture—*Boerhaave syndrome*—may develop from greatly increased esophageal pressure.

SMALL BOWEL AND COLON DISORDERS

The small bowel has diminished motility during pregnancy. Using a nonabsorbable carbohydrate, Lawson (1985) showed that small bowel mean transit times were 99, 125, and 137 minutes in each trimester, compared with 75 minutes when nonpregnant. In a study cited by Everson (1992), mean transit time for a mercury-filled balloon from the stomach to the cecum was 58 hours in term pregnant women compared with 52 hours in nonpregnant women.

Muscular relaxation of the colon is accompanied by increased absorption of water and sodium that predisposes to constipation. This complaint is reported by almost 40 percent of women at some time during pregnancy (Everson, 1992). Such symptoms are usually only mildly bothersome, and preventive measures include a high-fiber diet and bulk-forming laxatives. Wald (2003) has reviewed treatment options. We have encountered several pregnant women who developed megacolon from impacted stool. These women almost invariably had chronically abused stimulatory laxatives.

Acute Diarrhea

The estimated monthly prevalence of diarrhea among adults is 3 to 7 percent (DuPont, 2014). Diarrhea can be classified as acute (<2 weeks), persistent (2 to 4 weeks), and chronic (>4 weeks). Most cases of acute diarrhea are caused by infectious agents, and a third result from foodborne pathogens. The large variety of viruses, bacteria, helminths, and protozoa that cause diarrhea in adults inevitably also afflict pregnant women. Some of these are discussed in Chapter 64. Evaluation of acute diarrhea depends on its severity and duration. Some indications for evaluation include profuse watery diarrhea with dehydration, grossly bloody stools, fever >38°C, duration >48 hours without improvement, recent antimicrobial use, and diarrhea in the immunocompromised patient (Camilleri, 2015; DuPont, 2014). Cases of moderately severe diarrhea with fecal leukocytes or gross blood may best be treated with empirical antibiotics rather than evaluation. Some features of the more common acute diarrheal syndromes and their treatment are shown in Table 54-4.

TABLE 54-4

Etiology, Clinical Features, and Treatment of Common Acute Diarrheal Syndromes

Agents	Incubation	Emesis	Pain	Fever	Diarrhea	Treatment
Toxin producers 1. <i>Staphylococcus</i> 2. <i>C perfringens</i> 3. <i>E coli</i> (enterotoxin) 4. <i>B cereus</i>	1–72 hr	3–4+	1–2+	0–1+	3–4+, watery	1. None 2. None 3. Ciprofloxacin 4. None
Enteroadherent 1. <i>E coli</i> 2. <i>Giardia</i> 3. Helminths	1–8 days	0–1+	1–3+	0–2+	1–2+, watery, mushy	1. Ciprofloxacin 2. Tinidazole 3. As detected
Cytotoxin producers 1. <i>C difficile</i> 2. <i>E coli</i> (hemorrhagic)	1–3 days	0–1+	3–4+	1–2+	1–3+, watery, then bloody	1. Metronidazole 2. None
Inflammatory Minimal 1. <i>Rotavirus</i> 2. <i>Norovirus</i>	1–3 days	1–3+	2–3+	3–4+	1–3+, watery	1. None 2. None
Variable 3. <i>Salmonella</i> 4. <i>Campylobacter</i> 5. <i>Vibrio</i>	1–11 days	0–3+	2–4+	3–4+	1–4+ watery or bloody	3. Ciprofloxacin 4. Azithromycin 5. Doxycycline
Severe 6. <i>Shigella</i> 7. <i>E coli</i> 8. <i>Entamoeba histolytica</i>	1–8 days	0–1+	3–4+	3–4+	1–2+, bloody	6. Ciprofloxacin 7. Ciprofloxacin 8. Metronidazole

B cereus = *Bacillus cereus*; *C difficile* = *Clostridium difficile*; *C perfringens* = *Clostridium perfringens*; *E coli* = *Escherichia coli*.

Data from Camilleri, 2015; DuPont, 2014.

The mainstay of treatment is intravenous hydration using normal saline or Ringer lactate with potassium supplementation in amounts to restore maternal blood volume and to ensure uteroplacental perfusion. Vital signs and urine output are monitored for signs of sepsis syndrome. For moderately severe nonfebrile illness without bloody diarrhea, antimotility agents such as [loperamide](#) (Imodium) may be useful. [Bismuth subsalicylate](#) (Pepto-Bismol) may also alleviate symptoms.

Judicious use of antimicrobial agents is warranted. For moderate to severely ill women, some recommend empirical treatment with [ciprofloxacin](#), 500 mg twice daily for 3 to 5 days. Specific pathogens are treated as needed when identified (see [Table 54-4](#)). Syndromes for which treatment is usually unnecessary include those caused by *Escherichia coli*, staphylococcal species, *Bacillus cereus*, and Norwalk-like virus. Severe illness caused by *Salmonella* spp is treated with [ciprofloxacin](#) or trimethoprim-sulfamethoxazole; by *Campylobacter* spp with [azithromycin](#); by *Clostridium difficile* with oral [metronidazole](#) or [vancomycin](#); and by *Giardia* spp and *Entamoeba histolytica* with [metronidazole](#) (DuPont, 2014; Rocha-Castro, 2016).

***Clostridium Difficile* Infection**

This anaerobic gram-positive bacillus is transmitted by the fecal-oral route. It is the most frequent nosocomial infection in the United States. In 2011, 453,000 cases of *C difficile* and 29,000 associated deaths were reported by the Centers for Disease Control and Prevention (CDC) ([Lessa, 2015](#)). The most important risk factor is antibiotic use, and the highest risk is with aminopenicillins, [clindamycin](#), cephalosporins, and fluoroquinolones. Other risk factors include inflammatory bowel disease, immunosuppression, advanced age, and gastrointestinal surgery. Most cases are hospital-acquired, however, community-acquired cases are becoming common ([Leffler, 2015](#)). With severe colitis, the infection-related mortality rate is 5 percent.

Diagnosis is by enzyme immunoassay for toxins in the stool, or by DNA-based tests that identify toxin genes. Only patients with diarrhea should be tested, and posttreatment testing is not recommended. Prevention is by soap-and-water hand washing, and infected individuals are isolated.

Treatment is oral [vancomycin](#) or [metronidazole](#). The risk of recurrence after an initial episode is 20 percent. Fecal microbial transplantation may become standard for recurrent clostridial colitis.

Inflammatory Bowel Disease

Two presumably noninfectious forms of intestinal inflammation are ulcerative colitis and Crohn disease. Differentiation between these is important because treatment differs. That said, they both share common features, and sometimes are indistinguishable if Crohn disease involves the colon. The salient clinical and laboratory features shown in [Table 54-5](#) permit a reasonably confident diagnostic differentiation in most cases. The etiopathogenesis is enigmatic in both, but a genetic predisposition is suspected. Inflammation is thought to result from dysregulated mucosal immune function in response to commensal microbiota, with or without an autoimmune component ([Friedman, 2015](#)).

TABLE 54-5

Some Shared and Differentiating Characteristics of Inflammatory Bowel Disease

	Ulcerative Colitis	Crohn Disease
Shared Characteristics		
Hereditary	More than 100 disease-associated genetic loci—a third shared; Jewish predominance; familial in 5–10% of cases; Turner syndrome; immune dysregulation	
Other	Chronic and intermittent with exacerbations and remissions; extraintestinal manifestations: arthritis, erythema nodosum, uveitis	
Differentiating Characteristics		
Major symptoms	Diarrhea, tenesmus, rectal bleeding, cramping pain; chronic, intermittent	<u>Fibros</u> tenotic—recurrent RLQ colicky pain; fever <u>Fistulizing</u> —cutaneous, bladder, interenteric
Bowel involvement	Mucosa and submucosa of large bowel; usually begins at rectum (40% proctitis only); continuous disease	Deep layers small and large bowel; commonly transmural; discontinuous involvement; strictures and fistulas
Endoscopy	Granular and friable erythematous mucosa; rectal involvement	Patchy; rectum spared; perianal involvement
Serum antibodies	Antineutrophil cytoplasmic (pANCA) ~70%	Anti- <i>S cerevisiae</i> ~50%
Complications	Toxic megacolon; strictures; arthritis; cancer (3–5%)	Fistulas; arthritis; toxic megacolon
Management	Medical; proctocolectomy curative	Medical; segmental and fistula resection

RLQ = right lower quadrant; *S cerevisiae* = *Saccharomyces cerevisiae*.

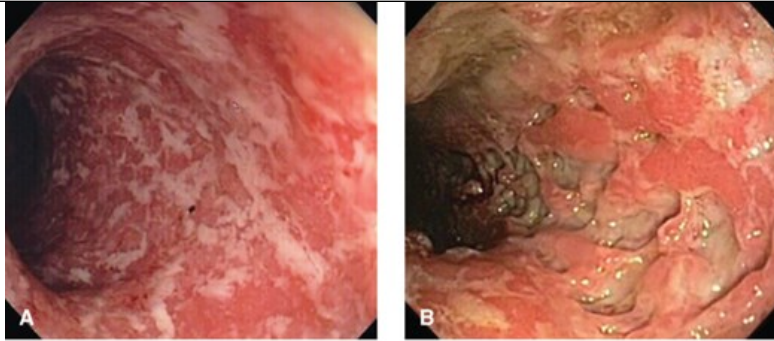
Data from [Friedman, 2015](#); [Lichtenstein, 2009](#); [Podolsky, 2002](#).

Ulcerative Colitis

This is a mucosal disorder with inflammation confined to the superficial luminal layers of the colon. It typically begins at the rectum and extends proximally for a variable distance. In approximately 40 percent of cases, disease is confined to the rectum and rectosigmoid, but 20 percent have pancolitis. For unknown reasons, prior appendectomy protects against development of ulcerative colitis ([Friedman, 2015](#)). Endoscopic findings include mucosal granularity and friability that is interspersed with mucosal ulcerations and a mucopurulent exudate ([Fig. 54-2](#)).

FIGURE 54-2

Causes of colitis. **A.** Chronic ulcerative colitis with diffuse ulcerations and exudates. **B.** Crohn colitis with deep ulcers. (Reproduced with permission from Song LM, Topazian M: Gastrointestinal endoscopy. Kasper DL, Fauci AS, Hauser SL, et al (eds): Harrison's Principles of Internal Medicine, 19th ed. New York: McGraw-Hill Education; 2015.)



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Major symptoms of ulcerative colitis include diarrhea, rectal bleeding, tenesmus, and abdominal cramps. The disease can be acute or intermittent and is characterized by exacerbations and remissions. *Toxic megacolon* and catastrophic hemorrhage are particularly dangerous complications that may necessitate colectomy. *Extraintestinal manifestations* include arthritis, uveitis, and erythema nodosum. Another serious problem is that the risk of colon cancer approaches 1 percent per year. With either ulcerative colitis or Crohn disease, there is also concern for possible increased risks for venous thromboembolism (Kappelman, 2011; Novacek, 2010).

Crohn Disease

Also known as regional enteritis, Crohn ileitis, and granulomatous colitis, Crohn disease has more protean manifestations than ulcerative colitis. It involves not only the bowel mucosa but also the deeper layers, and sometimes involvement is transmural (see Fig. 54-2). Lesions can be seen throughout the entire gastrointestinal tract, from the mouth to the anus, but it typically is segmental (Friedman, 2015). Approximately 30 percent of patients have small-bowel involvement, 25 percent have isolated colonic involvement, and 40 percent have both, usually with the terminal ileum and colon involved. Perianal fistulas and abscesses develop in a third of those with colonic involvement.

Symptoms depend on which bowel segment(s) is involved. Thus, complaints may include lower-right-sided cramping abdominal pain, diarrhea, weight loss, low-grade fever, and obstructive symptoms. The disease is chronic with exacerbations and remissions, and importantly, it cannot be cured medically or surgically. Approximately a third of patients require surgery within the first year after diagnosis, and thereafter, 5 percent per year. Reactive arthritis is common, and the gastrointestinal cancer risk, although not as great as with ulcerative colitis, is increased substantially.

Inflammatory Bowel Disease and Fertility

Subfertility is commonly linked to chronic medical disease, but Mahadevan (2006a) cited a normal fertility rate for inflammatory bowel disease unless severe disease warranted surgery. Similarly, Alstead (2003) reported that decreased female fertility from active Crohn disease returned to normal with remission. For women requiring surgical resection, laparoscopic anastomosis has a higher subsequent fertility rate (Beyer-Berjot, 2013). With colectomy, however, even though fertility is improved, up to half of women will be persistently infertile (Bartels, 2012). Sexual function and fertility are only modestly affected by ileal pouch-anal anastomosis (Hor, 2016). Subfertility may also be partially due to sulfasalazine, which causes reversible sperm abnormalities (Feagins, 2009).

Inflammatory Bowel Disease and Pregnancy

Because ulcerative colitis and Crohn disease are relatively common in young women, they are encountered with some frequency in pregnancy. In this regard, a few generalizations can be made. First, consensus supports that pregnancy does not increase the likelihood of an inflammatory bowel disease flare (Mahadevan, 2015). Indeed, in a 10-year surveillance of women in the European Collaborative on Inflammatory Bowel Disease, the likelihood of a flare during pregnancy was decreased compared with the preconceptional rate (Riis, 2006). Although most women with quiescent disease in early pregnancy do not have relapses, when a flare develops, it may be severe. Also, active disease in early pregnancy increases the likelihood of poor pregnancy outcome, which is discussed subsequently. In general, most usual treatment regimens may be continued during pregnancy. Diagnostic evaluations should be undertaken if needed to direct management, and surgery should be performed if indicated. For women who successfully complete pregnancy, about half experience improvement in their health-related quality of life (Ananthakrishnan, 2012).

At first glance, it appears that adverse pregnancy outcomes are increased with inflammatory bowel disease (Boyd, 2015; Cornish, 2012; Getahun, 2014).

Initially, this was attributed to the fact that most studies included women with either form of disease. Specifically, Crohn disease was noted to be linked to excessive morbidity ([Dominitz, 2002](#); [Stephansson, 2010](#)). But, according to [Reddy \(2008\)](#) and others, these adverse outcomes were in women with severe disease and multiple recurrences. Indeed, in the prospective European case-control *ECCO-EpiCom study* of 332 pregnant women with inflammatory bowel disease, [Bortoli and coworkers \(2011\)](#) found similar outcomes in women with ulcerative colitis or Crohn disease compared with normally pregnant women. Importantly, perinatal mortality rates are not appreciably increased.

Ulcerative Colitis and Pregnancy

Ulcerative colitis does not significantly alter the course of pregnancy in affected women. In one review of 755 pregnancies, colitis that was quiescent at conception worsened in approximately a third of pregnancies ([Fonager, 1998](#)). In women with active disease at the time of conception, approximately 45 percent worsened, 25 percent remained unchanged, and only 25 percent improved. These observations are similar to those previously described in an extensive review by [Miller \(1986\)](#) and a later report from [Oron and colleagues \(2012\)](#).

Osteoporosis is a significant complication in up to a third of these women, and thus vitamin D—800 IU daily—and calcium—1200 mg daily—are given. [Folic acid](#), 4 mg orally daily, is recommended preconceptionally and during the first trimester for neural-tube defect prevention. This high dose counteracts the antifolate actions of [sulfasalazine](#). Flares may be caused by psychogenic stress, and reassurance is important.

Management for colitis for the most part mirrors that outside of pregnancy. Treatment of active colitis and maintenance therapy incorporate drugs that deliver 5-aminosalicylic acid (5-ASA) or [mesalamine](#). [Sulfasalazine](#) (*Azulfidine*) is the prototype, and its 5-ASA moiety inhibits prostaglandin synthase in colonic mucosa. Others include [olsalazine](#) (*Dipentum*), [balsalazide](#) (*Colazal*), and delayed-release 5-ASA derivatives (*Apriso*, *Asacol*, *Pentasa*, *Lialda*). Glucocorticoids are given orally, parenterally, or by enema for moderate or severe disease that does not respond to 5-ASA. However, these latter drugs are not given for maintenance therapy. Recalcitrant disease is managed with immunomodulating drugs, including [azathioprine](#), 6-mercaptopurine, or [cyclosporine](#), which appear relatively safe in pregnancy ([Briggs, 2015](#); [Mozaffari, 2015](#)). Importantly, [methotrexate](#) is contraindicated in pregnancy.

In the past, biological therapy was reserved for recalcitrant moderate to severe disease. Because of their considerable efficacy, these medications are now frequently given *initially* for severe disease to prevent future complications. These agents are antibodies against tumor necrosis factor-alpha (TNF-alpha). Those approved for treatment of ulcerative colitis include [infliximab](#) (*Remicade*), [adalimumab](#) (*Humira*), and [golimumab](#) (*Simponi*). These drugs are administered intravenously or subcutaneously. Several studies indicate that they are safe for use in pregnancy, although there are concerns that their discontinuance may prompt a relapse ([Torres, 2015](#)). Another worry is that they may cause immunosuppression in the neonate ([Bröms, 2016](#); [Diav-Citrin, 2014](#); [Gisbert, 2013](#)).

Colorectal endoscopy is performed as indicated ([Katz, 2002](#)). During pregnancy, colectomy and ostomy creation for fulminant colitis may be needed as a lifesaving measure, and it has been described during each trimester. [Dozois \(2006\)](#) reviewed 42 such cases and found that, in general, outcomes have been good in recent reports. Most women underwent partial or complete colectomy, but [Ooi and colleagues \(2003\)](#) described decompression colostomy with ileostomy in a 10- and a 16-week pregnancy. Parenteral nutrition discussed in [Upper Gastrointestinal Tract Disorders](#) is occasionally necessary for women with prolonged exacerbations.

For women with an ileal pouch and an anal anastomosis performed before pregnancy, sexual function and fertility are improved ([Cornish, 2007](#)). Disadvantages that temporarily worsen in pregnancy include frequent bowel movements, fecal incontinence, and pouchitis. The last is an inflammatory condition of the ileoanal pouch probably due to bacterial proliferation and stasis. Pouchitis usually responds to cephalosporins or [metronidazole](#). In one rare case, adhesions to the growing uterus led to ileal pouch perforation ([Aouthmany, 2004](#)).

Women who have had a prior proctocolectomy and ileal pouch–anal anastomosis can be safely delivered vaginally ([Ravid, 2002](#)). [Hahnloser \(2004\)](#) reviewed routes of delivery in women with 235 pregnancies before and 232 pregnancies after ileoanal pouch surgery. Functional outcomes were similar, and it was concluded that cesarean delivery should be reserved for obstetrical indications. Postcesarean delivery ileoanal pouch obstruction has been described ([Malecki, 2010](#)).

To reiterate, ulcerative colitis likely has minimal adverse effects on pregnancy outcome. [Modigliani \(2000\)](#) reviewed perinatal outcomes in 2398 pregnancies and reported them to be not substantively different from those in the general obstetrical population. Specifically, the incidences of spontaneous abortion, preterm delivery, and stillbirth were remarkably low. In a population-based cohort study of 107 women from Washington state, perinatal outcomes, with two exceptions, were similar to those of 1308 normal pregnancies ([Dominitz, 2002](#)). One exception was an inexplicably

increased incidence of congenital malformations. These authors and others also describe a cesarean delivery rate that was substantially increased compared with that for normal controls (Mahadevan, 2015). The previously described ECCO-EpiCom study reported similar outcomes in 187 gravidas with ulcerative colitis compared with normal pregnant controls (Bortoli, 2011).

Crohn Disease and Pregnancy

In general, Crohn disease activity during pregnancy is related to its status around the time of conception. In a cohort study of 279 pregnancies in 186 women whose disease was inactive at conception, a fourth relapsed during pregnancy (Fonager, 1998). In 93 with active disease at conception, however, two thirds either remained active or worsened. Miller (1986) had described similar findings from his earlier review, as did Oron and associates (2012).

Calcium, vitamin D, and folic acid supplementation mirror that for ulcerative colitis. For maintenance during asymptomatic periods, no regimen is universally effective. Sulfasalazine is effective for some, but the newer 5-ASA formulations are better tolerated. Prednisone therapy may control moderate to severe flares but is less effective for small-bowel involvement. Immunomodulators such as azathioprine, 6-mercaptopurine, and cyclosporine are used for active disease and for maintenance. These appear relatively safe during pregnancy (Briggs, 2015; Chande, 2015). As discussed in Chapter 12 (Antimicrobial Drugs and Immunosuppressant Medications), methotrexate, mycophenolate mofetil, and mycophenolic acid are contraindicated in pregnancy (Briggs, 2015; Food and Drug Administration, 2008).

As with ulcerative colitis, treatment with antitumor necrosis factor monoclonal antibodies is often used initially for active Crohn disease and maintenance (Casanova, 2013; Cominelli, 2013; Friedman, 2015). These biological compounds include infliximab, adalimumab, certolizumab (Cimzia), natalizumab (Tysabri), and vedolizumab (Entyvio). As discussed in Inflammatory Bowel Disease and Fertility, this class of immunomodulators is considered safe in pregnancy (Briggs, 2015; Clowse, 2015). Their discontinuance may be followed by a relapse (Torres, 2015).

Endoscopy or conservative surgery is indicated for complications. Patients with small-bowel involvement are more likely to require surgery for complications that include fistulas, strictures, abscesses, and intractable disease. An abdominal surgical procedure was required during 5 percent of pregnancies described by Woolfson (1990). Parenteral hyperalimentation has been used successfully during severe recurrences (Russo-Stieglitz, 1999). Those with an ileal loop colostomy may have significant problems. Women with a perianal fistula—unless these are rectovaginal—usually can undergo vaginal delivery without complications (Forsnes, 1999; Takahashi, 2007).

As discussed, the likelihood is greater that Crohn disease is associated with adverse pregnancy outcomes compared with ulcerative colitis (Stephansson, 2010). Outcomes are probably related to disease activities. In a case-control Danish study, Norgård (2007) reported a twofold risk of preterm births. Dominitz (2002) reported a two- to threefold increased risk for preterm delivery, low birthweight, fetal growth restriction, and cesarean delivery in 149 women with Crohn disease. Recall, however, that the prospective ECCO-EpiCom study found outcomes to be similar to those for normal pregnancies.

Ostomy and Pregnancy

A colostomy or an ileostomy can be problematic during pregnancy because of its location (Hux, 2010). In a report of 82 pregnancies in 66 women with an ostomy, stomal dysfunction was common, but it responded to conservative management in most cases (Gopal, 1985). Surgical intervention was necessary, however, in three of six women who developed bowel obstruction and in another four with ileostomy prolapse—almost 10 percent overall. In this older study, only a third of 82 women underwent cesarean delivery, but Takahashi (2007) described six of seven cesarean deliveries in women with Crohn disease and a stoma. Although adhesions usually are involved with an obstructed ileostomy, the enlarging uterus may act to obstruct (Porter, 2014). Finally, Farouk and coworkers (2000) reported that pregnancy did not worsen long-term ostomy function.

Intestinal Obstruction

The incidence of bowel obstruction is not increased during pregnancy, although it generally is more difficult to diagnose. Meyerson (1995) reported a 20-year incidence of 1 in 17,000 deliveries at two Detroit hospitals. In one study, adhesive disease leading to small-bowel obstruction was the second most common cause of an acute abdomen in pregnancy following appendicitis—15 versus 30 percent, respectively (Unal, 2011). Approximately half of cases are due to adhesions from previous pelvic surgery that includes cesarean delivery (Al-Sunaidi, 2006; Andolf, 2010; Lyell, 2011). Another 25 percent of bowel obstruction cases are caused by volvulus—sigmoid, cecal, or small bowel. These have been reported in late pregnancy or early puerperium (Bade, 2014; Biswas, 2006; Al Maksoud, 2015). Small-bowel obstruction has been reported in pregnancy following the currently popular

Roux-en-Y gastric bypass for weight loss (Bokslag, 2014; Wax, 2013). Intussusception is occasionally encountered (Bosman, 2014; Harma, 2011). Bowel obstruction subsequent to colorectal surgery for cancer was increased threefold in women who had open versus laparoscopic surgery (Hagggar, 2013). Finally, Serra and colleagues (2014) described a massive ventral hernia with intestinal obstruction.

Most cases of intestinal obstruction during pregnancy result from pressure of the growing uterus on intestinal adhesions. According to Davis and Bohon (1983), this more likely occurs around midpregnancy when the uterus becomes an abdominal organ; in the third trimester when the fetal head descends; or immediately postpartum when uterine size acutely shrinks. Perdue (1992) reported that 98 percent of affected pregnant women had either continuous or colicky abdominal pain, and 80 percent had nausea and vomiting. Abdominal tenderness was found in 70 percent, and abnormal bowel sounds noted in only 55 percent. Plain abdominal radiographs following soluble contrast showed evidence of obstruction in 90 percent of women (Fig. 54-3). Plain radiographs, however, are less accurate for diagnosing small-bowel obstruction, and we and others have found that CT and MR imaging can be diagnostic (Biswas, 2006; Essilfie, 2007; McKenna, 2007). Colonoscopy can be both diagnostic and therapeutic for colonic volvulus (Dray, 2012; Khan, 2012).

FIGURE 54-3

Characteristic “bent inner tube” seen with sigmoid volvulus on abdominal radiograph. (Reproduced with permission from Song LM, Topazian M: Gastrointestinal endoscopy. Kasper DL, Fauci AS, Hauser SL, et al (eds): Harrison’s Principles of Internal Medicine, 19th ed. New York: McGraw-Hill Education; 2015.)



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During pregnancy, mortality rates with obstruction can be excessive because of difficult and thus delayed diagnosis, reluctance to operate during pregnancy, and the need for emergency surgery (Firstenberg, 1998; Shui, 2011). In an older report of 66 pregnancies, *Perdue and associates* (1992) described a 6-percent maternal mortality rate and 26-percent fetal mortality rate. Two of the four women who died were in late pregnancy, and they had bowel perforation from sigmoid or cecal volvulus caused by adhesions.

Colonic Pseudo-obstruction

Also known as *Ogilvie syndrome*, pseudo-obstruction is caused by adynamic colonic ileus. It is characterized by massive abdominal distention with cecal and right-hemicolon dilatation. Approximately 10 percent of all cases are associated with pregnancy, and its frequency has been reported as high as 1 in 1500 deliveries (Reeves, 2015). The syndrome usually develops postpartum—most commonly after cesarean delivery—but it has been reported antepartum (Tung, 2008). Rarely, the large bowel may rupture (Singh, 2005). Treatment with an intravenous infusion of neostigmine, 2 mg, usually results in prompt decompression (Song, 2015). In some cases, colonoscopic decompression is performed, and laparotomy is needed for perforation (De Giorgio, 2009; Rawlings, 2010).

Appendicitis

The lifetime incidence for appendicitis ranges from 7 to 10 percent (Flum, 2015). Thus, it is not surprising that an evaluation for possible appendicitis is relatively common during pregnancy. Theilen and colleagues (2015) studied 171 such women during a 5-year period, but only 12 women ultimately were found to have pathologically confirmed appendicitis. After clinical and imaging evaluation, the frequency of suspected appendicitis is much lower and that of confirmed appendicitis in more than 8 million women ranged from 1 in 1000 to 1 in 5500 births (Abbasi, 2014; Hée, 1999; Mazze, 1991).

It is repeatedly—and appropriately—emphasized that pregnancy makes the diagnosis of appendicitis more difficult. Nausea and vomiting accompany normal pregnancy, but also, as the uterus enlarges, the appendix commonly moves upward and outward from the right lower quadrant (Baer, 1932; Erkek, 2015; Pates, 2009). Another often-stated reason for late diagnosis is that some degree of leukocytosis accompanies normal pregnancy. For these and other reasons, pregnant women—especially those late in gestation—frequently do not have clinical findings “typical” for appendicitis. Thus, it commonly is confused with cholecystitis, labor, pyelonephritis, renal colic, placental abruption, or uterine leiomyoma degeneration.

Most reports indicate increasing morbidity and mortality rates with advancing gestational age. And as the appendix is progressively deflected upward by the growing uterus, omental containment of infection becomes increasingly unlikely. It is indisputable that appendiceal perforation is more common during later pregnancy (Abbasi, 2014). In the studies by Andersson (2001) and Ueberrueck (2004), the incidence of perforation was approximately 8, 12, and 20 percent in successive trimesters.

Diagnosis

Persistent abdominal pain and tenderness are the most reproducible findings. Right-lower quadrant pain is the most frequent, although pain migrates upward with appendiceal displacement (Mourad, 2000). For initial evaluation, sonographic abdominal imaging is reasonable in suspected appendicitis, even if to exclude an obstetrical cause of pain (Butala, 2010). That said, *graded compression sonography* is difficult because of cecal displacement and uterine imposition (Pedrosa, 2009). *Appendiceal computed tomography* is more sensitive and accurate than sonography to confirm suspected appendicitis (Katz, 2012; Raman, 2008). Specific views can be designed to diminish fetal radiation exposure (Chap. 46, *Computed Tomography*). It is generally accepted that when available, MR imaging is the preferred modality for evaluation of suspected appendicitis in pregnancy (Fig. 54-4). MR imaging has high diagnostic yield and accuracy, and it also provides alternative diagnoses (Fonseca, 2014; Theilen, 2015). One metaanalysis cited positive- and negative-predictive values for MR imaging of 90 and 99.5 percent, respectively (Blumenfeld, 2011). Burke and associates (2015) reported similar findings. Using a decision-analysis model, CT and MR imaging were found to be cost effective (Kastenberg, 2013). This was verified in the clinical study of more than 7000 cases reported by Fonseca and coworkers (2014).

FIGURE 54-4

Anterior-posterior magnetic resonance image of a periappendiceal abscess in a midtrimester pregnancy. The abscess is approximately 5 × 6 cm, and the appendiceal lumen (arrow) is visible within the right-lower quadrant mass. The gravid uterus is seen to the right of this mass.



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Management

When appendicitis is suspected, treatment is prompt surgical exploration. Although diagnostic errors may lead to removal of a normal appendix, surgical evaluation is preferable to postponed intervention and generalized peritonitis (Abbasi, 2014). In earlier reports, the diagnosis was verified in only 60 to 70 percent of pregnant women. As indicated above, however, with CT and MR imaging, these figures have improved (Blumenfeld, 2011; Theilen, 2015). Still and importantly, the accuracy of diagnosis is inversely proportional to gestational age.

Currently, laparoscopy is almost always used to treat suspected appendicitis during the first two trimesters. In a report from a Swedish database of nearly 2000 laparoscopic appendectomies, perinatal outcomes were similar to those of more than 1500 open laparotomies done before 20 weeks' gestation (Reedy, 1997). Conversely, in their review, Wilasrusmee and coworkers (2012) reported a higher rate of fetal loss with laparoscopy. Authors of a more recent systematic review indicate that the level of evidence is not strong enough to demonstrate a preferred approach to appendectomy. They concede that laparoscopy may be associated with a higher risk of miscarriage (Walker, 2014). It has evolved that in many centers, laparoscopic appendectomy is also performed in most cases during the third trimester (Donkervoort, 2011). This is encouraged by the Society of American Gastrointestinal and Endoscopic Surgeons (Pearl, 2017; Soper, 2011). That said, most are of the opinion that laparoscopic surgery in pregnancy after 26 weeks' gestation should be performed only by the most experienced endoscopic surgeons (Parangi, 2007).

Before exploration, intravenous antimicrobial therapy is begun, usually with a second-generation cephalosporin or third-generation penicillin. Unless there is gangrene, perforation, or a periappendiceal phlegmon, antimicrobial therapy can usually be discontinued after surgery. Without generalized peritonitis, the prognosis is excellent. Seldom is cesarean delivery indicated at the time of appendectomy. Uterine contractions are common, and although some clinicians recommend tocolytic agents, we do not. De Veciana (1994) reported that tocolytic use substantially increased the risk for pulmonary-permeability edema caused by sepsis syndrome (Chap. 47, *Acute Pulmonary Edema*).

Antimicrobial versus Surgical Treatment

Because of European studies, some have advocated that many cases of appendicitis can be treated successfully with intravenous antimicrobials alone (Flum, 2015; Joo, 2017). At this time, we discourage this practice until appropriate studies have been done with pregnant women. In one study, 6 percent of pregnant women with appendicitis were treated medically, and these gravidas had "considerably" elevated risks for septic shock, peritonitis, and venous thromboembolism compared with surgically managed cases (Abbasi, 2014).

Pregnancy Outcomes

Appendicitis increases the likelihood of abortion or preterm labor, especially if peritonitis has developed. In two studies, spontaneous labor after 23

weeks ensued with greater frequency following surgery for appendicitis compared with surgery for other indications (Cohen-Kerem, 2005; Mazze, 1991). In one study, the fetal loss rate was 22 percent if surgery was performed after 23 weeks' gestation. Two large population-based studies attest to the adverse outcomes from appendicitis in pregnancy. From the California Inpatient File of 3133 pregnant women undergoing surgery for suspected appendicitis, the fetal loss rate was 23 percent, and it was doubled—6 versus 11 percent—with simple versus complicated disease (McGory, 2007). A nationwide study from Taiwan found that risks for low birthweight and preterm delivery rose 1.5- to 2-fold when outcomes in 908 women with acute appendicitis were compared with those of controls (Wei, 2012).

Long-term complications are not common. The possible link between sepsis and neonatal neurological injury has not been verified (Mays, 1995). Finally, appendicitis during pregnancy does not appear to be associated with subsequent infertility (Viktrup, 1998).

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