Almost all women will experience pain during pregnancy. Common musculoskeletal conditions can cause severe pain in an otherwise uncomplicated pregnancy. Some women will enter pregnancy with preexisting painful disorders, and management of the ongoing pain and painful exacerbations can be challenging. This chapter reviews the common painful musculoskeletal conditions of pregnancy and an approach to the management of chronic pain during pregnancy and in breastfeeding mothers.

**USE OF MEDICATIONS DURING PREGNANCY**

Medical management of pregnant patients should begin with attempts to minimize the use of all medications and use nonpharmacologic therapies whenever possible. When opting for drug therapy, the clinician must consider any potential for harm to the mother, the fetus, and the course of the pregnancy. The degree of protein binding and lipid solubility of the medication, the speed of maternal metabolism, and molecular weight all affect placental transfer of medications from mother to fetus. With the exception of large polar molecules (such as heparin and insulin), as well as ionized molecules (glycopyrrolate), almost all medications will reach the fetus to some degree.

Approximately 3% of newborns will have a significant congenital malformation. Only 25% of fetal malformations have a known genetic cause, and just 2% to 3% have a clear environmental link, such as maternal medication exposure during organogenesis. One of the major limitations in evaluating any medication’s potential for causing harm to a developing human fetus is the degree of species specificity for congenital defects. A classic example of such specificity is the drug thalidomide; nonprimate studies revealed no teratogenic effects, but severe limb deformities occurred in human offspring when thalidomide was prescribed during pregnancy.

The most critical period for minimizing maternal drug exposure is during early development, from conception through the 10th menstrual week of pregnancy (the 10th week following the start of the last menstrual cycle). Drug exposure before organogenesis (prior to the fourth menstrual week) usually causes an all-or-none effect—the embryo either does not survive or develops without abnormalities. Drug effects later in pregnancy typically lead to single- or multiple-organ involvement, developmental syndromes, or intrauterine growth retardation. Certain medications may not influence fetal organ development directly but have the potential to influence the physiology of pregnancy adversely. For example, nonsteroidal anti-inflammatory drugs (NSAIDs) may delay the onset of labor, decrease amniotic fluid volume, or place a newborn at risk for pulmonary hypertension or renal injury.

The U.S. Food and Drug Administration (FDA) has developed a five-category labeling system for all approved drugs in the United States (Table 35.1). This labeling system rates the potential risk for teratogenic or embryotoxic effects based on available scientific and clinical evidence. It is important to note that the FDA classification system has been revised to address neonatal influences other than teratogenicity. For example, ibuprofen is associated with decreased amniotic fluid and constriction of the ductus arteriosus. In fact, many NSAIDs used to be class B before 30 weeks and class D after 30 weeks. More recently, this has changed to class C before 30 weeks and class D thereafter. Because few medications have undergone large-scale testing during human pregnancy, most are category C, which indicates incomplete knowledge of the potential for benefit and harm with drug therapy. More specifically, our present knowledge about the adverse effects of uncontrolled pain, as well as the risks associated with administering medications during pregnancy, remains incomplete, and the physician is left to weigh the risks against the benefits of instituting pharmacologic therapy for each individual.

**USE OF MEDICATIONS IN BREAST-FEEDING MOTHERS**

The same physicochemical properties that facilitate transplacental drug transfer affect drug accumulation in breast milk. High lipid solubility, low molecular weight, minimal protein binding, and the un-ionized state all facilitate excretion of medications into breast milk. The neonatal dose of most medications obtained through breastfeeding is 1% to 2% of the maternal dose. Even with minimal exposure via breast milk, neonatal drug allergy and slower infant drug metabolism must be considered. Only small amounts of colostrum are excreted during the first few postpartum days; thus, early breastfeeding poses little risk to an infant whose mother received medications during delivery.

Most breast milk is synthesized and excreted during and immediately following breastfeeding. Taking medications after breastfeeding or when the infant has the longest interval between feedings and avoidance of long-acting medications will minimize drug transfer via breast milk. However, effective treatment of chronic pain often necessitates the
use of long-acting medications, particularly long-acting opioids. To aid physicians in drug selection and to provide advice to lactating mothers, the American Academy of Pediatrics has categorized medications in relation to the safety of ingestion by breastfeeding mothers (Table 35.2). Although many common pain medications are listed as category 3 (compatibility with breastfeeding), psychotropic medications, which are used frequently for the treatment of chronic pain, are category 2, for which the effects are unknown and caution is urged.

**Table 35.1 FDA Pregnancy Risk Classification for Pain Management Medications**

<table>
<thead>
<tr>
<th>FDA Classification</th>
<th>Definition</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category A</td>
<td>Controlled human studies have indicated no apparent risk to the fetus. The possibility of harm to the fetus seems remote.</td>
<td>Multivitamins</td>
</tr>
<tr>
<td>Category B</td>
<td>Animal studies have not indicated fetal risk or animal studies have indicated teratogenic risk, but well-controlled human studies have failed to demonstrate a risk.</td>
<td>Acetaminophen, caffeine, metoprolol, prednisolone, prednisone, aspirin, ketorolac, butorphanol, nalbuphine* codeine, fentanyl, hydrocodone, methadone, meperidine, morphine, oxycodone, oxymorphone* ibuprofen, naproxen, indomethacin† fluoxetine, duloxetine, gabapentin, pregabalin, lidocaine, mexiletine, nifedipine, propranolol, sumatriptan, amitriptyline, imipramine, diazepam, paroxetine, phenobarbital, phenytoin, valproic acid, ergotamine</td>
</tr>
<tr>
<td>Category C</td>
<td>Studies have indicated teratogenic or embryocidal risk in animals, but no controlled studies have been conducted in women; there have been no controlled studies in animals or humans.</td>
<td>Aspirin, ketorolac, butorphanol, nalbuphine* codeine, fentanyl, hydrocodone, methadone, meperidine, morphine, oxycodone, oxymorphone* ibuprofen, naproxen, indomethacin† fluoxetine, duloxetine, gabapentin, pregabalin, lidocaine, mexiletine, nifedipine, propranolol, sumatriptan, amitriptyline, imipramine, diazepam, paroxetine, phenobarbital, phenytoin, valproic acid, ergotamine</td>
</tr>
<tr>
<td>Category D</td>
<td>There has been positive evidence of human fetal risk, but in certain cases the benefits of the drug may outweigh the risks involved.</td>
<td>Aspirin, ketorolac, butorphanol, nalbuphine* codeine, fentanyl, hydrocodone, methadone, meperidine, morphine, oxycodone, oxymorphone* ibuprofen, naproxen, indomethacin† fluoxetine, duloxetine, gabapentin, pregabalin, lidocaine, mexiletine, nifedipine, propranolol, sumatriptan, amitriptyline, imipramine, diazepam, paroxetine, phenobarbital, phenytoin, valproic acid, ergotamine</td>
</tr>
<tr>
<td>Category X</td>
<td>There has been positive evidence of significant fetal risk, and the risk clearly outweighs any possible benefit.</td>
<td>Amitriptyline, imipramine, diazepam, paroxetine, phenobarbital, phenytoin, valproic acid, ergotamine</td>
</tr>
</tbody>
</table>

*All opioid analgesics are FDA risk category D if used for prolonged periods or in large doses near term.
†All nonsteroidal anti-inflammatory drugs are FDA risk category D after 30 weeks’ gestation.
FYD, U.S. Food and Drug Administration.

**MEDICATIONS COMMONLY USED FOR PAIN MANAGEMENT**

**NONSTEROIDAL ANTI-INFLAMMATORY DRUGS**

NSAIDs have both analgesic and anti-inflammatory properties and are commonly used for musculoskeletal pain. Although the exact mechanism of action is uncertain, NSAIDs decrease pain by acting as nonselective inhibitors of cyclooxygenase and thereby inhibiting prostaglandin synthesis. During pregnancy, prostaglandins modulate many key processes, including stimulating uterine activity, maintaining patency of the ductus arteriosus (essential for adequate intrauterine blood flow), and promoting fetal urine production (which contributes to the level of amniotic fluid in the second and third trimesters). As expected, alteration of prostaglandin metabolism then has varied effects on the pregnancy, depending on the timing and duration of use. For example, short-term use of indomethacin in the second trimester is effective for the treatment of pain caused by degenerating fibroids; use for long periods (more than 48 hours) in the third trimester has been associated with narrowing of the ductus arteriosus and oligohydramnios. To complicate this picture further, aspirin, the prototypical NSAID, is used in a therapeutic manner in low doses (80 to 160 mg/day) to decrease the incidence of pregnancy complications in certain high-risk groups but is associated with premature narrowing of the ductus arteriosus at higher doses. Therefore, NSAID use in pregnancy must be carefully planned to achieve the proposed benefit and avoid fetal risk. In general, if NSAID use is indicated, the duration should be short (less than 48 hours) in the absence of monitoring of fetal ductus flow and amniotic fluid volume. All NSAID use for pain should be discontinued by 34 weeks’ gestation to prevent pulmonary hypertension in the newborn.

NSAIDs are among the most frequently used drugs during the first trimester of pregnancy. Over-the-counter use of these medications is very common in this population. With their use so common, many women may not realize that there is a potential for deleterious effects on them or their developing fetuses. Further as the age of first-time
who filled prescriptions for NSAIDs in the first trimester births with congenital anomalies in 1056 women (8.8%) registry from 1997 to 2003 in Quebec, they identified 93 nont users of NSAIDs. Using a population-based pregnancy control study of the risk for congenital anomalies in pregnancy to date, Ostensen and Ostensen detailed a exposure and other congenital anomalies.18

There is controversy regarding the risk associated with maternal pulmonary hypertension in the newborn. However, there are well documented, and they are associated with premature narrowing of the ductus arteriosus, which can lead to pulmonary hypertension in the newborn. However, there is controversy regarding the risk associated with maternal exposure and other congenital anomalies.18

Table 35.2 Classification of Maternal Medication Use during Pregnancy

<table>
<thead>
<tr>
<th>Classification</th>
<th>Definition</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category 1</td>
<td>These medications should not be consumed during lactation. Strong evidence exists that serious adverse effects on the infant are likely with maternal ingestion of these medications during lactation.</td>
<td>Ergotamine</td>
</tr>
<tr>
<td>Category 2</td>
<td>Effects on human infants are unknown, but caution is urged.</td>
<td>Amitriptyline, desipramine, doxepin, fluoxetine, imipramine, trazodone, Diacepam, lorazepam, midazolam, Carbamazepine, phenytoin, valproate</td>
</tr>
<tr>
<td>Category 3</td>
<td>These medications are compatible with breastfeeding.</td>
<td>Atenolol, propranolol, diltiazem, Codeine, fentanyl, methadone, morphine, propoxyphene, Butorphanol, Lidocaine, mexiletine, Acetaminophen, Ibuprofen, indomethacin, ketorolac, naproxen, Caffeine</td>
</tr>
</tbody>
</table>


mothers increases, more women are likely to take NSAIDs for conditions such as joint and musculoskeletal pain. The effects of fetal exposure to NSAIDs in the third trimester are well documented, and they are associated with premature narrowing of the ductus arteriosus, which can lead to pulmonary hypertension in the newborn. However, there is controversy regarding the risk associated with maternal exposure and other congenital anomalies.18

There is no role for the routine use of NSAIDs for pain other than that related to rheumatologic disease or uterine fibroids. In the largest published series of NSAID use during pregnancy to date, Ostensen and Ostensen19 detailed a series of 88 women with rheumatic disease and compared the outcomes of 45 who received NSAID therapy during pregnancy with the outcomes of 43 who were not treated during pregnancy. The most common agents used were naproxen (23/45) and ibuprofen (8/45). NSAIDs were most frequently used during the first and second trimesters because many patients stopped therapy once pregnancy was recognized; many of the rheumatic conditions remitted later in pregnancy. They found no significant differences in pregnancy outcome (duration of pregnancy and labor, vaginal delivery rate, maternal bleeding requiring transfusion, or incidence of congenital anomalies) or the health status of offspring at long-term follow-up (ranging from 6 months to 14 years). The authors concluded that NSAID therapy limited to periods of active rheumatic disease until weeks 34 to 36 did not adversely affect the neonate.19 It is of note, however, that women with rheumatic disease have poor pregnancy outcomes in general, so these outcome data should not be applied to the general obstetric population.

More recently, Ofori and colleagues18 published a case-control study of the risk for congenital anomalies in pregnant users of NSAIDs. Using a population-based pregnancy registry from 1997 to 2003 in Quebec, they identified 93 births with congenital anomalies in 1056 women (8.8%) who filled prescriptions for NSAIDs in the first trimester of pregnancy versus 2478 in 35,331 (7%) women who did not. They concluded that there may be a greater risk of NSAID users having children with congenital anomalies, particularly those related to cardiac septal closure.

Despite the physiologic effects of NSAIDs, the results of the Collaborative Perinatal Project suggested that first-trimester exposure to aspirin does not pose appreciable teratogenic risk,20 nor does ibuprofen or naproxen, the most commonly used NSAIDs. Patients who conceive while taking NSAIDs can be reassured that this will not impair the outcome of the pregnancy. However, NSAIDs can interfere with implantation and placental circulation. In a population-based cohort study, the risk for miscarriage was 1.8 (95% confidence interval [CI] = 1.0 to 3.2) with any NSAID use and increased to 8.1 (95% CI = 2.8 to 23.4) if used for more than 1 week around the time of conception.21

Aspirin has well-known platelet-inhibiting properties and, theoretically, may increase the risk for peripartum hemorrhage. Neonatal platelet function is inhibited for up to 5 days after delivery in aspirin-treated mothers.22 Although low-dose aspirin therapy (60 to 80 mg/day) has not been associated with maternal or neonatal complications, higher doses appear to increase the risk for intracranial hemorrhage in neonates born before 35 weeks’ gestation.15 Low-dose aspirin has been used to improve pregnancy outcomes in women with both preeclampsia and antiphospholipid antibodies.23 However, as with other NSAIDs, aspirin crosses the placenta. Even though it has not been implicated in causing congenital abnormalities, it has been associated with an increased risk for vascular disruptions, particularly gastrochisis.23,24 Data from two retrospective meta-analyses suggest that there may be a twofold to threefold increased risk for gastrochisis with aspirin exposure.24,25 However, reassuring data from more than 30,000 women enrolled in randomized, controlled trials of low-dose aspirin versus placebo have not shown any significant risk for intraventricular hemorrhage, other neonatal bleeding, or poor pregnancy outcomes.25
Ketorolac is an NSAID available for oral and parenteral administration. According to the manufacturer’s prescribing information, ketorolac did not cause birth defects in the offspring of pregnant rabbits. However, ketorolac administration during labor did lead to dystocia in rodents. Ketorolac shares the platelet-inhibiting properties of other NSAIDs. Although ketorolac has not undergone evaluation for its effects on the fetal ductus arteriosus or renal vasculature, it is likely to have effects similar to those of other NSAIDs. Until more information is available, it may be prudent to choose the more extensively studied NSAIDs for use during pregnancy.

Based on our clinical experience and a review of the available literature, we have formulated guidelines for the use of NSAIDs during pregnancy (Box 35.1). NSAID use in pregnancy must be planned carefully to achieve benefit and avoid fetal risk. In general, if NSAID use is indicated, the duration should be short (48 hours) in the absence of monitoring of fetal ductus flow and amniotic fluid volume. Chronic use of NSAIDs should be avoided in pregnancy, especially in the third trimester. Before the 24th week of pregnancy, NSAIDs should be used with caution. It is preferable to use both low-dose and short-half-life NSAIDs.

Because of the antiplatelet properties of NSAIDs, many anesthesiologists are concerned about the risk for epidural hematoma formation as a result of epidural catheter placement. To date, there are no outcome studies on which to base recommendations. There is no evidence that low-dose aspirin therapy or the use of other NSAIDs increases the risk for epidural hematoma formation following spinal or epidural placement. As part of our routine history and physical examination of parturients, we screen for any evidence of bleeding diathesis or easy bruising and, in their absence, proceed with epidural placement without further laboratory testing. This practice is consistent with the guidelines published by the American Society of Regional Anesthesia.

In breastfeeding women, salicylate transport into breast milk is limited by its highly ionized state and high degree of protein binding. Caution should still be exercised if more than occasional or short-term aspirin use is contemplated during lactation because neonates have very slow elimination of salicylates. High-dose aspirin can lead to rashes, platelet abnormalities, and bleeding in nursing infants. The American Academy of Pediatrics considers diclofenac, flufenamic acid, ibuprofen, indomethacin, naproxen, ketorolac, piroxicam, and tolmetin to be compatible with breastfeeding. Both ibuprofen and naproxen are also minimally transported into breast milk and are considered compatible with breastfeeding; these agents are generally better tolerated than indomethacin. Little information is available on the safety of maternal ketorolac use during lactation. One study found that ketorolac concentrations ranged from 1% to 4% of maternal serum levels in breast milk. Analysis of breast milk in 10 women given ketorolac, 10 mg orally every 6 hours for 4 days, resulted in clinically insignificant levels that the nursing infant would be exposed to. Taking into account the bioavailability of ketorolac after oral administration, this would probably result in neonatal blood levels between 0.16% and 0.40% of the maternal dose. The American Academy of Pediatrics considers ketorolac to be compatible with breastfeeding.

Acetaminophen is a analgesic and antipyretic drug used frequently by pregnant women. It provides similar analgesia without the anti-inflammatory effects seen with NSAIDs. Acetaminophen has no known teratogenic properties, does not inhibit prostaglandin synthesis or platelet function, and is hepatotoxic only in extreme overdosage. As with most drugs, there are no controlled studies in pregnant women in the first trimester. In animal studies, acetaminophen has not demonstrated fetal risk. Data obtained from 88,142 patients in the Danish National Birth Cohort (1996 to 2003) who had information on acetaminophen use during the first trimester of pregnancy indicated that ingestion of acetaminophen during pregnancy is not related to an overall increased prevalence of congenital abnormalities or to an increased prevalence of the most frequent abnormalities. If persistent pain demands use of a mild analgesic during pregnancy, acetaminophen appears to be a safe and effective first-choice agent. Acetaminophen does enter breast milk, although maximal neonatal ingestion would be less than 2% of a maternal dose. Acetaminophen is considered compatible with breastfeeding.

### OPIOID ANALGESICS

Many women of childbearing age are prescribed opioids for the management of intermittent or continual pain. In the United States, more than half of pregnancies are unplanned, which can lead to fetal medication exposure before a woman knows that she is pregnant. Much of our present knowledge about the effects of chronic opioid exposure during pregnancy is derived from the study of opioid-abusing patients. Chronic opioid use in pregnancy is associated with low birth weight and decreased head circumference, although the contribution of comorbid conditions, including polysubstance abuse and smoking, is not clear. Enrollment and compliance with methadone therapy for opioid dependence improve birth weight and prolong gestation, thus supporting the role of therapy during gestation.

Until recently there was no evidence to suggest a relationship between exposure to any of the opioid agonists or agonist-antagonists during pregnancy and large categories of major abnormalities.
or minor malformations. The Collaborative Perinatal Project monitored 50,282 mother-child pairs and studied exposure to codeine, propoxyphene, hydrocodone, meperidine, methadone, morphine, and oxycodone. Only codeine was found to have an association with malformation (respiratory), but this has not been confirmed by other studies. No evidence was found for either agent to suggest a relationship to large categories of major or minor malformations. In spring 2011, a study by Broussard and colleagues used data gathered from the National Birth Defects Prevention Study (1997 to 2005), which consisted of an ongoing multisite, population-based, case-control study of more than 30 types of major structural birth defects. They reported that opioid treatment from 1 month before pregnancy through the first trimester was associated with a greater risk for conoventricular septal defects, atrophicventricular septal defects, hypoplastic left heart syndrome, spina bifida, and gastrochisis. Codeine and hydrocodone represented 69% of all reported exposures. However, these results should be interpreted with caution because some sample sizes were borderline and further investigation is necessary. It is important to understand that the increased relative risk for a rare birth defect with exposure to medications usually translates into only a modest absolute increase in risk above baseline. All opioid analgesics are now teratogenic risk category C when used for a short time. It is critical that health care providers weigh the risks and benefits when prescribing opioids to pregnant women or to those of childbearing age.

It is important to note that all opioid medications are risk category D when used for long periods during pregnancy. This increased risk warning is due to the potential for neonatal opioid dependence when mothers are treated with opioid medications for prolonged periods during pregnancy. Abrupt cessation of opioids by an opioid-dependent patient late in pregnancy can precipitate fetal withdrawal in utero, which is characterized by fetal tachycardia and fetal death. Therefore, pregnant women who are opioid dependent, regardless of whether use is prescription or illicit, should not undergo acute withdrawal late in pregnancy without careful fetal monitoring. The general recommendation is to offer continuation of narcotic medication (for prescription use) or opioid substitution therapy such as methadone or buprenorphine plus entry into treatment programs for women using illicit drugs. Additional benefits of treatment programs include improved prenatal care, higher birth weight, and reduction of infectious risk to the neonate. Neonates exposed to opioid medications in utero can develop dependence and manifest withdrawal symptoms in the first few days of life, known as neonatal abstinence syndrome (NAS). Although NAS is characterized by irritability and increased tone in mild cases, severe neonatal withdrawal is associated with poor feeding and seizures. NAS occurs in 30% to 90% of infants exposed to heroin, methadone, or buprenorphine in utero when mothers are treated for illicit opioid use. Patients requiring methadone for the treatment of chronic pain tend to require lower doses of methadone, and their infants have a lower incidence of NAS, approximately 11%. Most infants who undergo narcotic withdrawal are symptomatic by 48 hours postpartum, but there are reports of withdrawal symptoms beginning 7 to 14 days postpartum. Neonates with prenatal exposure to opioids for long periods may require very slow weaning (as slow as a 10% reduction every third day) to prevent withdrawal symptoms. The American Academy of Pediatrics considers methadone to be compatible with breastfeeding.

Recognition of infants at risk for NAS and institution of appropriate supportive and medical therapy typically result in little short-term consequence to the infant. The long-term effects of in utero opioid exposure are unknown. Chasnoff considered the environmental and socioeconomic factors that influence child development and concluded that no definitive data demonstrate long-term developmental sequelae from in utero opioid exposure.

Buprenorphine, a partial µ-opioid agonist and κ-opioid antagonist, is currently used for office-based treatment of opioid dependence but is increasing in use for the treatment of chronic pain. Obstetricians and anesthesiologists will therefore encounter patients treated with buprenorphine with increasing frequency. This drug’s low intrinsic receptor efficacy results in a ceiling effect and diminished risk for overdose when compared with methadone. Although methadone has been used for more than 40 years for the treatment of opioid dependence, buprenorphine has recently been advocated as first-line therapy. The literature reporting use of buprenorphine in pregnancy remains limited, but buprenorphine has been found to be superior to methadone in reducing signs of withdrawal in newborns, thus requiring less medication and hospitalization time for the babies. In a randomized, double-blind trial comparing 175 women and infants treated with methadone versus buprenorphine, infants who had prenatal exposure to buprenorphine required significantly less morphine for treatment of the infant may be required. In buprenorphine-maintained patients, though, acute pain can be difficult to treat because of the partial antagonist activity at the µ receptor. Whereas treatment of opioid dependence requires only once-daily dosing, opioid-dependent patients with mild pain who are receiving buprenorphine may attain analgesia simply by splitting the same daily dose into intervals of every 6 hours.

According to the drug manufacturer’s insert, buprenorphine is not recommended during breastfeeding; however, it appears to be safe. Because of low levels in breast milk, as well as poor oral bioavailability in infants, an infant is exposed to about 1% to 1.4% of the maternal weight-adjusted dose. Breast milk–induced addiction appears to be unlikely, and there is no reason to time breastfeeding to avoid peak levels of buprenorphine. The amount of buprenorphine in milk may not be sufficient to prevent neonatal withdrawal, and treatment of the infant may be required.

Fentanyl is one of the most common parenteral opioid analgesics administered during the perioperative period. As with all opioid analgesics, administration of fentanyl to the mother immediately before delivery may lead to respiratory depression in the newborn. Maternal administration of fentanyl or other opioids may also cause loss of the normal variability in fetal heart rate. Loss of fetal heart rate variability can signal fetal hypoxemia, so administration of opioids during labor may deprive obstetric caregivers of a useful tool for assessing fetal well-being.
Meperidine undergoes extensive hepatic metabolism to normeperidine, which has a long elimination half-life (18 hours). Repeated dosing can lead to accumulation, especially in patients with renal insufficiency. Normeperidine causes excitation of the central nervous system manifested as tremors, myoclonus, and generalized seizures. Significant accumulation of normeperidine is unlikely in a parturient who receives single or infrequent doses; however, meperidine offers no advantages over other parenteral opioids.

Although mixed agonist-antagonist opioid analgesic agents are widely used to provide analgesia during labor, they do not appear to offer any advantage over pure opioid agonists. In a blinded randomized comparison of meperidine and nalbuphine during labor, the two agents appeared to provide comparable analgesic effects, as well as similar neonatal Apgar and neurobehavioral scores. Use of nalbuphine or pentazocine during pregnancy can lead to NAS. Nalbuphine may also cause a sinusoidal fetal heart rate pattern after maternal administration, thereby complicating fetal assessment.

Low-affinity opioid agonists, such as tramadol (Ultram), are being used with increasing frequency, in part because of a perceived lessening of the abuse and addiction potential. There is no evidence that acute use of tramadol for labor analgesia has any advantages over more traditional opioids. According to the manufacturer’s prescribing information, no drug-related teratogenic effects were observed in the progeny of rats treated orally with combination tramadol and acetaminophen at 1.6 times the maximum human daily dose. However, at this dose embryo and fetal toxicity consisted of decreased fetal weight and increased supernumerary ribs. Tramadol administered intramuscularly to mothers in labor reaches the neonate almost freely, thus confirming a high degree of placental permeability. The neonate already possesses the complete hepatic capacity for metabolism of tramadol into its active metabolite, but renal elimination of the active tramadol metabolite M1 is delayed, in line with the slow maturation process of renal function in neonates. Neonates born to women who are chronically taking tramadol during pregnancy carry a risk for withdrawal. No studies have compared the relative rate of NAS with tramadol versus other opioid analgesics. Breastfeeding is of unknown risk when the mother is taking tramadol.

Postoperative analgesia for most pregnant women undergoing nonobstetric surgery can be provided readily with narcotic analgesics (Tables 35.3 and 35.4). Fentanyl, morphine, and hydromorphone are all safe and effective alternatives when a potent opioid is needed for parenteral administration. There are a range of safe and effective oral analgesics—fentanyl requirements while providing excellent analgesia. Spinal or epidural delivery of opioids can be used to minimize

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**Table 35.3 Oral Analgesics for Treating Pain during Pregnancy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>How Supplied</th>
<th>Equianalgesic Oral Dose (mg)</th>
<th>FDA Risk Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>—</td>
<td>325-, 500-mg tablets; 500 mg/5 mL elixir</td>
<td>B</td>
</tr>
<tr>
<td>Codeine</td>
<td>60</td>
<td>15-, 30-, 60-mg tablets; 15 mg/5 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Acetaminophen with codeine</td>
<td>—</td>
<td>300 · 15-, 300 · 30-, 300 · 60-mg tablets; 120-12/5 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>60</td>
<td>—†</td>
<td>C†</td>
</tr>
<tr>
<td>Acetaminophen with hydrocodone</td>
<td>—</td>
<td>500 · 2.5-, 500 · 5-, 500 · 7.5-, 660-10-mg tablets; 500-7.5/15 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>10</td>
<td>5-mg tablets; 5 mg/5 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Acetaminophen with oxycodone</td>
<td>—</td>
<td>325 · 5-, 500 · 5-mg tablets; 325 · 5/5 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Morphine</td>
<td>20</td>
<td>15-, 30-mg tablets; 10, 20 mg/5 mL elixir</td>
<td>C†</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>2</td>
<td>2-, 4-, 8-mg tablets; 5 mg/5 mL elixir</td>
<td>C†</td>
</tr>
</tbody>
</table>

*There is wide variability in the duration of analgesic action from patient to patient. All the oral agents listed are generally started with dosing every 4 to 6 hours. The dosing interval can then be adjusted as needed to maintain adequate analgesia.

†All opioid analgesics are FDA risk category D if used for prolonged periods or in large doses near term.

‡No oral formulation of hydrocodone alone is available in the United States.

*There is wide variability in the duration of analgesic action from patient to patient. All the parenteral agents listed are generally started with dosing every 3 to 4 hours and the oral agents every 4 to 6 hours. The dosing interval can then be adjusted as needed to maintain adequate analgesia.

---

**Table 35.4 Analgesics for Moderate to Severe Pain during Pregnancy**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Equianalgesic Parenteral Dose</th>
<th>Equianalgesic Oral Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>50 µg</td>
<td>—</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>1 mg</td>
<td>2-4 mg</td>
</tr>
<tr>
<td>Morphine</td>
<td>5 mg</td>
<td>30-60 mg</td>
</tr>
<tr>
<td>Meperidine</td>
<td>50 mg</td>
<td>150-300 mg</td>
</tr>
</tbody>
</table>

*There is wide variability in the duration of analgesic action from patient to patient. All the parenteral agents listed are generally started with dosing every 3 to 4 hours and the oral agents every 4 to 6 hours. The dosing interval can then be adjusted as needed to maintain adequate analgesia.
maternal plasma concentrations, thereby reducing placental transfer to the fetus or exposure of breastfeeding infants.

Opioids are excreted into breast milk. Pharmacokinetic analysis has demonstrated that breast milk concentrations of codeine and morphine are equal to or somewhat higher than maternal plasma concentrations. Use of meperidine by breastfeeding mothers via patient-controlled analgesia (PCA) has resulted in significantly greater neurobehavioral depression of the breastfeeding newborn than seen with equianalgesic doses of morphine. After absorption from the infant’s gastrointestinal tract, opioids contained in ingested breast milk undergo significant first-pass hepatic metabolism. Morphine undergoes glucuronidation to inactive metabolites, whereas meperidine undergoes N-demethylation to the active metabolite normeperidine. The half-life of normeperidine is markedly prolonged in newborns, so regular breastfeeding leads to accumulation and the resultant risk for neurobehavioral depression and seizures. The American Academy of Pediatrics considers the use of many opioid analgesics, including codeine, fentanyl, methadone, morphine, and propoxyphene, to be compatible with breastfeeding. There are insufficient data to determine the safety of buprenorphine with breastfeeding; however, excretion of buprenorphine into breast milk is minimal.

LOCAL ANESTHETICS

Few studies have focused on the potential teratogenicity of local anesthetics. Lidocaine and bupivacaine do not appear to pose significant developmental risk to the fetus. In the Collaborative Perinatal Project, only mepivacaine was found to have any suggestion of teratogenicity; however, the number of patient exposures was inadequate to draw conclusions. Animal studies have found that continuous exposure to lidocaine throughout pregnancy does not cause congenital anomalies but may decrease neonatal birth weight. Continuous exposure to local anesthetics is unusual but might be seen with the frequent use of local anesthetic patches or creams, which are used for post-herpetic neuralgia and other neuropathic pain states.

Neither lidocaine nor bupivacaine appears in measurable quantities in breast milk after epidural local anesthetic administration during labor. Intravenous infusion of high doses (2 to 4 mg/min) of lidocaine for suppression of cardiac arrhythmias has led to minimal levels in breast milk. Based on these observations, continuous epidural infusion of dilute local anesthetic solutions for postoperative analgesia should result in only small quantities of drug actually reaching the fetus. The American Academy of Pediatrics considers local anesthetics to be safe for use in nursing mothers.

Mexiletine is an orally active antiarrhythmic agent with structural and pharmacologic properties similar to those of lidocaine. This agent has shown promise in the treatment of neuropathic pain. Mexiletine is lipid-soluble and crosses the placenta freely. There are no controlled studies in humans of mexiletine use during pregnancy. However, studies in rats, mice, and rabbits involving doses of up to four times the maximum daily dose in humans have demonstrated an increased risk for fetal resorption but not teratogenicity. Mexiletine appears to be concentrated in breast milk, but based on expected breast milk concentrations and average daily intake of breast milk, the infant would receive only a small fraction of the usual pediatric maintenance dose of mexiletene. Mexiletine is rated risk category C by the FDA, and its use should be undertaken cautiously during pregnancy. The American Academy of Pediatrics considers the use of mexiletine to be compatible with breastfeeding.

STEROIDS

Corticosteroids may be used commonly in pregnant patients with autoimmune disease, as well as in those with premature rupture of membranes. There is variability in placental metabolism and transplacental passage of steroids, depending on the preparation. Most corticosteroids cross the placenta, although prednisone and prednisolone are inactivated by the placenta, whereas dexamethasone and betamethasone do not undergo significant metabolism. Fetal serum concentrations of prednisone are less than 10% of maternal levels. In 145 patients exposed to corticosteroids during their first trimester of pregnancy, no increase in malformations was seen. The use of corticosteroids during a limited trial of epidural steroid therapy in a pregnant patient probably poses minimal fetal risk (see further discussion later in this chapter).

In a mother who is breastfeeding, less than 1% of a maternal prednisone dose appears in the nursing infant over the next 3 days. This amount of steroid exposure is unlikely to affect infants’ endogenous cortisol secretion.

BENZODIAZEPINES

Benzodiazepines are among the most frequently prescribed of all drugs and are often used as anxiolytic agents, for the treatment of insomnia, and as skeletal muscle relaxants in patients with chronic pain. First-trimester exposure to benzodiazepines may be associated with an increased risk for congenital malformations. Diazepam may be associated with cleft lip or cleft palate, as well as with congenital inguinal hernia. However, epidemiologic evidence has not confirmed the association of diazepam with cleft abnormalities; the incidence of cleft lip and palate remained stable after the introduction and widespread use of diazepam. Epidemiologic studies have confirmed the association of diazepam use during pregnancy with congenital inguinal hernia. Benzodiazepine use immediately before delivery also increases the risk for fetal hypothermia, hyperbilirubinemia, and respiratory depression.

Two other benzodiazepines have been evaluated for teratogenicity. Chlordiazepoxide has been reported to produce a fourfold increase in congenital anomalies, including spastic diplegia, duodenal atresia, and congenital heart disease. However, a study of more than 200,000 Michigan Medicaid recipients did not support these earlier findings. Instead, this study found a high co-prevalence of alcohol and illicit drug use in patients receiving benzodiazepines. Benzo- diazepine use alone did not appear to be a risk factor for congenital anomalies. Oxazepam use during pregnancy has also been associated with congenital anomalies, including a syndrome of dysmorphic facial features and central nervous system defects. In addition to the risk for teratogenesis, neonates who are exposed to benzodiazepines in utero may experience withdrawal symptoms immediately after birth.
In a breastfeeding mother, diazepam and its metabolite desmethyldiazepam can be detected in the infant’s serum for up to 10 days after a single maternal dose. This is due to the slower metabolism in neonates than in adults. Clinically, infants who are nursing from mothers receiving diazepam may exhibit sedation and poor feeding. It appears most prudent to avoid any use of benzodiazepines during organogenesis, near the time of delivery, and during lactation.

**ANTIDEPRESSANTS**

Antidepressants are often used for the management of migraine headaches, as well as for analgesic and antidepressant purposes in chronic pain states. Although they are an effective therapy in nonpregnant patients, the most commonly used medications of this class are FDA category C or D. Selective serotonin reuptake inhibitors (SSRIs) have become the mainstay for the treatment of depression and are widely prescribed. As with most medications, increased use has been associated with increased reports of adverse effects in pregnancy and the neonate. Though initially thought to be safe in early pregnancy, unpublished epidemiologic reports from GlaxoSmithKline have raised concern that paroxetine, one of the most widely prescribed antidepressants, may be associated with an increase in malformations, particularly cardiovascular malformations, when used in the first trimester. This recent retrospective epidemiologic study of 3581 pregnant women exposed to paroxetine or other antidepressants during the first trimester suggested that paroxetine has an increased risk for overall major congenital malformations relative to other antidepressants (odds ratio [OR] = 2.20; 95% CI = 1.34 to 3.63). The risk for cardiovascular malformations was also increased with the use of paroxetine versus other antidepressants (OR = 2.08; 95% CI = 1.03 to 4.23); 10 of the 14 infants with cardiovascular malformations had ventricular septal defects. In addition, use late in pregnancy has recently become a concern, with reports of NAS, including jitteriness or seizures and pulmonary hypertension, occurring in the newborn.

These data initiated a re-evaluation of the risks and benefits of SSRIs during pregnancy and raised the FDA risk category from B to C. It is important to note that although the relative risk for adverse outcomes has increased, the incidence of malformations (1% to 3%) and pulmonary hypertension (0.5% to 1%) remains low, whereas the presence of severe depression in pregnant women is high (15%). As with all medications, the risk associated with no medication must be carefully weighed against the risk related to treatment; there are many women who will need to keep taking their antidepressant throughout pregnancy, and the low incidence of adverse outcomes remains reassuring.

Although tricyclic antidepressants have had a more limited role in the treatment of depression, they can be of benefit in patients with chronic pain. Amitriptyline, nortriptyline, and imipramine are all rated risk category D by the FDA. Desipramine and all other conventional antidepressant medications are category C. Amitriptyline is teratogenic in hamsters (encephaloceles) and rats (skeletal defects) and has been associated with increased congenital defects in rabbits, but not in rats, mice, or monkeys. Although there have been case reports of human neonatal limb deformities after maternal use of amitriptyline and imipramine, large human population studies have not revealed an association with any congenital malformation, with the possible exception of cardiovascular defects after maternal imipramine use. There have been no reports linking maternal desipramine use with congenital defects. Withdrawal syndromes have been reported in neonates born to mothers taking nortriptyline, imipramine, and desipramine, with symptoms including irritability, colic, tachypnea, and urinary retention.

Amitriptyline, nortriptyline, and desipramine are all excreted into human milk. Pharmacokinetic modeling has suggested that infants are exposed to about 1% of the maternal dose. In a critical review of the literature regarding the use of antidepressants during breastfeeding, Wisner and colleagues concluded that amitriptyline, nortriptyline, desipramine, clomipramine, and sertraline are not found in quantifiable amounts in nurseries and reported no adverse effects; they recommended use of these agents as the antidepressants of choice for breastfeeding women. Fluoxetine is also excreted into human milk, and has a milk-to-plasma ratio of about 0.3. No controlled studies are available to guide fluoxetine therapy during lactation; however, colic and high infant serum levels have been reported. Maternal doxepin use has also been associated with elevated plasma levels of the metabolite N-desmethyldoxepin and respiratory depression in a nursing infant. The American Academy of Pediatrics considers all antidepressants to have unknown risk during lactation.

Duloxetine, a selective serotonin-norepinephrine reuptake inhibitor (SSNRI), is representative of a new class of drug that combines inhibition of serotonin and norepinephrine reuptake. Duloxetine is efficacious for depression and neuropathic pain and may have particular efficacy for diabetic neuropathy. Duloxetine is FDA pregnancy category C, a class indicating potential risks and benefits. Neonates born to mothers receiving SSRi or SSNRI drugs may have a withdrawal reaction, as discussed earlier. Although the relative risks and benefits of breastfeeding when a woman is receiving duloxetine have not been fully evaluated, the manufacturer advises against its use during breastfeeding.

**ANTICONVULSANTS**

A number of anticonvulsant medications are used in chronic pain management. However, most data on the risk for major malformation in fetuses of mothers taking anticonvulsants are derived from the treatment of epilepsy. Although epilepsy itself is not associated with an increased risk for congenital malformations, some theoretical risk may exist. Nonetheless, data from anticonvulsant use in epileptic women are used to assess the risk associated with the same medications when used for pain conditions. Recently, the American Academy of Neurology and the American Epilepsy Society subcommittee undertook a systematic review of the evidence for teratogenic potential and perinatal outcomes in pregnant women taking antiepileptic medication. The review found that exposure to valproic acid, especially in the first trimester, contributes to neural tube defects, facial clefts, and possibly hypospadias. They also found that neonates of women taking anticonvulsants were also more likely to be small for gestational age and have
lower Apgar scores. Treatment with valproic acid is more likely to be associated with a major congenital malformation than is treatment with carbamazepine or lamotrigine. There is a possible dose relationship for the development of congenital malformations when valproic acid is taken during the first trimester. Though not consistent throughout all the studies, a dose of valproic acid greater than 1000 mg daily may be associated with the greatest risk for malformations.

In the same review, carbamazepine was associated with an increased risk for cleft palate, but this was not confirmed by another study focusing specifically on carbamazepine and using the EUROCAT (European Surveillance of Congenital Anomalies) database. Although this study did not find an association between carbamazepine and clefts, it did find an association with spina bifida.

Data suggest that topiramate (Topamax) increases the risk for cleft lip and cleft palate in babies born to women who use the medication during pregnancy. Its use has also been linked to low birth weight. The FDA has recently changed its pregnancy category from C to D.

Gabapentin is a newer anticonvulsant that is being used for the treatment of neuropathic pain syndromes. Little information exists about the safety of gabapentin in pregnant women, and thus far, the Gabapentin Registry Study has not shown an increased risk for adverse maternal and fetal events. In their prescribing information, the manufacturer has reported a series of nine women who received gabapentin during their pregnancies. Four women elected termination of their pregnancy, four had normal outcomes, and one neonate had pyloric stenosis and an inguinal hernia. Insufficient data exist to counsel patients regarding the fetal risk associated with gabapentin use during pregnancy.

A drug similar to gabapentin is pregabalin, which combines anticonvulsant activity and affinity for the γ-aminobutyric acid receptor. The main applications of pregabalin are for the treatment of pain associated with diabetic neuropathy and post-herpetic neuralgia. Pregabalin is listed as FDA pregnancy risk category C, but the risk during breastfeeding is unknown.

Patients contemplating childbearing who are taking anticonvulsants should have their pharmacologic therapy critically evaluated. Those taking anticonvulsants for neuropathic pain should strongly consider discontinuation during pregnancy, particularly during the first trimester. Consultation with a perinatologist is recommended if continued use of anticonvulsants during pregnancy is being contemplated. Frequent monitoring of serum anticonvulsant levels and folate supplementation should be initiated, and maternal α-fetoprotein screening may be considered to detect fetal neural tube defects.

The use of anticonvulsants during lactation does not seem to be harmful to infants. Phenytoin, carbamazepine, and valproic acid appear in small amounts in breast milk, but no adverse effects have been noted. No data exist on the use of gabapentin during lactation.

**ERGOT ALKALOIDS**

Ergotamine can have significant therapeutic efficacy for the episodic treatment of migraine headaches. However, even low doses of ergotamine are associated with significant teratogenic risk, and higher doses have caused uterine contractions and spontaneous abortion. During lactation, ergot alkaloids are associated with neonatal convulsions and severe gastrointestinal disturbances. Occasionally, methylergonovine is administered systemically to treat uterine atony and maternal hemorrhage immediately after delivery. This brief exposure is not a contraindication to breastfeeding.

**CAFFEINE**

Caffeine is a methylxanthine often used in combination with analgesics for the management of vascular headaches. It is readily absorbed from the gastrointestinal tract and crosses the placenta such that concentrations in the fetus are similar to maternal plasma levels. Early studies of caffeine ingestion during pregnancy suggested an increased risk for intrauterine growth retardation, fetal demise, and premature labor, but more recent studies do not. Although the data against caffeine use in pregnancy are not strongly compelling, most obstetricians recommend that pregnant women limit caffeine intake to less than 300 mg/day. To date, there is no evidence for birth defects related to caffeine.

Caffeine use is also associated with certain cardiovascular changes. Ingestion of modest doses of caffeine (100 mg/m², a dose similar to that found in two cups of brewed coffee) by caffeine-naïve subjects produces modest cardiovascular changes in the mother and fetus, including increased maternal heart rate and mean arterial pressure, increased peak aortic flow velocity, and decreased fetal heart rate. The modest decrease in fetal heart rate and increased frequency of fetal heart rate accelerations may confound the interpretation of fetal heart tracings. Caffeine ingestion is also associated with an increased incidence of tachyarrhythmia in the newborn, including supraventricular tachyarrhythmia, atrial flutter, and premature atrial contractions. Many over-the-counter analgesic formulations contain caffeine (typically in amounts of 30 to 65 mg per dose), and use of these preparations must be considered when determining total caffeine exposure.

Moderate ingestion of caffeine during lactation (up to two cups of coffee per day) does not appear to affect the infant. Breast milk usually contains less than 1% of the maternal dose of caffeine, with peak breast milk caffeine levels appearing 1 hour after maternal ingestion. Excessive caffeine use may cause increased wakefulness and irritability in the infant.

**SUMATRIPTAN**

Sumatriptan is a selective serotonin agonist that has achieved widespread use because of its efficacy in the treatment of migraine headaches. It has been associated with fetal malformations in rabbits, but not in rats. Limited data in humans have not demonstrated any strong teratogenic effects. Sumatriptan is advantageous in the treatment of migraine headaches in pregnancy because it does not share uterine contractile properties with ergotamine and would probably not have abortifacient effects. Beginning in January 1996, Glaxo Wellcome established a registry to prospectively evaluate the risk associated with sumatriptan use during pregnancy. The accumulated evidence from the Sumatriptan Pregnancy Registry and other studies...
suggested that this drug is a safe therapeutic option for the treatment of migraine attacks in pregnant women. Sumatriptan is labeled risk category C by the FDA.

A minimal amount of sumatriptan is excreted into breast milk, and it is considered safe for breastfeeding. The use of sumatriptan during lactation has not been well studied. One study of a single 6-mg subcutaneous dose of sumatriptan given to lactating women found total breast milk sumatriptan level to be only 0.24% of the maternal dose. Because sumatriptan is poorly absorbed from the infant’s gastrointestinal tract, only 14% of the drug ingested by the fetus would be bioavailable. Even this minor exposure could be largely avoided by expressing and discarding all milk for 8 hours after injection.\(^\text{114}\)

**\(\beta\)-BLOCKERS**

Propranolol and other \(\beta\)-blockers are used for chronic prophylaxis against migraine and nonmigraine vascular headaches. Most of the studies on \(\beta\)-blocker use during pregnancy involve women being treated for hypertension, as opposed to migraine prophylaxis, and hypertension itself may increase the risk for small-for-gestational-age fetuses.\(^\text{115}\) A 2009 Cochrane review looking at \(\beta\)-blocker use for mild to moderate hypertension during pregnancy found that the effect of \(\beta\)-blockers on perinatal outcome is unclear.\(^\text{116}\) There is no evidence that propranolol is teratogenic. Fetal effects noted with maternal consumption of propranolol include decreased weight, potentially because of a modest decrease in maternal cardiac output with consequent diminished placental perfusion.\(^\text{117}\) Patients should be aware that fetal toxicity can result in complications, including intrauterine growth retardation, hypoglycemia, bradycardia, and respiratory depression.\(^\text{117}\) Longer-acting agents should lead to less fluctuation in both maternal and fetal blood concentrations and perhaps less fluctuation in the drug’s effects on fetal heart rate. The FDA rates all \(\beta\)-blockers as class C with the exception of atenolol, which is rated class D.

In a lactating mother, propranolol doses of up to 240 mg/day appear to have minimal neonatal effects. The average neonatal exposure at this maternal dose is less than 1% of the therapeutic dose.\(^\text{118}\) Atenolol is concentrated in breast milk but still results in subtherapeutic levels in the infant.\(^\text{119}\)

**EVALUATION AND TREATMENT OF PAIN DURING PREGNANCY**

We have been asked to consult on numerous patients with uncontrolled pain during the course of pregnancy. Frequently, severe pain was arising from an extreme form of one of the more common musculoskeletal pain syndromes of pregnancy. Thus, a working knowledge of the painful musculoskeletal conditions that occur during pregnancy is essential. We also discuss evaluation of back pain and migraine headaches during pregnancy because these are among the most common problems encountered in practice. Although sickle cell pain crisis is less common, it provides a good example of the approach to managing chronic recurrent pain during the course of pregnancy.

**ABDOMINAL WALL AND LIGAMENTOUS PAIN**

Abdominal wall pain during pregnancy typically results in prompt evaluation by an obstetrician. One of the most common causes of abdominal pain early in pregnancy is miscarriage, which is manifested as abdominal pain and vaginal bleeding. Unruptured ectopic pregnancy and ovarian torsion may cause vague hypogastric pain and supra-pubic tenderness. Once these conditions, which require the immediate attention of an obstetrician, have been ruled out, myofascial causes of abdominal pain should be considered.

The round ligaments stretch as the uterus rises in the abdomen. If the pull is too rapid, small hematomas may develop in the ligaments (Fig. 35.1). This usually begins at 16 to 20 weeks’ gestation, with pain and tenderness being localized over the round ligament and radiating to the pubic tubercle.\(^\text{120}\) Treatment is bed rest and local warmth, along with oral analgesics in more severe cases.

Less common is abdominal pain arising from hematoma formation within the sheath of the rectus abdominis muscle (Fig. 35.2). As the uterus expands, the muscles of the abdominal wall become greatly overstretched. Rarely, the rectus muscle may dehisce or the inferior epigastric veins may rupture behind the muscle. Severe pain localized to a single segment of the muscle often follows a bout of sneezing. A diagnosis of rectus hematoma is made when the localized pain is exacerbated by tightening the abdominal muscles (raising one’s head in the supine position). Ultrasound can be helpful in confirming the diagnosis. Conservative management consisting of bed rest, local heat, and mild analgesics is often all that is needed.
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