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Analgesics in Pregnancy and Lactation

The following chart includes information to help guide decisions regarding analgesic use in pregnancy and lactation. FDA pregnancy categories have several limitations and are not included. Topical analgesics are covered in our chart, *Topical Medications in Pregnancy and Lactation*.

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Acetaminophen	• Generally considered the analgesic/antipyretic of choice in pregnant women, but use the lowest dose for the shortest duration necessary.[3,28] • For longer duration use (e.g., weeks), accumulating observational evidence suggests an association with neurodevelopmental concerns (e.g., ADHD, autism), early puberty in girls, and cryptorchidism.[1,4,7,22,28,29] • High-dose animal studies suggest that acetaminophen may have the potential to affect neurodevelopmental or reproductive development.[28]	• Good analgesic/antipyretic choice for nursing moms.[2] Amount in milk less than therapeutic doses given to infants.[2] • Case report of rash.[1]
Aspirin	• Analgesic doses used around 20 weeks or later may cause perinatal renal impairment and/or oligohydramnios and its complications.[5,23] Consider ultrasound monitoring of amniotic fluid if used for >48 hours.[5,23] Increased risk of maternal and newborn hemorrhage.[1] • Third trimester use poses risk of premature closure of ductus arteriosus (30 weeks or later[5]) and inhibition of labor.[1] • Avoid as an analgesic or antipyretic; use acetaminophen instead.[1] • Low doses (e.g., 81 mg once daily) may have favorable risk/benefit for certain complicated pregnancies.[1,5,23] • Small to moderate association between first trimester use and a variety of birth defects including cleft palate, congenital heart defects, gastroschisis, and neural tube defects.[6,7]	• Hemolysis (in a glucose-6-phosphate dehydrogenase-deficient infant), metabolic acidosis, and thrombocytopenia reported.[2] • Theoretical risk of Reye's syndrome.[2] • Low-dose aspirin 81 mg once daily can be considered.[2] • Acetaminophen is a safer analgesic choice.[2]
NSAIDs *Continued…*	• Analgesic doses used around 20 weeks or later may cause perinatal renal impairment and/or oligohydramnios and its complications.[5,23] Consider ultrasound monitoring of amniotic fluid if used for >48 hours.[5] Increased risk of maternal and newborn hemorrhage.[1] • Third trimester use poses risk of premature closure of ductus arteriosus (30 weeks or later[5]) and inhibition of labor.[1] • Use before week 20 possibly linked to miscarriage; data inconclusive.[7]	• Ibuprofen is the NSAID of choice for nursing moms; half-life short, amount in milk less than therapeutic doses given to infants.[2]

Drug or Drug Class	Use in Pregnancy	Use in Lactation
NSAIDs, continued	• Small to moderate association between first trimester use and a variety of birth defects including cleft palate, congenital heart defects, gastroschisis, and neural tube defects.[6,7] • There is no proof topical NSAIDs are safer than systemic agents in pregnancy.	
Opioids[a,b] (See footnotes for more information about opioid use during pregnancy/labor/postpartum.)		
Buprenorphine	• Most info based on use for opioid dependence, not analgesia.[1] • Buprenorphine was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Can be used in pregnancy for opioid use disorder. Single-agent product preferred due to concerns that naloxone component could cause withdrawal in fetus.[24-26]	• Poor oral absorption.[1] • Use considered "acceptable" based on oral use for opioid dependence.[2] • Monitor for sleepiness, breathing or feeding problems, or limpness.[2] • Extradural use for postpartum pain may suppress feeding.[2]
Butorphanol	• No reports of congenital malformations.[1] • Use during labor associated with sinusoidal fetal heart rate and neonatal depression.[1] • Butorphanol was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7]	• Poor oral absorption.[2] • Probably compatible with breastfeeding,[1] but no info with repeated, high, intravenous, or intranasal doses.[2] • Monitor for sleepiness, breathing or feeding problems, or limpness.[2] • Consider alternatives due to paucity of information, especially if nursing preterm infant or newborn.[2]
Codeine *Continued…*	• Unproven association with a variety of malformations in humans (e.g., heart defects, cleft lip and palate, musculoskeletal defects, hernia, hydrocephaly, gastrointestinal defects).[1] • Codeine was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] Specifically, codeine was associated with perimembranous ventricular septal defect.[8]	• Not recommended (Canada: contraindicated).[15,21] Risk of fatal morphine (codeine metabolite) toxicity if mom is an ultrarapid CYP2D6 metabolizer (see footnote c).[1]

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Codeine, continued	• Codeine was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Avoid in first trimester and third trimesters.[1]	
Fentanyl	• Fentanyl was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Fentanyl was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7]	• Considered compatible with breastfeeding,[1] but use smallest dose necessary for shortest duration necessary.[3] If used epidurally, may affect infant for first 24 hours and impair initial breastfeeding efforts if good support is not available.[2]
Hydrocodone (e.g., *Norco* [U.S.])	• Hydrocodone was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] Specifically, hydrocodone was associated with cleft palate alone or with cleft lip, perimembranous ventricular septal defect, and tetralogy of Fallot.[8] • Hydrocodone was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7]	• Excessive sleepiness and cyanosis reported in two case reports.[2] • Active metabolite (hydromorphone) formed through CYP2D6 is more potent than oxycodone.[2] • Theoretical risk of hydromorphone (hydrocodone metabolite) toxicity if mom is an ultrarapid CYP2D6 metabolizer (see footnote c).[2] • Use smallest dose necessary (e.g., daily dose 30 mg max) for shortest duration necessary.[2]
Hydromorphone (*Dilaudid*) *Continued…*	• Hydromorphone was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10]	• Excreted in breast milk.[1] Case report of excessive sleepiness, intermittent bradycardia, and apnea in infant.[3] Use smallest dose necessary for shortest duration necessary.[3]

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Hydromorphone, continued	• Hydromorphone was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Anticipate neonatal respiratory depression if used during labor.[1]	
Meperidine	• Unproven possible association between first trimester use and inguinal hernia.[1] • Meperidine was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Meperidine was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Newborns clear meperidine slowly. Concerns about neurologic effects on newborn if used during labor.[1] Anticipate neonatal respiratory depression if used during labor.[1]	• Not recommended.[12] • Newborns have trouble clearing meperidine.[1] • Fentanyl preferred for intravenous or intramuscular use for breastfeeding moms, especially if nursing a newborn or preterm infant.[2] • Higher risk vs morphine.[2] • Single dose for maternal anesthesia usually not problematic in older infants.[2] • Postpartum epidural PCA usually not sedating to breastfed infants.[2]
Methadone	• An option for opioid use disorder in pregnancy.[24] • Most human pregnancy data is from use for opioid use disorder.[1] • Methadone was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Potential for neonatal withdrawal and low birth weight.[1]	• Probably compatible.[1] • Breast milk concentrations are too low to be relied upon to prevent neonatal abstinence syndrome.[1] • Other agents are preferred for pain control during breastfeeding.[2] • Initiation of methadone postpartum, or increasing the dose to >100 mg/day, poses a particular risk of infant sedation and respiratory depression, especially if the infant is opioid-naive.[2]

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Morphine	• Unproven possible association between anytime use and inguinal hernia.[1] • Morphine was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Morphine was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Anticipate neonatal respiratory depression if used during labor.[1]	• Low-dose morphine may be preferred when an opioid is needed.[2,12] • Newborns and infants do not clear morphine as rapidly as adults.[12] • Infant can have detectable morphine levels, which may be within the therapeutic range.[12] • Epidural administration leads to lower levels in milk than oral or intravenous administration.[2] • Use smallest dose necessary for shortest duration necessary.[2]
Nalbuphine (*Nubain*)	• No reports of congenital malformations.[1] • Nalbuphine was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] • Use during labor associated with sinusoidal fetal heart rate and late and variable decelerations.[1] Fetal distress and respiratory depression may be comparable to meperidine.[1]	• Amount in milk less than therapeutic doses given to infants. Poor oral absorption. Unlikely to affect infant.[2]
Oxycodone (e.g., *Percocet*, etc) *Continued…*	• Oxycodone was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Oxycodone was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7]	• Not recommended.[12] • Not safer than codeine; one in five infants of moms taking oxycodone experience CNS depression, similar to codeine.[13] • Accumulates in breast milk.[1] • Oxycodone elimination is impaired in young infants and varies interindividually.[2] • Theoretical risk of oxymorphone (oxycodone metabolite) toxicity if

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Oxycodone, continued		mom is a CYP2D6 ultrarapid metabolizer (see footnote c).[14] But oxycodone is metabolized mainly by CYP3A4 to a weak metabolite (noroxycodone).[13] • Use smallest dose necessary (e.g., daily dose 30 mg max) for shortest duration necessary.[2]
Oxymorphone (*Opana*, etc)	• No human data, other than neonatal respiratory depression, as expected, if used during labor.[1] • Probably crosses placenta.[1] • Animal data suggest fetotoxicity, but no congenital malformations at exposures not causing maternal toxicity.[1]	• No data in humans.[1,3] • Probably excreted in breast milk.[1]
Tapentadol (*Nucynta*, *Nucynta ER* [U.S.]; *Nucynta IR*, *Nucynta CR* [Canada])	• No human data.[1] • Probably crosses placenta.[1] • Animal data suggest no congenital malformations at exposures not causing maternal toxicity.[1]	• Potential to accumulate in breast milk based on physicochemical properties.[1]
Tramadol (e.g., *Ultram*) *Continued…*	• Embryotoxic, fetotoxic, and maternally toxic, but not teratogenic, in animals at doses greater than the maximum daily human dose.[1] • Crosses placenta.[1] • Although not a "typical" opioid, use near term linked to respiratory depression and withdrawal in newborns.[1] • Tramadol was included in the National Birth Defects Prevention Study. The study authors concluded that opioid use between one and three months after conception is associated with a number of birth defects (including neural tube defects). However, the risk, if it exists, is likely small.[10] • Tramadol was included in the Birth Defects Study (Pregnancy Health Interview Study), which found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of neural tube defects in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000	• Not recommended (Canada: contraindicated) because tramadol and its active metabolite are excreted in breast milk.[20,30] Tramadol has the same risks associated with ultrarapid CYP2D6 metabolism as does codeine (see codeine and footnote c).[20,30]

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Tramadol, continued	live births), so a two-fold increased risk would represent a small increase in absolute risk.[7]	

a. Reserve opioids for postpartum pain that can't be managed with acetaminophen or ibuprofen.[17] Use lowest effective dose for shortest time necessary.[11] Watch baby for limpness, difficulty feeding or breathing, or sleeping more than usual (e.g., more than four hours at a time).[3,15]
b. Occasional doses of opioids during pregnancy generally considered low risk,[3] but pose risks in the first and third trimester.[7-10,18] Opioid use during labor can cause neonatal respiratory depression, and long-term use during pregnancy may result in neonatal opioid withdrawal (abstinence) syndrome.[18] Symptoms of neonatal withdrawal include vomiting, diarrhea, poor feeding, irritability, tremor, and high-pitched crying.[16] Neonatal opioid withdrawal can be life-threatening and requires management according to protocols developed by neonatology experts.[19]
c. Ultrarapid CYP2D6 metabolism occurs in up to 1% to 10% of White Europeans or North Americans; 3% to 4% of Blacks; 1% to 2% of Chinese, Japanese, and Koreans; and >10% in Oceanic, North African, Middle Eastern, and Puerto Rican populations, and Ashkenazi Jews.[20] In a U.S. urban population, individuals identifying as Caucasian or Hispanic had an incidence of ~11%, with variability within subpopulations.[27]

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