

## Guidelines for endoscopy in pregnant and lactating women

*This is one of a series of statements discussing the use of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. This guideline updates a previously issued guideline on this topic.<sup>1</sup> In preparing this guideline, we performed a search of the medical literature by using PubMed. Additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When few or no data exist from well-designed, prospective trials, emphasis was given to results from large series and reports from recognized experts. Guidelines for appropriate use of endoscopy are based on a critical review of the available data and expert consensus at the time that the guidelines are drafted. Further controlled clinical studies may be needed to clarify aspects of this guideline. This guideline may be revised as necessary to account for changes in technology, new data, or other aspects of clinical practice. The recommendations are based on reviewed studies and are graded on the strength of the supporting evidence (Table 1).<sup>2</sup> The strength of individual recommendations is based on both the aggregate evidence quality and an assessment of the anticipated benefits and harms. Weaker recommendations are indicated by phrases such as "We suggest . . .," whereas stronger recommendations are typically stated as "We recommend. . ."*

*This guideline is intended to be an educational device to provide information that may assist endoscopists in providing care to patients. This guideline is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment. Clinical decisions in any particular case involve a complex analysis of the patient's condition and available courses of action. Therefore, clinical considerations may lead an endoscopist to take a course of action that varies from these guidelines.*

### THE ROLE OF ENDOSCOPY IN PREGNANT PATIENTS

The safety and efficacy of GI endoscopy in pregnant patients is not well-studied. Invasive procedures during

pregnancy are justified when it is clear that failure to perform the procedure could expose the fetus and/or mother to harm. Informed consent should include risks to the fetus as well as to the mother. Studies involving humans tend to be small and retrospective, and much of the drug safety data is based on animal studies.

GI endoscopy in pregnant patients is inherently risky because the fetus is particularly sensitive to maternal hypoxia and hypotension, either of which can cause hypoxia that can lead to fetal demise.<sup>3</sup> Maternal oversedation resulting in hypoventilation or hypotension or maternal positioning precipitating inferior vena cava compression by the gravid uterus can lead to decreased uterine blood flow and fetal hypoxia. Other risks to the fetus include teratogenesis (from medications given to the mother and/or ionizing radiation exposure) and premature birth.<sup>4</sup> In situations where therapeutic intervention is necessary, endoscopy offers a relatively safe alternative to radiologic or surgical interventions.<sup>3,5-10</sup> The main indications for endoscopy in pregnancy are outlined in Table 2, and general principles that apply to endoscopy in pregnancy are shown in Table 3.

### SAFETY DURING PREGNANCY OF MEDICATIONS COMMONLY USED FOR ENDOSCOPY

The U.S. Food and Drug Administration lists 5 categories of drugs with regard to safety during pregnancy (Table 4). There are no category A drugs used for endoscopy. For endoscopic procedures, category B and category C drugs are recommended. For most procedures, the level of sedation should be anxiolysis or moderate sedation. A trained anesthesia provider should administer deep sedation. Caution should be used in administering any level of sedation to a pregnant patient because of the increased risk of aspiration and potentially difficult airway. Pregnancy-induced physiologic changes involving the cardiopulmonary and GI systems as well as anatomic changes in the airway, such as swelling of the oropharyngeal tissues and decreased caliber of the glottic opening, make careful monitoring of the sedated pregnant patient mandatory.<sup>11</sup>

### Narcotic analgesics

Two large studies<sup>12-13</sup> have confirmed that meperidine (category B) does not appear to be teratogenic, and it is preferred over morphine (category C), which

**TABLE 1. GRADE system for rating the quality of evidence for guidelines<sup>2</sup>**

Quality of evidence	Definition	Symbol
High quality	Further research is very unlikely to change our confidence in the estimate of effect.	⊕⊕⊕⊕
Moderate quality	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.	⊕⊕⊕○
Low quality	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.	⊕⊕○○
Very low quality	Any estimate of effect is very uncertain.	⊕○○○

**TABLE 2. Indications for endoscopy in pregnancy**

Significant or continued GI bleeding
Severe or refractory nausea and vomiting or abdominal pain
Dysphagia or odynophagia
Strong suspicion of colon mass
Severe diarrhea with negative evaluation
Biliary pancreatitis, symptomatic choledocholithiasis, or cholangitis
Biliary or pancreatic ductal injury

**TABLE 3. General principles guiding endoscopy in pregnancy**

Every endoscopic procedure requires a preoperative consultation with an obstetrician, regardless of fetal gestational age.
Always have a strong indication, particularly in high-risk pregnancies.
Defer endoscopy to second trimester whenever possible.
Use lowest effective dose of sedative medications.
Use category B drugs whenever possible.
Minimize procedure time.
Position patient in left pelvic tilt or left lateral position to avoid vena cava or aortic compression.
The decision to monitor fetal heart rate should be individualized and will depend on gestational age of the fetus and available resources.
Before 24 weeks of fetal gestation, it is sufficient to confirm the presence of the fetal heart rate by Doppler before sedation is begun and after the endoscopic procedure.
After 24 weeks of fetal gestation, simultaneous electronic fetal heart and uterine contraction monitoring should be performed before and after the procedure. Ideally, procedures should be done at an institution with neonatal and pediatric services. If possible, the fetal heart rate and uterine contractions should be monitored before, during, and after the procedure by a qualified individual, with obstetric support readily available in case of fetal distress or a pregnancy-related complication.
Endoscopy is contraindicated in placental abruption, imminent delivery, ruptured membranes, or uncontrolled eclampsia.

crosses the fetal blood-brain barrier more rapidly. Meperidine may cause loss of fetal beat-to-beat cardiac variability that can last up to 1 hour after drug administration, but this does not indicate fetal distress.<sup>14</sup> Fentanyl (category C) has a rapid onset of action and shorter patient recovery time than meperidine. It is not teratogenic, but is embryocidal in rats.<sup>15</sup> Although fentanyl appears safe in humans when given in low doses typical for endoscopy, meperidine is preferred over fentanyl in pregnancy.

### Naloxone (category B)

This rapidly acting opiate antagonist crosses the placenta within 2 minutes of intravenous administration.<sup>16</sup> It

does not appear to be teratogenic. Its use in mothers dependent on opiates is contraindicated because it can precipitate opiate withdrawal symptoms.<sup>8</sup> It should be used only in respiratory depression, hypotension, or unresponsiveness in a closely monitored setting. The potential for re-sedation as the agent is metabolized should be recognized and anticipated.<sup>17</sup>

### Benzodiazepines (category D)

Diazepam should not be used for sedation in pregnant women. Sustained use of diazepam during pregnancy has been associated with cleft palate and, when used later in pregnancy, neurobehavioral disorders.<sup>18-20</sup> Midazolam has not been associated with congenital abnormalities. It is the preferred benzodiazepine when sedation with meperidine alone is inadequate.<sup>8</sup> Midazolam should be avoided in the first trimester, if possible.

**TABLE 4. U.S. Food and Drug Administration categories for drugs used in pregnancy**

Category	Description
A	Adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
B	Animal studies have revealed no evidence of harm to the fetus; however, there are no adequate and well-controlled studies in pregnant women. <b>or</b> Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
C	Animal studies have shown an adverse effect, and there are no adequate and well-controlled studies in pregnant women. <b>or</b> No animal studies have been conducted, and there are no adequate and well-controlled studies in pregnant women.
D	Adequate, well-controlled, or observational studies in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
X	Adequate, well-controlled, or observational studies in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are, or may become, pregnant.

**Flumazenil (category C)**

Little is known of the safety profile of this benzodiazepine antagonist in pregnancy. Although it is not teratogenic in rats and mice, it does produce subtle neurobehavioral changes in male offspring of rats exposed to the drug in utero.<sup>21</sup>

**Propofol (category B)**

In the pregnant patient, it is recommended that propofol be administered by a trained anesthesia provider because of its narrow therapeutic index and the importance of close monitoring. Safety in the first trimester has not been well-studied.<sup>22-23</sup>

**Simethicone (category C)**

Simethicone is a category C drug because of lack of evaluation in pregnancy, but it is commonly administered and probably safe.<sup>24</sup>

**Glucagon (category B)**

Glucagon, an antispasmodic agent commonly used during ERCP, is not contraindicated during pregnancy.<sup>24</sup>

**Topical anesthetics**

Topical anesthetics such as lidocaine (category B) often are used to decrease the gag reflex and make intubation easier. One study showed no fetal malformations in 293 infants with first trimester exposure to lidocaine.<sup>13</sup> It may be prudent to ask the patient to gargle and spit out the drug, rather than swallow, when its use is deemed necessary.

**Summary of anesthetic agents**

According to a joint statement from the American Society of Anesthesiologists and the American College of Obstetrics and Gynecology, none of the currently used anesthetic agents, when used in standard concentrations at any gestational age, have been shown to have any teratogenic effect in humans.<sup>25</sup>

**Antibiotics**

The indications for prophylactic use of antibiotics to pregnant patients and nonpregnant patients are similar as discussed in other American Society for Gastrointestinal Endoscopy guidelines.<sup>26</sup> It is important to realize that some antibiotics are contraindicated in pregnancy because of adverse fetal effects, whereas others are safe only in certain trimesters. Table 5 summarizes the current recommendations regarding the use of antibiotics during pregnancy. Further details can be obtained from sources such as *Drugs in Pregnancy and Lactation*.<sup>12</sup>

**Colon cleansing agents**

The safety of polyethylene glycol electrolyte isotonic cathartic solutions has not been studied in pregnancy. Polyethylene glycol solutions are classified as pregnancy category C. Sodium phosphate preparations (category C) may cause fluid and electrolyte abnormalities and should be used with caution.<sup>27</sup> Tap water enemas may be sufficient for flexible sigmoidoscopy in a pregnant patient.

**PROCEDURAL CONSIDERATIONS IN PREGNANCY**

Endoscopy should be deferred to the second trimester whenever possible and should always have a strong indication with a careful assessment of risk versus benefit.<sup>28</sup> Every endoscopic procedure requires a preoperative consultation with an obstetrician, regardless of the gestational age of the fetus.<sup>25</sup> The decision to monitor fetal heart rate and uterine contractions should be made with an obstetrician and should depend on the gestational age of the fetus and available resources (Table 3).<sup>25</sup>

For all GI endoscopic procedures, patients in the second or third trimester should not be positioned on their backs before, during, or after the procedure, because the pregnant uterus can compress the aorta or the inferior vena cava, resulting in maternal hypotension and decreased placental perfusion. Most procedures are done

**TABLE 5. Antibiotic safety in pregnancy**

Safe in pregnancy	Avoid in pregnancy	Avoid in first trimester	Avoid in third trimester
Penicillins	Quinolones	Metronidazole	Sulfonamides
Cephalosporins	Streptomycin		Nitrofurantoin
Erythromycin (except estolate)	Tetracyclines		
Clindamycin			

with the patient in the left lateral position, where vascular compression is not an issue.<sup>11</sup> Vascular compression can be prevented before or after the procedure by placing a wedge or pillow under the patient's right hip and creating a pelvic tilt or by having the patient sit up. Pregnant patients also are more likely to aspirate gastric contents or secretions than nonpregnant ones.<sup>11</sup> In addition to the usual patient monitoring, maternal-fetal monitoring should be performed as depicted in Table 3.

Upper endoscopy (EGD) is performed as in nonpregnant patients. Case series and case-control studies suggest that EGD is safe and effective in pregnancy.<sup>29-31</sup> In a case-control study of 83 EGDs performed during pregnancy, the diagnostic yield for upper GI bleeding was 95%.<sup>30</sup> In this study, EGD did not induce premature labor, and no congenital malformations were reported. Studies assessing the safety of colonoscopy in pregnancy involve very small numbers, limiting the ability to detect uncommon adverse outcomes.<sup>32-34</sup> In late pregnancy, patients should not be placed supine or prone during colonoscopy. If external abdominal pressure is required, great care should be taken to apply mild force and direct it away from the uterus.

ERCP should be used during pregnancy only when therapeutic intervention is intended. Biliary pancreatitis, symptomatic choledocholithiasis, or cholangitis are the usual indications and can lead to fetal loss if not treated properly. Only experienced endoscopists should attempt the procedure. Several studies have confirmed the safety of ERCP in pregnancy,<sup>35-39</sup> although one study demonstrated an increased risk of pancreatitis after ERCP, occurring in 16% of 65 patients evaluated.<sup>39</sup> A major concern during pregnancy is fetal radiation exposure. True radiation exposure to the fetus depends on multiple factors, including patient body size, fetal gestational age, and exposure techniques, and may exceed 10 millisievert (mSv) during prolonged or complicated cases.<sup>40</sup> External shielding of the fetus with lead placed under the pelvis and lower abdomen is common practice; however, the majority of the fetal radiation dose occurs as a result of radiation scatter within the pregnant patient.<sup>40</sup> Thus, the most effective method to reduce radiation-associated risk is to limit fluoroscopy time and overall radiation exposure. Radiation exposure to the fetus also can be reduced by colli-

imating the beam to the area of interest<sup>40</sup> and by using brief "snapshots" of fluoroscopy to confirm cannula position and common bile duct stones, with a low-dose-rate setting when available.<sup>41</sup> Endoscopists should avoid taking hard copy x-ray films, because these involve greater amounts of radiation. They should also consider adjusting the patient's position to minimize fetal radiation exposure.<sup>41</sup> With thoughtful precaution, fetal exposure can be well below the 50 to 100 mSv level considered to be of concern for radiation-induced teratogenesis.<sup>35,42-43</sup> As with medications administered during endoscopic procedures, radiation exposure time and dose should be documented.

ERCP can be performed without fluoroscopy by using a wire-guided cannulation technique. Bile duct cannulation can be confirmed by bile aspiration or visualization of bile around the guidewire.<sup>44-46</sup> After biliary sphincterotomy and balloon sweeping, stone extraction can be confirmed by normalization of laboratory indices<sup>44</sup> or by inspection of the bile duct with choledochoscopy<sup>45</sup> or EUS. EUS performed before ERCP can help to delineate anatomy and determine the number, size, and location of stones.<sup>45-46</sup> In cases of suspected incomplete stone removal, biliary stents can be placed to avoid excessive fluoroscopy. A 2-stage approach has been described whereby pregnant patients are initially treated with sphincterotomy and stent placement, with definitive ERCP and stone clearance performed after delivery.<sup>47</sup> However, stent placement may require subsequent procedures during pregnancy. The risks and benefits of repeat endoscopy must be weighed against any potential radiation exposure to the developing fetus in order to determine the optimal treatment strategy.

### Electrocautery

Amniotic fluid can conduct electrical current to the fetus.<sup>48</sup> The grounding pad should be placed such that the uterus is not between the electrical catheter and the grounding pad whenever possible. Bipolar electrocautery should be used to minimize the risk of "stray" currents going through the fetus. Although electrocautery is relatively safe when used for sphincterotomy and hemostasis, polyp removal involving electrocautery should be postponed until after delivery.

## The role of endoscopy in lactating patients

Diagnostic and therapeutic GI endoscopy in lactating women does not vary from that in pregnant women in terms of indications/contraindications, preprocedure preparation, procedural monitoring, radiation exposure, and endoscopic equipment. Caution should be exercised in the use of certain medications because these drugs may be transferred to the infant through breast milk. In situations where there is a concern regarding medication or metabolite transfer to the infant, the woman should be advised to pump her breast milk and discard it as indicated for the individual medication after the procedure is complete.

## SAFETY DURING LACTATION OF MEDICATIONS COMMONLY USED FOR ENDOSCOPY

The sensitivity to and risks of sedation in a lactating woman are similar to those for any adult.<sup>14</sup>

### Midazolam

Midazolam is excreted in breast milk. However, a study of 12 women receiving midazolam 15 mg orally found no measurable concentrations (<10 nmol/L) in milk samples 7 hours after ingestion.<sup>49</sup> Additional investigation of two women showed that midazolam and its metabolite hydroxymidazolam were undetectable after 4 hours.<sup>49</sup> Most recently, in a study of 5 lactating women undergoing premedication with 2 mg of intravenous midazolam prior to induction of general anesthesia, exposure of nursing infants within 24 hours was 0.004% of the maternal dose of midazolam, and no interruption of breastfeeding was recommended.<sup>50</sup> However, the American Academy of Pediatrics considers the effects of midazolam on the nursing infant unknown.<sup>51</sup> Based on the paucity of data, it is advisable to recommend withholding nursing of the infant for at least 4 hours following administration of midazolam.

### Fentanyl

Fentanyl is excreted in breast milk, but the concentrations are too low to be pharmacologically significant and fall to undetectable levels by 10 hours.<sup>52</sup> A study of 5 lactating women undergoing induction for general anesthesia with 100 µg of intravenous fentanyl demonstrated that the exposure of nursing infants within 24 hours was 0.024% of the maternal dose, and no interruption of breastfeeding was recommended.<sup>50</sup> The American Academy of Pediatrics considers fentanyl to be compatible with breastfeeding.<sup>51</sup>

### Meperidine

Meperidine is concentrated in breast milk, and may be detected up to 24 hours after administration.<sup>53</sup> Studies have suggested that meperidine can be transferred to the breastfed infant and may have neurobehavioral

**TABLE 6. Antibiotic safety in breastfeeding**

Safe	Avoid
Penicillins	Sulfonamides
Cephalosporins	Ciprofloxacin
Erythromycin	Ofloxacin
Tetracycline	Metronidazole (effect on infant unknown, may be of concern)
Nitrofurantoin (except in infants with glucose-6-phosphate dehydrogenase deficiency)	

effects.<sup>54-56</sup> While the American Academy of Pediatrics classified meperidine as compatible with breastfeeding in their 1983 statement,<sup>51</sup> it may be reasonable to use an alternative such as fentanyl whenever possible, especially when the patient is nursing a newborn or preterm infant.<sup>57</sup>

### Propofol

Propofol is excreted in breast milk with maximum concentrations at 4 to 5 hours.<sup>58</sup> A study of 5 lactating women undergoing induction for general anesthesia who received a total of 180 to 200 mg of propofol demonstrated that exposure of nursing infants within 24 hours was 0.015% of the maternal dose. The effects of small oral doses of propofol on the infant are unknown, so no interruption of breastfeeding is recommended.<sup>50</sup>

### Reversal agents

The safety of naloxone and flumazenil in this setting is unknown. Naloxone is not orally bioavailable, so it is unlikely to affect the breastfed infant.<sup>59</sup>

### Antibiotics

Penicillins and cephalosporins are excreted in breast milk in trace amounts and are considered compatible with breastfeeding.<sup>51</sup> Ofloxacin and ciprofloxacin are excreted in breast milk, and their toxicity has not been well-studied. Because there is a potential for arthropathy in the infant, quinolones should be avoided in the lactating woman.<sup>60</sup> It is recommended that sulfonamides be avoided in breastfeeding mothers of infants who are ill, premature, and glucose-6-phosphate dehydrogenase deficient.<sup>61</sup> The safety of commonly used antibiotics is summarized in Table 6.

## RECOMMENDATIONS

### Pregnancy

- We recommend that endoscopy during pregnancy should be done only when there is a strong indication

and should be postponed to the second trimester whenever possible (⊕○○○).

- We recommend the close involvement of obstetrical staff to assist with management, including determination of the degree of maternal and fetal monitoring (⊕○○○).
- We suggest that for endoscopic procedures involving moderate sedation during pregnancy, meperidine is the preferred agent followed by small doses of midazolam as needed (⊕○○○).
- We recommend deep sedation, when needed, be administered by an anesthesia provider (⊕○○○).
- Therapeutic ERCP is generally safe in pregnancy. We recommend that care be taken to minimize radiation exposure to the fetus (⊕⊕○○) and risks to the mother (⊕⊕○○).
- We recommend that when electrocautery is required, bipolar electrocautery be used. If monopolar electrocautery must be used, the grounding pad should be placed to minimize flow of electrical current through the amniotic fluid (⊕○○○).
- We recommend that in late pregnancy, women should be in the lateral decubitus position before, during, and after the procedure (⊕○○○).
- We recommend that antibiotic choice in the context of endoscopic procedures consider patient-specific factors and stage of fetal development. Although many antibiotics can be safely used in pregnancy, some are contraindicated (quinolones, streptomycin, tetracyclines) while others are safe only in certain stages of fetal development (⊕⊕○○).

### Lactation

- We suggest that breastfeeding may be continued after maternal fentanyl administration (⊕⊕○○).
- We suggest that infants not be breastfed for at least 4 hours after maternal midazolam administration (⊕⊕○○).
- We suggest that breastfeeding may be continued after maternal propofol administration as soon as the mother has recovered sufficiently from general anesthesia to nurse (⊕⊕○○).
- We recommend that quinolones and sulfonamides be avoided (⊕○○○).
- Penicillins, cephalosporins, tetracyclines, and erythromycin are compatible with breastfeeding (⊕⊕○○).

### DISCLOSURE

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