This is one of a series of statements discussing the utilization of GI endoscopy in common clinical situations. The Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy prepared this text. In preparing this guideline, a MEDLINE literature search was performed and additional references were obtained from the bibliographies of the identified articles and from recommendations of expert consultants. When little or no data exist from well-designed prospective trials, emphasis is given to results from large series and reports from recognized experts.

Guidelines for appropriate utilization of endoscopy are based on a critical review of the available data and expert consensus. Further controlled clinical studies are needed to clarify aspects of this statement, and revision may be necessary as new data appear. Clinical consideration may justify a course of action at variance to these recommendations.

INTRODUCTION

The safety and the efficacy of GI endoscopy in pregnant patients is not well studied. Studies involving humans tend to be small and retrospective. Much of the drug safety data is based on animal studies. Invasive procedures are justified when it is clear that by not doing so could expose the fetus and/or the mother to harm. Informed consent should include risks to the fetus as well as the mother.

The fetus is particularly sensitive to maternal hypoxia and hypotension, either of which may cause fetal hypoxia that can lead to fetal demise. Maternal oversedation, with resulting hypoventilation or hypotension, or maternal positioning that might lead to inferior vena caval compression by the gravid uterus can lead to decreased uterine blood flow and fetal hypoxia. Other potential risks to the fetus include teratogenesis (both from medication given to the mother and radiation exposure from fluoroscopy) and premature birth.

In situations where therapeutic intervention is necessary, endoscopy offers a relatively safe alternative to radiologic or surgical intervention. The main indications for endoscopy in pregnancy are outlined in Table 1. General principles that apply to endoscopy in pregnancy are shown in Table 2.

SAFETY OF COMMONLY USED MEDICATIONS FOR ENDOSCOPY DURING PREGNANCY

The U.S. Food and Drug Administration lists 5 categories of drugs with regard to safety during pregnancy (Table 3). There are no category A drugs used for endoscopy. For use during endoscopic procedures, category B and, when necessary, category C drugs are recommended. Category D drugs may be used when the benefits clearly outweigh the risks. These categories are of limited value for determining the safety of one-time use; therefore, consultation with an obstetrician regarding medication should be considered. For most procedures, the level of sedation should be anxiolysis or moderate sedation. If deep sedation is necessary, it should be administered by an anesthesiologist.

Meperidine (category B)

Meperidine does not appear to be teratogenic as reported in two large studies. It is preferred over morphine (category C), which crosses the fetal blood–brain barrier more rapidly, and fentanyl (category C).

Fentanyl (category C)

This narcotic has a rapid onset of action and a shorter patient recovery time than meperidine. Fentanyl is not teratogenic but was embryocidal in rats. It appears safe in humans when given in low doses typical for endoscopy.

Naloxone (category B)

This rapidly acting opiate antagonist crosses the placenta within 2 minutes of intravenous administration. It does not appear to be teratogenic. Its use is contraindicated in mothers dependent on opiates, because it can precipitate opiate-withdrawal symptoms. It should only be used in respiratory depression, hypotension, or unresponsiveness in a closely monitored setting. The
potential for re-sedation as naloxone is metabolized should be recognized.

Benzodiazepines (category D)
Sustained use of diazepam during early pregnancy (first trimester) has been associated with cleft palate and, when used later in the pregnancy, neurobehavioral disorders, although this association is challenged by some investigators. Diazepam should not be used for sedation in pregnant women.

Midazolam, although also category D, has not been reported to be associated with congenital abnormalities. Midazolam is the preferred benzodiazepine when sedation with meperidine is inadequate. Avoid the use of midazolam in the first trimester if possible.

Flumazenil (category C)
Little is known of the safety profile of this benzodiazepine antagonist. 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.

Propofol (category B)
In the pregnant patient, it is recommended that propofol be administered by an anesthesiologist, because of its narrow therapeutic index and the importance of close monitoring. Safety in the first trimester has not been well studied.

Simethicone (category C)
This is a category C drug because of a lack of studies, but, it commonly is given to pregnant women and probably is safe.

Glucagon (category B)
Glucagon is an antispasmodic, commonly used during ERCP, that is not contraindicated during pregnancy.

Topical anesthetics
Topical anesthetics, e.g., lidocaine (category B), often are used to decrease the gag reflex and to make intubation easier.
easier. One study showed no fetal malformations in 293 infants with first trimester exposure. It may be prudent to ask the patient to gargle and to spit out the drug instead of swallowing it when its use is deemed necessary.

Antibiotics

Most antibiotics can be safely used in pregnancy, and the indications for their prophylactic use are similar to those in nonpregnant patients. However, some antibiotics are contraindicated because of adverse fetal effects, and others are safe in only certain trimesters. Table 4 summarizes the recommendations at present. Further details can be obtained from sources, e.g., Drugs in Pregnancy and Lactation.

Colon-cleansing agents

The safety of polyethylene glycol (PEG) electrolyte isotonic cathartic solutions has not been studied in pregnancy. PEG solutions are category C. Sodium phosphate preparations (category C) may cause fluid and electrolyte abnormalities and should be used with caution. Tap water enemas may be sufficient for flexible sigmoidoscopy.

PROCEDURES

For all endoscopy procedures, it is suggested that the patient who is in the second or third trimester not lie on her back while waiting for the procedure or afterward in recovery. This is because the pregnant uterus can compress the aorta and/or the inferior vena cava (IVC), causing maternal hypotension and decreased placental perfusion. By placing a wedge or pillow under the right hip, a “pelvic tilt” is created to prevent this. The patient also may sit up if she so prefers, because this will prevent IVC compression. Most procedures are done in the left lateral position where this is not an issue. Pregnant patients also are more likely to aspirate gastric contents or secretions than nonpregnant ones. In addition to the usual patient monitoring, maternal–fetal monitoring should be performed as in Table 2. Consultation with an obstetrician should be considered before endoscopy.

Procedural considerations in pregnancy

Upper endoscopy is performed as in nonpregnant patients. Case series and case-control studies suggest it is safe and effective. In a case-control study of 83 upper endoscopies (EGD) performed during pregnancy, the diagnostic yield for upper-GI bleeding was 95%. In this study, EGD did not induce premature labor and no congenital malformations were reported. Studies assessing the safety of colonoscopy in pregnancy involve extremely small numbers, limiting the ability to detect uncommon adverse outcomes. 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 to direct it away from the uterus.

ERCP

ERCP should only be used when therapeutic intervention is intended. Biliary pancreatitis, choledocholithiasis, or cholangitis are the usual indications, and can lead to fetal loss if not treated properly. Several studies have confirmed the safety of ERCP in pregnancy. The fetus should be shielded from the ionizing radiation. Lead shields are placed under the pelvis and lower abdomen, remembering that the x-ray beam originates from beneath the patient. Measuring radiation exposure to the area of the uterus also should be considered. Radiation exposure is reduced by collimating the beam to the area of interest. Use brief “snapshots” of fluoroscopy to confirm cannula position and common bile-duct stones. Avoid taking hard-copy x-ray films, because these involve additional radiation. Consultation with a radiologist or a hospital radiation safety officer may be useful in minimizing the radiation exposure to the fetus. With thoughtful precaution, the fetal exposure is well below the 5- to 10-rad level considered to be of concern for radiation-induced teratogenesis. Only experienced endoscopists should attempt the procedure.

Electrocautery and hemostasis

Amniotic fluid can conduct electrical current to the fetus. The grounding pad should be placed in such a position that the uterus is not between the electrical
catheter and the grounding pad. Bipolar electrocautery should be used to minimize this risk of “stray” currents going through the fetus. Although electrocautery is relatively safe when used for sphincterotomy and hemostasis, polyp removal should be postponed until after pregnancy.

Epinephrine is pregnancy category C and causes a decrease in uterine blood flow. Its safety, when used as an endoscopic injectant, has not been studied, although, when given in low-dose combinations for analgesia, it is safe. Its use for hemostasis should balance the benefits with the potential risks.

BREAST-FEEDING

Indications and contraindications
Diagnostic and therapeutic endoscopy in lactating women do not vary in terms of indication, procedural preparation, procedural monitoring, radiation exposure, and endoscopic equipment. Caution needs to be exercised in the use of certain medications, because these drugs may be transferred to the infant through breast milk. In these instances, where there is a concern regarding the transfer to the infant, the woman should be advised to pump her breast milk and discard it, with the timing dependent upon the agent of concern.

Sedation and analgesia
The sensitivity to and risks of sedation in a lactating woman is similar to any adult.

Midazolam. Midazolam is excreted in breast milk. However, a study of 12 women receiving 15 mg midazolam orally found no measurable concentrations (<10 nmol/L) in milk samples obtained 7 hours after ingestion. Additional investigations on two women showed that midazolam and its metabolite, hydroxymidazolam, were undetectable after 4 hours. The American Academy of Pediatrics considers the effects of midazolam unknown on the nursing infant, but the drug may be of concern.

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 after administration. The American Academy of Pediatrics considers fentanyl to be compatible with breast-feeding.

Meperidine. Meperidine is concentrated in breast milk and may be detectable up to 24 hours after administration. Studies have suggested that meperidine can be transferred to the breast-fed infant and may have neurobehavioral effects. Whereas, the American Academy of Pediatrics classified meperidine as compatible with breast-feeding in their 1983 statement, it may be reasonable to use an alternative, e.g., fentanyl, where possible.

Propofol. Propofol is excreted in breast milk, with maximum concentrations at 4 to 5 hours after administration. The effects of small oral doses of propofol on the infant is unknown. Continued breast-feeding after propofol exposure is not recommended, although the period of prohibition has yet to be determined.

Naloxone and flumazenil. The safety of naloxone and flumazenil in this setting is unknown.

Antibiotics
Penicillins and cephalosporins. Penicillins and cephalosporins are excreted in breast milk in trace amounts and are considered compatible with breast-feeding.

Ofloxacin and ciprofloxacin. Ofloxacin and ciprofloxacin are excreted in breast milk, and their toxicity has not been well studied.

Quinolones. As there is a potential for arthropathy in the infant, quinolones should be avoided.

Sulfonamides. Sulfonamides are contraindicated when nursing infants younger than 2 months because of the risk of kernicterus. It is recommended that sulfonamides be avoided in infants that are ill, premature, and glucose-6-phosphate dehydrogenase deficient. The safety of commonly used antibiotics are summarized in Table 5.

SUMMARY
For the following points: (A), Prospective controlled trials. (B), observational studies. (C), Expert opinion.

- Endoscopy during pregnancy should only be done when there is a strong indication and should be postponed to the second trimester whenever possible.
- The close involvement of obstetrical staff is recommended.

TABLE 5. Antibiotic safety in breast-feeding

<table>
<thead>
<tr>
<th>Safe</th>
<th>Avoid</th>
</tr>
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<tbody>
<tr>
<td>Penicillins</td>
<td>Sulfonamides</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Quinolones</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Metronidazole</td>
</tr>
<tr>
<td></td>
<td>(effect on infant unknown, may be of concern)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td></td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>(except in infants with glucose-6-phosphate dehydrogenase deficiency)</td>
</tr>
</tbody>
</table>
• The degree of maternal and fetal monitoring needs to be individualized. (C)
• For procedural sedation during pregnancy, meperidine alone is preferred, followed by small doses of midazolam as needed. (C)
• If deep sedation is needed, it should be administered by an anesthesiologist. (C)
• EGD and colonoscopy generally are safe during pregnancy. (C)
• ERCP generally is safe, provided care is taken to minimize radiation exposure to the fetus (B) and risks to the mother. (C)
• Bipolar electrocautery is preferred over monopolar. The monopolar grounding pad should be placed to minimize flow of electrical current through the amniotic fluid. (C)
• In late pregnancy, women should be placed in the lateral decubitus position during and after the procedure. (C)
• Although many antibiotics can be safely used in pregnancy, some are contraindicated (quinolones, streptomycin, tetracyclines), whereas others are safe only in certain stages of fetal development. (B)
• Breast-feeding may be continued after maternal fentanyl administration (B), which is preferred over meperidine. (C)
• Infants should not be breast-fed for at least 4 hours after maternal midazolam administration. (B)
• Continued breast-feeding after maternal propofol exposure is not recommended, although the period of prohibition is unknown. (C)
• Penicillins, cephalosporins, tetracyclines, and erythromycin are compatible with breast-feeding. Quinolones and sulfonamides should be avoided. (C)

ACKNOWLEDGMENT

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