Risks of and Recommendations for Flexible Bronchoscopy in Pregnancy*

A Review

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Key words: bronchoscopy; complications; pregnancy

Abbreviations: FB = flexible bronchoscopy; FDA = Food and Drug Administration

Generally, medical procedures such as flexible bronchoscopy (FB) are avoided in pregnancy as a result of procedure- and sedation-related risks to the mother and the fetus. However, there are situations in which these procedures might be diagnostically or therapeutically indicated and should not be delayed.

The current published knowledge about FB in pregnancy is limited to a few case reports1–8 and one review article9; however, upper and lower GI endoscopy during pregnancy is well described, and the lessons learned may be partially extrapolated to FB.

The published studies on endoscopy during pregnancy are mostly retrospective and small.10 The only exception is a large, case-control study11 comparing 83 pregnant women undergoing esophagogastroduodenoscopy with matched pregnant (not undergoing the procedure) and nonpregnant (undergoing the same procedure) women as control subjects. The study reported no increase in adverse events among the pregnant treatment group. However, statistical power was insufficient to exclude a small, but clinically important, fetal risk from endoscopy.

Bronchoscopy during pregnancy has its own specific risks from inserting instruments into the airway, such as impaired gas exchange, severe violent cough, and barotrauma (pneumothorax and pneumomediastinum), which may actually be more hazardous to the pregnant patient. Medications used during endoscopy, and thus bronchoscopy, seem to be responsible for many of the endoscopic risks during pregnancy, but their risks are imprecisely defined, apart from the direct effect of each drug on the fetus.

In this review, we describe the major issues of performing FB in pregnant women, such as changes in the respiratory system, the potential risks associated with FB, the major indications for FB, the use of diagnostic radiation, and the monitoring of the mother and the fetus during FB. Finally, we list some general recommendations for performing bronchoscopy in pregnant patients.

RESPIRATORY SYSTEM CHANGES DURING PREGNANCY

The respiratory system undergoes multiple physiologic and anatomic changes during pregnancy. The bronchoscopist should understand the implications of these changes when planning, preparing, and monitoring the procedure in pregnant women.

Functional Respiratory Changes in Pregnancy

Large airway function does not seem to change during pregnancy.12 The respiratory centers in the brain do appear to change homeostatic set points during pregnancy, as manifested by increased respiratory drive, which is probably a function of increasing levels of progesterone.13 The mechanism of this change is thought to involve an increasing sensitivity of the medulla to carbon dioxide, such that increases in PaCO₂ elicit an exaggerated respiratory effort, although a direct effect of progesterone on the respiratory center cannot be excluded.14

Residual volume and expiratory reserve volume

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both decrease in pregnancy; hence, the decrease in functional residual capacity of approximately 18%. However, the increased inspiratory capacity results in minimal decreases in total lung capacity, and it leaves vital capacity virtually unchanged. The decrease in functional residual capacity is caused by diaphragmatic elevation (caused by increased intra-abdominal pressure) and possibly by increased pulmonary blood flow. These changes likely result in increased uptake and elimination of inhalational anesthetics and with rapid oxygen desaturation during hypoventilation episodes, and this in turn makes endotracheal intubation at term more hazardous.

Relative hyperventilation begins in the first trimester of pregnancy, with the minute ventilation rising by almost 50% at term. The increase in minute ventilation is primarily the result of a large (up to 40%) increase in tidal volume; the respiratory rate does not change. Pregnant women with normal respiratory rates often complain of dyspnea, which is usually the result of these respiratory adaptations.

Oxygen consumption increases by almost 20% during pregnancy, to meet the increased metabolic demands of the placenta, fetus, and maternal organs. However, as mentioned above, minute ventilation rises disproportionately, leading to a rise in alveolar and arterial oxygen levels (normal PaO2 in pregnant women ranges from 100 to 110 mm Hg). In addition, PaCO2 decreases from the nonpregnant average of 40 mm Hg to a plateau of 27 to 32 mm Hg during pregnancy. This respiratory alkalosis is followed by compensatory renal excretion of bicarbonate so that the resultant arterial pH is normal to slightly alkalotic (usually a pH between 7.40 and 7.45). The decrease in PaCO2 probably helps the fetus to eliminate carbon dioxide across the placenta.

Anatomic Respiratory Changes in Pregnancy

Increased estrogen levels during pregnancy cause several changes in the upper airway mucosa, such as hyperemia, glandular hyperactivity, increased phagocytic activity, and increased mucosal mucopolysaccharide content. These changes, in turn, lead to the so-called “rhinitis of pregnancy,” which occurs in approximately 30% of all pregnancies, and pregnancy-induced gingivitis, which occurs in 40 to 100% of all pregnancies. The result is increased mucosal edema and likelihood of bleeding, which makes the case for oral, rather than nasal, bronchoscope insertion in the pregnant women.

Changes in the thorax and abdomen appear to occur early in pregnancy, well before simple displacement from the enlarging uterus could cause such an effect. In the first trimester, the subcostal angle can change from 68° to as much as 103°. The diaphragm rises by up to 4 cm, and the chest diameter can increase ≥ 2 cm. Diaphragmatic excursion is not limited by the uterus, and actually increases by up to 2 cm. The result of these changes is a more “barrel-chested” appearance during pregnancy.

Other Changes in Pregnancy Relevant to Bronchoscopy

The increased prevalence of gastroesophageal re-flux during pregnancy involves both mechanical and intrinsic factors that reduce lower esophageal sphincter tone, which in turn increases the theoretical risk of aspiration during conscious sedation and bronchoscopy.

Uterine enlargement beyond 20 weeks of gestational age can compress the inferior vena cava, markedly reducing cardiac preload and causing the so-called “supine hypotensive syndrome” in approximately 8% of all pregnancies. This syndrome is characterized by the symptoms and signs of reduced cardiac output, mean arterial pressure decrease of > 15 mm Hg, and sympathetic activation, within 3 to 10 min of lying supine, and can harm the mother and the fetus. A sedated patient may not be able to respond to early warning signs appropriately. Therefore, procedures such as FB should be done with the patient in the left lateral tilt position, which is achieved by placing a wedge under the right side, having the patient lie on her left side, or adjusting the operating table to a 30° left lateral tilt.

Potential Risks of Bronchoscopy in Pregnancy

Risks associated with FB can be classified into those related to conscious sedation and medications and those related to the procedure itself. Risks from conscious sedation and other medications used during the procedure include medication-related teratogenesis, induction of premature labor, maternal cardiac arrhythmias, and depressed mental status with resultant hypoventilation (which in turn can cause hypoxemia), airway vulnerability, and possible pulmonary aspiration or respiratory distress. Risks associated with the procedure itself generally include pneumothorax, hypoxemia, airway hyperreactivity, pulmonary hemorrhage, and systemic hypotension or hypertension.

The fetus is particularly sensitive to maternal hypoxia and hypotension. Maternal hypoxia can result from medications vagally mediated bronchospasm, and pulmonary aspiration.
published information on the pulmonary complications associated with FB in pregnancy.

Medications Commonly Used During Bronchoscopy and Pregnancy

Medications used during FB should be considered carefully before being administered to pregnant women, as a result of the potential risks of inducing hemodynamic effects in the mother that can affect the fetus (Table 1). Also, the possible direct effects on the fetus, other than the other usual effects of sedatives and analgesics, must be considered (Table 2).

Patient and Fetal Monitoring During Bronchoscopy

As in other procedures done under conscious sedation, monitoring of pregnant women undergoing FB under conscious sedation should include the following: (1) an initial assessment of the medical history, including previous instances of complicated conscious sedation and allergies, and a general physical examination with specific attention to airway patency; (2) continuous monitoring with intermittent sphygmomanometry, cardiac rhythm and rate monitoring, and pulse oximetry (see below); capnography is optional (see below), but special attention should be paid to the presence of apnea and hypopnea; and (3) there are no formal recommendations regarding fetal heart monitoring during FB. The few case series that address endoscopy during pregnancy suggest that fetal heart monitoring is indicated only in high-risk pregnancies or in procedures done during the third trimester.38 However, anesthesia departments may require fetal heart monitoring during any procedure done under conscious sedation.

Pulse Oximetry

Maraneta et al39 evaluated changes in hemoglobin oxygen saturation with pulse oximetry during diagnostic bronchoscopy in 100 patients. They reported an average oxygen desaturation of 5.6% in approximately 97% of the patients, a recuperation time of 1 to 34 min, and increased desaturation when patients were examined while seated. These findings stress the importance of pulse oximetry during bronchoscopy, especially in pregnant women, given the potential detrimental effect of hypoxemia on the fetus described above. Therefore, oxygen should be administered during the procedure to keep oxygen saturation at 97 to 100% at all times.

Capnography

Studies40–42 have documented the occurrence of marked hypercapnia in the absence of profound hypoxemia in patients receiving sufficient amounts of oxygen, even though these results have been put into question. In an animal study,43 the fetal heart rate response to either hypoxemia or hypercapnia consisted of slowing and increased variability. Slowing was more consistent with hypercapnia than with hypoxemia.

Cognitive skills were lower in 26 preterm-birth preschool and early school-age children with a slight-to-moderate risk for perinatal hypoxia when compared with matched control subjects; however this study44 was retrospective and the patients had marked hypoxemia in addition to hypercapnia, and its applicability is therefore limited. Other evidence

Table 1—FDA Categories of Fetal Risk From Drugs Administered During Pregnancy

<table>
<thead>
<tr>
<th>FDA Pregnancy Risk Category</th>
<th>Fetal Risk From Drugs Administered During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Controlled studies in women show no risk to the fetus in the first trimester (and there is no evidence of risk in later trimesters), and the possibility of fetal harm appears remote.</td>
</tr>
<tr>
<td>B</td>
<td>Animal reproduction studies have reported no fetal risk, and there are no controlled studies in pregnant women, or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).</td>
</tr>
<tr>
<td>C</td>
<td>Studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal, or other) and there are no controlled studies in women, or studies in women and animals are not available. Drug should be administered only if the potential benefit justifies the potential risk to the fetus.</td>
</tr>
<tr>
<td>D</td>
<td>There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg, if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).</td>
</tr>
<tr>
<td>X</td>
<td>Studies in animals or humans have reported fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.</td>
</tr>
<tr>
<td>Medication</td>
<td>FDA Pregnancy Risk Category</td>
</tr>
<tr>
<td>-------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Lidocaine B (manufacturer)</td>
<td>B (manufacturer)</td>
</tr>
<tr>
<td></td>
<td>C (expert analysis)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>β2-agonists</td>
<td>C</td>
</tr>
<tr>
<td>Inhaled</td>
<td>B</td>
</tr>
<tr>
<td>ipratropium</td>
<td>C</td>
</tr>
<tr>
<td>Atropine</td>
<td></td>
</tr>
<tr>
<td>(subcutaneous</td>
<td></td>
</tr>
<tr>
<td>injection)</td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>C</td>
</tr>
<tr>
<td>(submucosal</td>
<td></td>
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<tr>
<td>injection)</td>
<td></td>
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<tr>
<td>Benzodiazepine</td>
<td></td>
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<tr>
<td>Diazepam</td>
<td>D</td>
</tr>
<tr>
<td>Midazolam</td>
<td>D</td>
</tr>
<tr>
<td>Meperidine</td>
<td>B</td>
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<tr>
<td>Fentanyl</td>
<td>C</td>
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<tr>
<td>Propofol</td>
<td>B</td>
</tr>
<tr>
<td>Flumazenil</td>
<td>C</td>
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<tr>
<td>Naloxone</td>
<td>B</td>
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</tbody>
</table>
of mild and temporary respiratory acidosis effects on human fetal growth and development is lacking; however, until such evidence is obtained, hyperventilation should be avoided during procedures in pregnant women.

End-tidal PaCO₂ (capnometry) is a more sensitive measure of the hyperventilation that is being masked by supplemental oxygen delivery than is direct visual monitoring. A controlled trial evaluating this approach in 195 patients undergoing endoscopic retrograde cholangiopancreatography found that hypercapnia was not reliably detected by clinical observations or by pulse oximetry in patients receiving supplemental oxygen. The addition of transcutaneous carbon dioxide monitoring prevented severe hypercapnia more effectively than intensive clinical monitoring and pulse oximetry alone. Routine capnometry, however, is not currently widely available or included in current recommendations for monitoring patients undergoing conscious sedation.

**Indications for Bronchoscopy in Pregnancy**

The indications for bronchoscopy in pregnant patients are similar to those for patients who are not pregnant (Table 3).

**Emergent Bronchoscopy in Pregnancy**

As in any other emergent situations, lifesaving procedures should be performed in pregnant women regardless of the stage of pregnancy or the status of the fetus. Emergent bronchoscopy is no exception. Emergent indications for FB include airway maintenance in cases of upper airway obstruction caused by critical subglottic-tracheal stenosis, marked lung collapse caused by an obstructing foreign body, or massive hemoptysis caused by tumors. The primary concern should be the safety and survival of the mother. However, harm to the fetus can be minimized by fetal monitoring, adequate oxygenation of the mother during the procedure, and avoiding hypotension-inducing drugs. Well-trained operators working in well-controlled settings, such as in the operating room, also decrease risk.

**Nonemergent Bronchoscopy in Pregnancy**

The decision to perform nonemergent bronchoscopy should be individualized to each patient and should depend on the clinical setting, indication, mother’s health status, and stage of pregnancy. In addition, the following considerations are important:

- If possible, postpone diagnostic bronchoscopy until the patient has given birth. Timing will be dictated by clinical needs.

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**Table 3—Indications for FB During Pregnancy**

<table>
<thead>
<tr>
<th>Diagnostic uses</th>
<th>Therapeutic uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>To evaluate lung lesions of unknown cause that appear on chest radiographs</td>
<td>To remove retained secretions or mucous plugs not mobilized by conventional noninvasive techniques</td>
</tr>
<tr>
<td>To assess airway patency</td>
<td>To remove foreign bodies</td>
</tr>
<tr>
<td>To investigate unexplained hemoptysis, unexplained cough, localized wheeze, or stridor</td>
<td>To remove abnormal endobronchial tissue or foreign material by use of forceps or laser techniques</td>
</tr>
<tr>
<td>To search for the origin of a suspicious or positive sputum cytology sample</td>
<td>To perform difficult intubations</td>
</tr>
<tr>
<td>To investigate unexplained paralysis of a vocal cord, hemidiaphragm, superior vena cava syndrome, chylothorax, or unexplained pleural effusion</td>
<td>Conditions involving increased risk</td>
</tr>
<tr>
<td>To evaluate problems associated with endotracheal tubes, such as tracheal damage, airway obstruction, or tube placement</td>
<td>Lack of patient cooperation</td>
</tr>
<tr>
<td>To stage lung cancer preoperatively and subsequently to evaluate, when appropriate, the response to therapy</td>
<td>Recent myocardial infarction or unstable angina</td>
</tr>
<tr>
<td>To determine the location and extent of respiratory tract injury after acute inhalation of noxious fumes or aspiration of gastric contents</td>
<td>Partial tracheal obstruction</td>
</tr>
<tr>
<td>To obtain material for microbiologic studies in suspected pulmonary infections</td>
<td>Unstable bronchial asthma</td>
</tr>
<tr>
<td>To evaluate the airways for suspected bronchial tear or other injury after thoracic trauma</td>
<td>Respiratory insufficiency associated with moderate-to-severe hypoxemia or any degree of hypercarbia</td>
</tr>
<tr>
<td>To evaluate a suspected tracheoesophageal fistula</td>
<td>Uremia and pulmonary hypertension (possible serious hemorrhage after biopsy)</td>
</tr>
<tr>
<td>To determine the location and extent of respiratory tract injury after acute inhalation of noxious fumes or aspiration of gastric contents</td>
<td>Lung abscess (danger of flooding the airway with purulent material)</td>
</tr>
<tr>
<td>To obtain material for study from the lungs of patients with diffuse or focal lung diseases</td>
<td>Immunosuppression (danger of postbronchoscopy infection)</td>
</tr>
<tr>
<td>To perform difficult intubations</td>
<td>Obstruction of the superior vena cava (possibility of bleeding and laryngeal edema)</td>
</tr>
<tr>
<td>Conditions involving increased risk</td>
<td>Dehiscence and malnutrition</td>
</tr>
<tr>
<td>Lack of patient cooperation</td>
<td>Unstable cardiac arrhythmia</td>
</tr>
<tr>
<td>Recent myocardial infarction or unstable angina</td>
<td>Respiratory failure requiring mechanical ventilation</td>
</tr>
<tr>
<td>Partial tracheal obstruction</td>
<td>Disorders requiring laser therapy, biopsy of lesions obstructing large airways, or multiple transbronchial lung biopsies</td>
</tr>
<tr>
<td>Unstable bronchial asthma</td>
<td>Danger of a serious complication from bronchoscopy is especially high in patients with:</td>
</tr>
<tr>
<td>Respiratory insufficiency associated with moderate-to-severe hypoxemia or any degree of hypercarbia</td>
<td>Malignant arrhythmia</td>
</tr>
<tr>
<td>Uremia and pulmonary hypertension (possible serious hemorrhage after biopsy)</td>
<td>Profound refractory hypoxia</td>
</tr>
<tr>
<td>Lung abscess (danger of flooding the airway with purulent material)</td>
<td>Severe bleeding diathesis that cannot be corrected when biopsy is anticipated</td>
</tr>
<tr>
<td>Immunosuppression (danger of postbronchoscopy infection)</td>
<td>Contraindications</td>
</tr>
<tr>
<td>Obstruction of the superior vena cava (possibility of bleeding and laryngeal edema)</td>
<td>Absence of consent from the patient or his or her representative</td>
</tr>
<tr>
<td>Dehiscence and malnutrition</td>
<td>Inexperienced bronchoscopist working without direct supervision</td>
</tr>
<tr>
<td>Unstable cardiac arrhythmia</td>
<td>Lack of adequate facilities and personnel to care for emergencies, such as cardiopulmonary arrest, pneumothorax, or bleeding</td>
</tr>
<tr>
<td>Respiratory failure requiring mechanical ventilation</td>
<td>Inability to adequately oxygenate the patient during the procedure</td>
</tr>
</tbody>
</table>

*From Baughman et al.*
• If possible, postpone bronchoscopy until there is
good chance of delivering a viable healthy new-
born, usually after 28 weeks of pregnancy.
• New technologies can, in selected cases, substitute
for bronchoscopy. For example, three-dimensional
CT and virtual bronchoscopy can be used to follow
an endobronchial lesion in a patient who has
undergone an initial diagnostic FB. However, the
limitations and potential harmful effects (such as
radiation, see below) of these technologies on the
mother and the fetus must be kept in mind.

Radiation Exposure During Pregnancy

The potential harmful consequences of radiation
for the fetus can be classified into four categories:
intrauterine death, malformations, growth and devel-
opmental disturbances, and mutagenic and carci-
nonic effects. The danger to the fetus from radia-
tion during fluoroscopic procedures depends on the
dose of radiation (which in turn is related to exposure
time, the number of films obtained, beam size, and
imaging area) and gestational age. The preimplanted
embryo is most at risk from the lethal effects of
radiation.

The risk is greatly diminished by appropriate and
complete abdominal lead shielding, a short radiation
exposure time, and performance of the procedure
after the 14th week of gestation, when organogenesis
has already been achieved. A study of radiation in
pregnant women with appropriate abdominal shielding
reported no abnormalities related to radiation.

The exact dose of radiation received during fluo-
roscopic FB is not known; however, a study of
cardiac catheterization and valvuloplasty reported no
adverse fetal effects of ionizing radiation at doses of
< 5 rad. The margin of safety is augmented by the
fact that most exposures to diagnostic imaging radia-
tion are spread over a period of time; this type of
exposure is less harmful than acute exposure. The
same risk-benefit analysis should be applied when
deciding to use fluoroscopy for diagnostic FB, keep-
ing in mind that fluoroscopy does not improve the
yield for transbronchial biopsy, especially in diffuse
lung diseases.

General Recommendations for
Bronchoscopy During Pregnancy

1. When possible, defer bronchoscopy until after
the pregnancy is ended or, if that is not possible,
until after the 28th week of pregnancy.
2. Explain to the patient the risks and benefits of
the procedure, as well as the associated med-
ications, to her and to the fetus. Obtain in-
formed and written consent to perform the
procedure.
3. Perform the bronchoscopy in a well-equipped
hospital with ready access to anesthesia, obstet-
ric, and neonatology services in case of
emergency.
4. Consult a pharmacologist regarding the ter-
atogenicity of any medications to be used.
5. Consult an anesthesiologist about options for
conscious sedation.
6. Consider an obstetric consultation to help
identify and manage at-risk pregnancies.
7. For conscious sedation, use the lowest effec-
tive dose of the drug. Do not use US Food and
Drug Administration (FDA) category X or
category D drugs (Tables 1, 2).
8. Avoid using optional drugs. When alternative
drugs are available, use the drug that is safest
for the fetus.
9. Perform continuous cardiac monitoring, pulse
oximetry, and intermittent sphygmomanome-
try during the procedure.
10. Capnography has not been studied in preg-
nant women during procedures that require
conscious sedation and therefore is not rec-
ommended.
11. Monitor the fetus if possible.
12. Position the patient in the left lateral decubi-
tus position if possible, and if not, in a seated
position.
13. Complete the procedure as soon as possible.
For example, avoid lengthy examination of the
distal airways if it is not indicated during
preprocedure planning.
14. Terminate poorly tolerated procedures.
15. Have the most experienced bronchoscopist
available perform the procedure.
16. Base the decision to use fluoroscopy in FB
during pregnancy on an individual risk-benefit
analysis.
17. Consider alternatives to bronchoscopy when
appropriate, such as imaging technologies.
18. Consider referrals to a specialized center if
you are unsure whether all needed services
(anesthesia, critical care, obstetrics, neonatol-
ogy) are available.

Summary

When performing FB on pregnant women, com-
mon sense and generally used precautions should be
considered, including appropriate planning and care-
ful review of medication effects on the fetus. No
studies, other than some case reports, have tested
the utility and safety of bronchoscopy and other associated diagnostic and therapeutic procedures during pregnancy. Until such studies are published, bronchoscopy should be reserved for indications that cannot wait until the postpartum period. Advances in the diagnosis and treatment of lung and airway diseases, such as endobronchial ultrasound, CT fluoroscopy, and virtual bronchoscopy, may be combined with FB to decrease the risks to the mother and the fetus.

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