Nonobstetric Surgery During Pregnancy

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Surgery during pregnancy: indications and incidence

• 0.75%-2% of pregnant women undergo non-obstetric surgery
  
  Brodsky JB. *Am J Obstet Gynecol* 1980; 138:1165

• May occur at any time during pregnancy
  – 5405 Swedish women
    • 42% occurred during the first trimester
    • 35% during the second trimester
    • 23% during the third trimester
  

• The true incidence may be higher, as women may undergo surgery before realizing they are pregnant
  
  Manley S. *Anesthesiology* 1995; 83:690
Maternal Mortality

- Maternal mortality can occur even in early pregnancy
  - Hemorrhage
  - Sepsis
  - Thromboembolism
  - Anesthesia
Risks to the Fetus

- Disease process or related therapy
- Teratogenicity of anesthetic agents or other drugs
- Intraoperative perturbations of uteroplacental perfusion and/or fetal oxygenation
- Abortion/preterm delivery
Maternal physiologic changes during pregnancy

• Inhalation anesthetic requirements
  – Decreased by approximately 30% during pregnancy, as early as the first trimester
    Chan MT. Anesthesiology 1996; 85:782
    Gin T. Anesthesiology 1994; 81:829
  – Elevated circulating endorphins
    Gintzler AR. Prog Brain Res 2001; 133:83
  – Elevated progesterone
    Datta S. Anesth Analg 1989; 68:46
Maternal physiologic changes during pregnancy

• Local anesthetic requirements
  – Decreased by 30% to 40% during pregnancy
  – Decreased volume of CSF in subarachnoid space secondary to engorgement of the epidural veins
    Igarashi T. *Anesthesiology* **2000**; 92:1631
  – Vagus nerves obtained from pregnant rabbits show increased sensitivity to local anesthetic-induced blockade of nerve conduction
  – Nerves obtained from non-pregnant rabbits bathed in a progesterone-containing solution do not display increased sensitivity
    Bader AM. *Anesth Analg* **1990**; 71:545
Maternal physiologic changes during pregnancy

• Cardiovascular
  – Blood volume
    • ↑15% by 12 weeks
    • ↑50% by end of 2nd trimester
    • Minimal increase during third trimester

Bernstein IM. *Obstet Gynecol* 2001; 97:669
Maternal physiologic changes during pregnancy

• Cardiovascular
  – Cardiac output
    • ↑35-40% at end of 1st trimester
    • Initial change due to increased HR, followed by increased stroke volume
    • Intrinsic contractility (LVSWI) unchanged
    • ↑50% at term

Maternal physiologic changes during pregnancy

• Respiratory
  – Oxygen consumption
    • ↑60%-fetus, placenta, uterus
  – Oxygen supply
    • FRC ↓20%
  – Implication: apnea⇒rapid desaturation
Published recommendations: airway management

- “Some consider all women at risk for aspiration of gastric content at 18-20 weeks”
  - “Any woman with symptoms of acid reflux should be considered at risk”
    Beilin Y. In Anesthesia for Obstetrics, 5th Edition

- “It seems prudent to consider any pregnant woman as having a higher risk for aspiration after mid-gestation; some anesthesia providers contend that pregnant women are at increased risk from the beginning of the second trimester”
  Van de Velde M. In Chestnut’s Obstetric Anesthesia, Fifth edition
Expert opinion

- “Anytime after conception”
- “12 weeks”
- “18-20 weeks, depending on size of uterus, symptomatic reflux”
- “18 weeks, earlier if they have morning sickness”
- “20 weeks if I can give metoclopramide and H₂ blocker”
Maternal physiologic changes during pregnancy

- Gastrointestinal system
  - Lower esophageal sphincter tone
  - Gastric volume/acidity
  - Gastric emptying
Lower esophageal sphincter tone

- The enlarging uterus displaces the stomach, altering the angle of the GE junction and predisposing to incompetence of the LES
  

- Smooth muscle relaxant effects of progesterone decrease LES tone

- Intragastric pressures are significantly increased by the enlarging uterus, exacerbated by multiple gestation or polyhydramnios

  Spence AA. *Anaesthesia* 1967; 22:249
Lower esophageal sphincter tone

• Decreased LES tone and increased intragastric pressure alters the pressure gradient across the GE junction in an unfavorable manner, predisposing to regurgitation
  

• It appears that the time course of these changes differs, with decreases in LES tone occurring early in pregnancy (especially in patients with heartburn), and increases in intragastric pressure occurring later in gestation
  
Lower esophageal sphincter tone

• This would suggest that, in the absence of symptoms of regurgitation, the risk of an altered LES gradient is not significant until approximately 20 weeks gestation
Gastric volume/acidity

- The volume and acidity of gastric secretions is increased by the polypeptide hormone gastrin
- Gastrin secretion is increased by gastrin-releasing peptide (GRP)
- Gastrin secretion is increased throughout pregnancy

Attia RR. *Anaesthesia* 1982; 37:18
# Gastric volume/acidity

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>T.O.P. (EGA 15±3)</th>
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<tbody>
<tr>
<td>pH</td>
<td>1.7</td>
<td>2.4</td>
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<tr>
<td>Gastric volume</td>
<td>28ml</td>
<td>28 ml</td>
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</tbody>
</table>

Wyner J, Cohen SE. *Anesthesiology* **1982;** 57:209
Gastric volume/acidity

- Ultrasonography demonstrates no change in gastric emptying during first and third trimesters compared to postpartum controls
  Chiloiro M. J Gastroenterol 2001; 36:538

- However, patients in labor, especially those receiving opioid analgesics, do appear to have delayed gastric emptying
Recommendations: Airway management during pregnancy

• A non-particulate antacid should be used throughout pregnancy when general anesthesia is planned
• Metoclopramide and an H$_2$ blocker should be added for high risk patients (symptomatic reflux, significant obesity), i.e., as would be done with any patient, pregnant or not
Recommendations: Airway management during pregnancy

- Rapid sequence induction with cricoid pressure and endotracheal intubation should be performed:
  - In patients with symptomatic reflux disease
  - In patients who are significantly obese
  - In the third trimester, or during the second trimester in patients with significant uterine enlargement
Teratogenicity
<table>
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<th>Causes of Developmental Defects in Humans</th>
<th>Percentage</th>
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<tr>
<td>Genetic transmission</td>
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<tr>
<td>Chromosomal aberration</td>
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<td>Environmental causes:</td>
<td></td>
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<tr>
<td>Radiation</td>
<td>&lt;1</td>
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<tr>
<td>Infection</td>
<td>2-3</td>
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<tr>
<td>Maternal metabolic imbalance</td>
<td>1-2</td>
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<tr>
<td>Drugs and environmental chemicals</td>
<td>2-3</td>
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<tr>
<td>Unknown</td>
<td>65-70</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
</tr>
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</table>
Teratogenic Agents in Human Beings

Radiation
Atomic weapons, radioiodine, therapeutic uses

Infections
Cytomegalovirus, herpes virus hominis, parvovirus B-19, rubella virus, syphilis, toxoplasmosis, Venezuelan equine encephalitis virus

Maternal Metabolic Imbalance
Alcoholism, cretinism, diabetes, folic acid deficiency, hyperthermia, phenylketonuria, rheumatic disease and congenital heart block, virilizing tumors

Drugs and Chemicals
Aminopterin and methylaminopterin, androgenic hormones, busulphan, captopril, chlorobiphenyls, cocaine, coumarin anticoagulants, cyclophosphamide, diethylstilbestrol, diphenylhydantoin, enalapril, etretinate, iodides (goiter), lithium, mercury (organic), methimazole (scalp defects), penicillamine, 13-cis-retinoic acid (Accutane), tetracyclines, thalidomide, trimethadione, valproic acid
Nitrous oxide

- Animal studies
  - Rats exposed to 50% N₂O for 2-6 days induced skeletal abnormalities and fetal resorption
    
  
  - Rats exposed to 50% N₂O for 4 hours daily on days 6-15 did not show an increased risk of malformations
    
    Mazze RI. *Teratology* **1984**; 30:259
Nitrous oxide

• Mechanism of teratogenicity
  – $\text{N}_2\text{O}$ inactivates vitamin $\text{B}_{12}$, a cofactor for methionine synthetase
  – This impairs production of tetrahydrofolate, essential for DNA synthesis, and methionine, an important component of methylation reactions
Nitrous oxide

- However, maximal depression of methionine synthetase activity occurs at $N_2O$ exposure levels far less than those required to produce congenital malformations.
- The ability of $N_2O$ to potentiate phenylephrine-induced situs inversus suggests that sympathetic stimulation is a major factor in the production of fetal toxicity.
• Human studies
  – Early studies suggested that exposure to trace levels of anesthetic gases contributed to poor obstetric outcomes in operating room personnel
  – Flaws: response bias, failure to account for confounding factors, lack of verification of adverse outcomes, and lack of dose-response information
  – The increases in poor obstetric outcomes are within the range of statistical error (relative risk ratios of 1.2-1.3) vs. 2-3 fold increase required to prove teratogenicity

Nitrous oxide
Nitrous oxide

• Surgery during pregnancy
  – 5405 operations performed in 720,000 pregnant women
  – 2252 in first trimester, 65% general anesthesia, most received N₂O
  – Incidence of congenital malformations was no higher among offspring of women who underwent surgery
  – Little evidence to support the blanket refusal to administer N₂O to pregnant women during the first trimester
Benzodiazepines

• 599 oral clefts reported to the Finnish Register of Congenital Malformations 1967-71
• Consumption of antineurotics (primarily diazepam) during the first trimester was two times more common among mothers of affected infants than in matched controls
• Retrospective: recall bias?

Saxen I. *Int J Epid* 1975; 4:37
Benzodiazepines

- 611 infants with cleft lip, cleft palate, or both, 2498 controls
- No evidence of increased risk of cleft in offspring of women who received diazepam during 1st trimester
  

- 599 women who called teratogen hotline during pregnancy due to BD exposure
- Followup of 460 pregnancies-no increase in incidence of congenital malformations
  
Behavioral teratology

• Some teratogens produce persistent behavioral abnormalities without any observable morphologic changes
• Brief intrauterine exposure to halothane adversely affects postnatal learning behavior and causes CNS degeneration and decreased brain weight in rats

Smith RF. Anesthesiology 1978; 49:319
Levin ED. Anesth Analg 1986; 65:653
Behavioral teratology

- Currently used general anesthetics act by one of two mechanisms:
  - Potentiation of gamma-aminobutyric acid (GABA<sub>A</sub>) receptors (inhalational agents, benzodiazepines, barbiturates)
  - Antagonism of N-methyl-D-aspartate (NMDA) receptors (Nitrous oxide, ketamine)

- Drugs that act by either of these mechanisms induce widespread neuronal apoptosis in the developing rat brain when administered during the period of synaptogenesis

Jevtovic-Todorovic V. *J Neurosci* 2003; 23:876
Animal studies

- Hartley guinea pig model
- Gestation 59-72 days
- Three groups:
  - 20-25 days (early stage of brain development)
  - 35-40 days (peak stage)
  - Over 50 days (late stage)
• Experimental group further subdivided into:
  – Isoflurane alone 0.55%
  – Isoflurane + N₂O 75%
  – Isoflurane + midazolam 1 mg/kg
  – Isoflurane + N₂O + midazolam
• In fetuses exposed to anesthetics at the time of peak brain development (35-40 days), caspase-3 activation (early marker of apoptosis) is elevated in multiple cortical regions within 2 hours of anesthesia.

• This effect is greatest in animals given all three agents, but is seen to a lesser extent even in those receiving isoflurane alone.
• In fetuses exposed at early period of brain development (20-25 days) increased apoptosis was again worse with triple drug exposure, but not seen with isoflurane alone
• In animals exposed in the late stages of brain development, there was no evidence of increased apoptosis in any drug treatment group
• Studies of postnatal animals remote from anesthetic exposure (1 week after birth) showed that early apoptotic changes were manifested as persistent decreased cell density in multiple cortical regions.

Rizzi S. Brain Path 2008; 18:198
Multiple animal studies have shown that exposure to general anesthetics during the period of brain development can impair neurodevelopment.

So the proposition that exposure to anesthetic agents during human pregnancy MAY cause post-natal neurocognitive effects must be answered in the affirmative.

And this proposition may be supported by studies of multiple anesthetic exposures in infancy.
• 8548 children born between January 1976 and December 1982 in Rochester, Minnesota
• 350 identified as having general anesthesia prior to age 2 years
  – 286 exposed once
  – 86 more than once
• 700 unexposed controls
• Incidence of learning disabilities by age 19
  – 21.3% in unexposed controls
  – 23.6% in those exposed once
  – 36.6% in those with multiple exposures

Flick RP. Pediatrics 2011; 128:e1053
• Retrospective study of 10,450 siblings born between 1999 and 2005
• 304 underwent surgery at less than 3 years of age
• 10,146 controls
• Incidence of developmental and behavioral disorders was 128 diagnoses/1000 person-years in exposed group
• 56 diagnoses/1000 person-years in control group
• Hazard ratio 1.6
  – 1.1 for one operation
  – 2.9 for two operations
  – 4.0 for three or more operations

DiMaggio C. Anesth Analg 2011; 113:1143
Should any of this change our practice?

- Multiple postnatal anesthetic exposures in humans do not necessarily have the same effect as a single exposure during pregnancy.
- A single exposure during human pregnancy cannot be assumed to have the same effect as a similar duration exposure during a much shorter animal gestation.
- Can we reliably correlate a particular period of brain development in animals with an analogous period in human gestation?
• We may not be able to separate anesthetic effects from the effects of the illness that required anesthesia during pregnancy
  – Fetal surgery for congenital malformations
  – Maternal intra-abdominal febrile infectious process
What are the most common surgical procedures performed during pregnancy?

- Cervical cerclage
- Ovarian cystectomy
- Appendectomy – 6.13/10,000 births
- Cholecystectomy – 5/10,000 births
- Surgery for trauma

None of these procedures can be delayed until after delivery, or even until the theoretically less risky third trimester.
• It is standard practice to utilize regional anesthetics whenever possible throughout pregnancy
  – Minimal fetal transfer
  – No documented teratogenic effects
  – Will usually avoid the complications of airway instrumentation (hypoxemia, aspiration, failed intubation)
There is no specific inhaled or intravenous anesthetic agent that has been shown to be any safer than the alternative anesthetics.

- 6 hour exposure of neonatal mice to 0.6 MAC isoflurane, desflurane, and sevoflurane produced identical patterns of neuronal cell death.

Istaphanous GK. *Anesthesiology* 2011; 114:578.
• Avoidance of multiple agents?
  – Not clear if increased toxicity is due to mixture of GABAergic and NMDA antagonist agents, or greater depth of anesthesia
  – Will using a larger dose of a single agent to achieve one MAC have a benefit or will it only increase complications of that single agent?
• “We believe that evidence is most consistent with the premise that anesthesia per se, given to an otherwise healthy child who needs only a routine surgical procedure, is not neurotoxic.
• “We have no doubt that that there are parents who are declining surgery entirely because of (fears of neurotoxicity)
• “Anesthetic neurotoxicity in children has become a modern day dragon in medicine…Dragons are very good at hiding from view, and they are very hard to kill.”

Thomas J. Anesth Analg 2011; 113:969
FH monitoring

• How might fetal monitoring affect perioperative management?
  – Emergency cesarean delivery if viability has been reached-practicality?
  – Initiate measures to improve uteroplacental perfusion and oxygen delivery
    • Positioning
    • Blood pressure
    • Oxygenation
    • Acid-base status
    • Inspection of operative site to r/o uterine compression
FH monitoring

• Normal changes in FH seen during general anesthesia:
  – Decreased baseline
  – Decreased short-term variability
  – Decreased long-term variability
FH monitoring

• When is fetal monitoring technically feasible?
  – Beyond 20 weeks gestation
  – Non-abdominal or pelvic surgery
    • Intraoperative doppler

• Who should monitor?
  – Obstetrician prepared for immediate cesarean section
  – Obstetric nurse
  – Anesthesia provider
The American College of Obstetricians and Gynecologists
Women’s Health Care Physicians

COMMITTEE OPINION

Number 474, February 2011 (Reaffirmed 2013, Replaces No. 284, August 2003)

Committee on Obstetric Practice
This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

Nonobstetric Surgery During Pregnancy
• If fetal monitoring is to be used, consider the following recommendations:
  – Surgery should be done at an institution with neonatal and pediatric services.
  – An obstetric care provider with cesarean delivery privileges should be readily available.
  – A qualified individual should be readily available to interpret the fetal heart rate patterns.
• General guidelines for fetal monitoring include the following:
  – If the fetus is considered pre-viable, it is generally sufficient to ascertain
    the fetal heart rate by Doppler before and after the procedure.
  – At a minimum, if the fetus is considered to be viable, simultaneous
    electronic fetal heart rate and contraction monitoring should be performed
    before and after the procedure to assess fetal well-being and the absence
    of contractions.
Intraoperative electronic fetal monitoring may be appropriate when all of the following apply:

- The fetus is viable.
- It is physically possible to perform intraoperative electronic fetal monitoring
- A health care provider with obstetric surgery privileges is available and willing to intervene during the surgical procedure for fetal indications
- When possible, the woman has given informed consent to emergency cesarean delivery
- The nature of the planned surgery will allow the safe interruption or alteration of the procedure to provide access to perform emergency delivery
• In select circumstances, intraoperative fetal monitoring may be considered for previable fetuses to facilitate positioning or oxygenation interventions.

• The decision to use fetal monitoring should be individualized and, if used, should be based on gestational age, type of surgery, and facilities available. Ultimately, each case warrants a team approach (anesthesia and obstetric care providers, surgeons, pediatricians, and nurses) for optimal safety of the woman and the fetus.
Laparoscopic surgery during pregnancy

• Advantages
  – Smaller incisions ⇒ less pain, more rapid recovery, decreased complications of immobilization
  – Earlier return of GI function
  – Smaller scars
  – Fewer incisional hernias
  – Shorter hospitalizations, decreased costs
Laparoscopic surgery during pregnancy

- Laparoscopic procedures performed during pregnancy:
  - Adnexal torsion/mass
  - Cholecystectomy
  - Appendectomy
Potential physiologic perturbations

• Secondary to increased intraabdominal pressure
  – Decreased maternal oxygenation
    • Secondary to decreased FRC; does not affect fetal oxygenation
      Cruz AM. *Anesthesiology* 1996; 85:1395
  – Decreased maternal cardiac output and decreased uteroplacental perfusion
    • Insignificant if distending pressure limited to 15 mm Hg
      Galan HL. *Anesthesiology* 1994; 81:A1160
      Barnard JM. *Obstet Gynecol* 1995; 85:669
• Maternal hypercarbia
  – In a fetal ewe model, CO₂ pneumoperitoneum consistently produced maternal and fetal hypercarbia and acidosis
  – The $p_a$CO₂-ETCO₂ gradient was widened during pneumoperitoneum
    • ETCO₂ therefore underestimates $p_a$CO₂
  – Attempts to correct maternal hypercarbia with hyperventilation led to partial improvement of fetal hypercarbia and acidosis, but this was exaggerated by capnometry, i.e. the $p_a$CO₂-ETCO₂ gradient widened even further during hyperventilation
Human studies

- The pregnancies of 4/7 women undergoing laparoscopic appendectomy or cholecystectomy ended in fetal death
  

- However, several larger series have demonstrated the safety of laparoscopy during pregnancy
Human studies

- 413 cases identified by mail survey (SLS)
  - 48% cholecystectomies, 28% adnexal operations, 16% appendectomies, 8% other
  - Trimester: 33% 1st, 54% 2nd, 13% 3rd
  - 5 intraoperative complications including 1 intrauterine needle placement
  - 10 postoperative complications including 5 SAB (all in first trimester, 5/134)
    
    Reedy MB. *J Reprod Med* 1997; 42:33

- Problems: select group of surgeons, retrospective underreporting of complications
Human studies

- 2,015,000 deliveries identified through three Swedish Health Registries, 1973-1993
- 2181 laparoscopies and 1522 laparotomies performed between 4-20 weeks of gestation
- Five parameters evaluated:
  - Birth weight <2500 gm
  - Gestational duration <37 weeks
  - IUGR
  - Infant death at one year
  - Fetal malformations
Human studies

• There was a tendency for infants in both groups to weigh <2500 gm, to be delivered before 37 weeks, and to be growth restricted

• However, there was no difference between groups in these or the other outcome parameters.

Reedy MB, Källén B. *Am J Obstet Gynecol* 1997; 177:673
Human studies

- It has been suggested that maternal $p_aCO_2$ be measured directly or via transcutaneous CO$_2$ monitoring.
- Is the $p_aCO_2$-ETCO$_2$ gradient altered during laparoscopy in humans?
  - 8 patients undergoing lap chole, 17-30 wks EGA
  - Insufflated with CO$_2$, 15 mm Hg peak
  - Ventilated to maintain ETCO$_2$ at 32 mm Hg
  - Gradient pre-insufflation: 2.4, during insufflation: 2.6, after termination: 1.9

Bhavani-Shankar K. Anesthesiology 2000; 93:370
Human studies

- Alternative techniques:
  - Gasless laparoscopy
    - Little experience, compromised exposure
  - Nitrous oxide
    - Supports combustion
- Fetal monitoring
  - Transabdominal FH monitoring may not be possible-transvaginal monitoring may be more reliable

SAGES Guidelines for laparoscopic surgery during pregnancy

• Obstetric consultation should be obtained preoperatively
• Operative intervention should be deferred until the second trimester whenever possible
• Because pneumoperitoneum enhances venous stasis in lower extremities, pneumatic compression stockings should be used
• Fetal and uterine status, as well as maternal ETCO$_2$ and/or ABG should be monitored
SAGES Guidelines for laparoscopic surgery during pregnancy

- Uterus should be protected with lead shield if cholangiography is used
- Access should be obtained via open technique to minimize risk of uterine injury
- Uterine displacement should be utilized
- Pneumoperitoneum: optimal 8-12 mm Hg, not to exceed 15 mm Hg

Society of American Gastrointestinal Endoscopic Surgeons
http://www.sages.org
From Rosen M. Management of anesthesia for the pregnant surgical patient. Anesthesiology 91:1159, 1999