

NON-OBSTETRIC SURGERY DURING PREGNANCY

Joy L. Hawkins, M.D.
University of Colorado SOM
(* I have no conflicts to disclose.*)

GOALS & OBJECTIVES

Upon completion of this presentation, participants will be able to:

1. Explain issues related to teratogenicity
2. Discuss the risks of occupational exposure to anesthetics
3. Cite outcome studies of parturients having surgery
4. Develop a rational approach to anesthetic management, including special surgical situations.

Br J Anaesth 2011; (S1): i72-i78

OUR PATIENTS ARE CONCERNED

Pregnant women who sought counseling after exposure to *non-teratogenic* drugs estimated they had a 25% risk of major malformations.

Am J Obstet Gynecol 1989;160:1190

THE PUBLIC IS CONCERNED

“The fetus usually dies from the anesthesia administered to the mother before the procedure begins . . . The intravenous anesthetic administered to the woman during the procedure induces a medical coma in the fetus and eventually a neurological fetal demise.”

Congressional Testimony 6/23/95

Too much oxygen may abort fetus

By Michael Day
New Scientist

For us, oxygen is a benign gas essential to life. But for a developing fetus, it can be a killer.

One in six pregnancies comes to a premature end, and oxygen might play a key role in these miscarriages, say scientists who have measured levels of oxygen in the placenta through the first third of pregnancy.

ANESTHESIOLOGISTS ARE CONCERNED

A retrospective survey of female veterinarians related preterm delivery (< 37 weeks) to self-reported occupational exposures.

- OR 2.5 for those who performed surgery without scavenging anesthetic gases vs. with scavenging
- OR 3.69 for those working > 45 hours a week.

Obstet Gynecol 2009;113:1008

Are Pregnant Moms Safe in OR for Child's Inhalation Induction?

To the Editor:

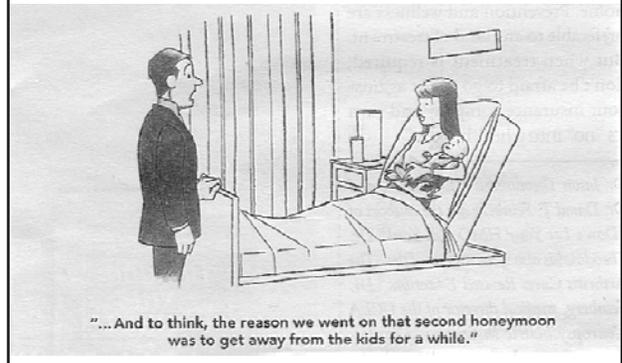
During a recent pediatric mask induction on a mother's lap, the mother happened to mention that she was 16 weeks pregnant. The next two patients' mothers, who also chose to be present for induction, were also pregnant but this information was only elicited after direct questioning.

CONTROVERSIAL ISSUES IN ANESTHETIC CARE DURING PREGNANCY

Controversy #1. Which patients need to have preoperative pregnancy testing?

Case: A healthy 25-year old woman presents to your operating room for knee arthroscopy on an outpatient basis. Does she need to have a pregnancy test?

50% of pregnancies in the U.S. are unplanned!



PREGNANCY TESTING

From the ASA *Practice Advisory for Pre-anesthesia Evaluation*:

"The Task Force recognizes that patients may present for anesthesia with early undetected pregnancy. The Task Force believes that the literature is inadequate to inform patients or physicians on whether anesthesia causes harmful effects on early pregnancy. Pregnancy testing may be *offered* to female patients of childbearing age and for whom the result would alter the patient's management."

PREGNANCY TESTING

For one year, all women of childbearing age having ambulatory surgical procedures had preoperative pregnancy testing.

- 7/2056 (0.3%) of tests were positive.
- All 7 patients elected to cancel surgery (2 were infertility procedures).
- The estimated cost to diagnose one pregnancy was \$2879.

Anesthesiology 1995;83:690

PREGNANCY TESTING

A specialty orthopedic hospital initiated mandatory pregnancy testing. After 1 year:

- 2588 tested→8 positives, but 4 were false positives.
- 3 of the false positives subsequently had a negative serum hCG, and surgery then proceeded.
- 4/2588 (0.15%) of tests were true positives and their surgery was canceled.
- NNT for 1 true positive : 647
- Cost for 1 true positive : \$3273

Anesth Analg 2008;106:1127

PREGNANCY TESTING

“...should a spontaneous abortion occur after surgery, or the baby be born with a congenital anomaly, this may be attributed to the surgery or anesthetic.....screening may decrease litigation, although potential cost savings are difficult to quantify.”

Anesth Analg 2008;106:1127

PREGNANCY TESTING

A retrospective review of 2 years of mandatory pregnancy testing in a freestanding pediatric hospital revealed that 2.4% of patients age 16 and older were positive. None were positive in patients less than 15 years of age (overall 1.3%).

Their conclusions: A policy of mandatory pregnancy testing in patients aged 15 and older is advisable. Specific written consent for the test is not necessary, but proper notification processes must be established.

Anesth Analg 1996;82:4-7

PREGNANCY TESTING

What about ethical and privacy concerns?

- Can you test without the patient's consent?
- Will you cancel the case if they refuse testing?
- If positive, can/should you inform a minor's parents?

If testing *is* required, patients should be informed they will be tested, that they could be denied their surgery if positive, and that the results will be on their medical record and therefore potentially available to insurance companies and/or their employers.

PREGNANCY TESTING

- Even if she *was* pregnant, how would you change your anesthetic management?

Since there are no modern anesthetic drugs that we know will affect the pregnancy or developing embryo, testing is not *medically* indicated for anesthetic management. Is testing an entire class of patient just to protect the provider from liability ethical?

PREGNANCY TESTING

Do pregnant women have greater morbidity after surgery than non-pregnant?

- Using the NSQIP database from 2005-9, 857 appendectomy and 436 cholecystectomy cases in pregnancy were reviewed.
- Morbidity was no different than non-pregnant.
- Pregnant women were more likely to be infected.

Obstet Gynecol 2011;118:1261

Controversy #2. Are benzodiazepines and nitrous oxide safe to use during pregnancy?

Case: A woman at 12 weeks gestation requests general anesthesia for a cervical cerclage placement scheduled for ~ 20 minutes. She is extremely anxious about the procedure and asks you for preoperative sedation.

DOCUMENTED TERATOGENS

- | | |
|---------------------|---------------|
| ACE Inhibitors | Lead |
| Alcohol | Lithium |
| Androgens | Mercury |
| Antithyroid Drugs | Phenytoin |
| Chemotherapy Agents | Streptomycin |
| Cocaine | Thalidomide |
| Coumadin | Trimethadione |
| Diethylstilbestrol | Valproic Acid |
| Isoretinoin | |

TERATOGENICITY

How long after a drug is marketed does it take to establish safety for use in pregnancy?

- Experts assessed 469 drugs approved by the FDA between 1980 and 2000, reviewing available studies.
- 91% of drugs were still classified as their risk of use during pregnancy being “undetermined”.
- Inadequate information is available for women and their physicians to determine risks of most drugs.

Obstet Gynecol 2002;100:465

NITROUS OXIDE

Pregnant rats given nitrous oxide 75% for 24 hours on day 9 of gestation had a 4-fold increase in resorptions (abortions) and a 15-fold increase in anomalies when compared to rats given equi-anesthetic concentrations of xenon.

Science 1980;210:899

NITROUS OXIDE

Why might N₂O cause adverse effects?

N₂O inactivates vitamin B₁₂, a coenzyme of methionine synthetase, causing depression of methionine synthetase activity and potentially affecting production of thymidine and DNA.



NITROUS OXIDE

However, even very low concentrations of N₂O (<1%) will abolish methionine synthetase activity, yet it requires 24 hours of high N₂O concentrations (75%) to cause teratogenesis.

Are the adverse effects of nitrous oxide biochemical (reduced methionine synthetase activity), or could they be due to hemodynamic effects?

NITROUS OXIDE

- N₂O enhances adrenergic tone and causes vasoconstriction.
- Halothane (a sympatholytic) and other volatile anesthetics administered with N₂O protect against major and minor anomalies in rodents. Folic acid does not.

Teratology 1988;38:121

NITROUS OXIDE

The largest retrospective study of exposure to surgery and anesthesia during pregnancy compared 5405 women who had surgery (of 720,000 total = 0.75%) to case controls.

- 54% had GETA, 97% of those had N₂O
- No difference in stillbirth or anomalies
- Increase in IUGR and prematurity

Am J Obstet Gynecol 1989;161:1178

NITROUS OXIDE: SUMMARY

- Teratogenic effects in animal studies may be due to vasoconstriction and decreased uterine blood flow. Combine N₂O with a sympatholytic agent.
- Adverse human effects have never been documented, even in large outcome studies.
- Studies in modern hospital settings with O.R. scavenging do not show an association with nitrous and adverse pregnancy outcomes.

BENZODIAZEPINES

Two studies in 1975 reported an association between maternal exposure to benzodiazepines (Valium® and Librium®) and cleft lip and/or palate.

Int J Epidemiol 1975; 4:37

Lancet 1975; 306:478

But later work refuted these reports.....

BENZODIAZEPINES

- 611 infants with cleft lip and/or palate were compared to 2498 control infants with other birth defects.
- The risk of clefts was no different between women who were or were not exposed to diazepam during first trimester of pregnancy.
- For cleft lip ± palate: RR 0.8 (0.4-1.7).
- For cleft palate alone: RR 0.8 (0.2-2.5).

NEJM 1983; 309:1282

BENZODIAZEPINES

- An NIH-supported prospective study did not find any increased risk of cleft anomalies associated with diazepam use:
RR 1.2 versus controls
95% CI 0.17-8.95

NEJM 1984; 311:919

BENZODIAZEPINES

- A meta-analysis of 7 cohort studies involving 1090 infants who were exposed to benzodiazepines found no increased risk of major malformations, or specifically oral clefts (RR 1.19, CI 0.34-4.15).
- “Even when the worst case scenario is assumed, benzodiazepines do not seem to be major human teratogens....”
BMJ 1998;317:839

BENZODIAZEPINES

ACOG Clinical Expert Series on Teratogenicity

- “Anxiolytics (benzodiazepines): No evidence of *significant* risk of teratogenicity”
- Initial findings of clefts have not been confirmed by long-term follow-up studies.
 - Overall results are reassuring, revealing no adverse effects on neurodevelopment.
 - May be beneficial adjunct for hyperemesis (!)
Obstet Gynecol 2009;113:166

BENZODIAZEPINES

“An increased risk of congenital malformations associated with the use of benzodiazepine drugs . . . has been suggested in several studies. If this drug is used during pregnancy, the patient should be apprised of the potential hazard to the fetus.”

Roche, package insert for Versed®

Controversy #3. When and how should fetal monitoring be used?

Case 1: An elective cholecystectomy done at 34 weeks gestation.

Case 2: An emergency femoral thrombectomy at 31 weeks gestation.

Case 3: A series of 5 ECTs performed between 17 and 19 weeks of gestation.

INTRAOP MONITORING

- Blood pressure (normal or slightly above)
- Oxygenation, ventilation
- Temperature (avoid hyperthermia)
- Blood glucose for longer cases
- Fetal heart rate (FHR) > 24 weeks: intermittent, or continuous if possible
- FHR < 24 weeks: preop and postop check

INTRAOP FETAL MONITORING

- This should *not* be discussed and decided as a medicolegal issue! It is a *medical* issue.
- Monitoring may help assess placental perfusion during induced hypotension, cardiopulmonary bypass, volume shifts/blood loss.
- It provides an important reassurance for the mother.
- Helps assure the intrauterine environment is optimized
- *But* FHR monitoring is imprecise and not predictive of outcome.

ELECTRONIC FETAL HEART RATE MONITORING (EFM)

- EFM has a 98% false positive rate, yet is used in 85% of births. Does it prevent brain injury and/or death?
- 13 RCT and 3 observational studies were reviewed.
 - EFM has no effect on cerebral palsy or perinatal death.
 - EFM use does parallel the increase in cesarean rates.
 - There are related increases in litigation and payments for negligent fetal injury, despite a lack of evidence that EFM can predict outcome.

Obstet Gynecol 2006;108:656

CASE 1: FETAL MONITORING

A patient at 34 weeks gestation required cholecystectomy. During skin prep (before any surgical intervention), severe persistent fetal bradycardia occurred. An emergency cesarean was performed and the umbilical cord was tightly coiled and twisted.

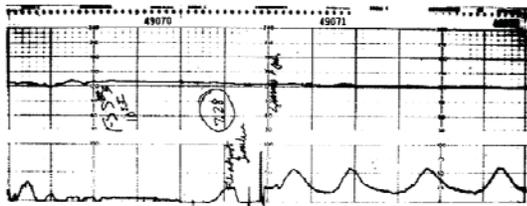
- Apgar scores = 1 / 5 / 7
- Umbilical cord pH = 7.17 and 7.18

Can J Anesth 2003;50:922

CASE 2: FETAL MONITORING

During the 30th week of an uncomplicated pregnancy, a patient underwent femoral thrombectomy under routine GETA. During surgery the fetal monitor showed absent variability, so an emergency cesarean delivery was performed for presumed fetal distress. Umbilical pH=7.23 (normal). The child was intubated for prematurity and had to be admitted to the ICU.

Br J Anaesth 2001; 87:791



CASE 3: FETAL MONITORING

A series of ECTs was required in a woman between 17 and 19 weeks gestation. FHTs checked before and after the first 4 procedures were normal. FHTs monitored during the 5th procedure showed a severe deceleration. No intervention was done due to non-viability. She went on to deliver a normal healthy baby at 38 weeks.

Acta Anaesthesiol Scand 2003;47:101

FETAL MONITORING

What should you do for intra-operative fetal distress?

- ↑ maternal FIO₂ and blood pressure
 - ↑ left uterine displacement or try the right side
 - Move the surgeons or their retractors
 - Administer a tocolytic (terbutaline 0.25mg)
 - Document your efforts in the record
- ** Remember: loss of BTBV is normal; decels are not.
 ** Consider preop / postop FHR monitoring for most cases in consultation with the obstetricians.

**Controversy #4. Should pregnant patients > 24 weeks gestation have surgery in a specialty hospital without L&D coverage?
 (no fetal monitoring, no capability for a C/S, no neonatologists)**

PERIOPERATIVE BACK-UP

Case: A woman at 28 weeks gestation was evaluated for deteriorating vision, and a large meningioma was found on MRI. Urgent craniotomy was planned to preserve her sight. The surgery proceeded without fetal monitoring or provision for cesarean delivery as obstetric care was not available at the hospital where neurosurgery was performed.

Can J Anesth 2004;51:573

ACOG / ASA JOINT STATEMENT “Non-obstetric Surgery During Pregnancy”

“Due to the difficulty of conducting large-scale randomized clinical trials in this population, there are **no data** to allow for specific recommendations... When non-obstetric surgery is planned, the primary obstetric provider should be notified. If that provider is not at the institution where surgery is to be performed, another **obstetric care provider with privileges at that institution should be involved.**”

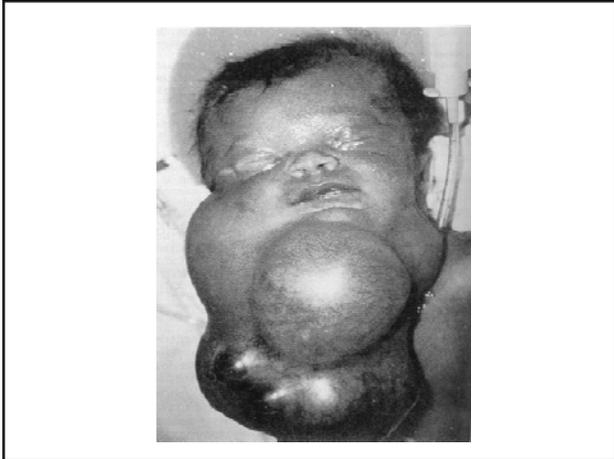
ACOG / ASA STATEMENT

If fetal heart rate monitoring is to be used: “Surgery should be done at an institution with neonatal and pediatric services; an obstetric provider with cesarean delivery privileges should be readily available, and a qualified individual should be readily available to interpret the fetal heart rate.”

www.asahq.org, October 2009

Controversy #5. What is the best way to manage the EXIT (ex-utero intrapartum treatment) procedure?

Case: A healthy gravida at term has a fetus with a large neck mass found on ultrasound. The mass is compromising its airway and intubation will be required immediately after delivery.



EXIT PROCEDURE

(Ex Utero Intrapartum Treatment)

1. Maternal GETA is maintained with 2 MAC volatile agent and narcotics for uterine relaxation and to provide adequate fetal anesthesia.
2. After uterine incision and hemostasis, only the head and arm are delivered. A pulse oximeter is placed, IM relaxant and narcotic are given to the fetus. The placenta remains intact.
3. The trachea is intubated or tracheostomy is performed. Surfactant may be administered.
4. Once the airway is secure, volatile agent is discontinued, delivery is completed and oxytocics are begun.

Anesthesiology 2011;114:1446



Controversy #6. Is there a “best” anesthetic during pregnancy to protect the fetal brain from neurotoxicity?

Do anesthetic drugs cause developing neurons to commit suicide (apoptosis)?

Case: A healthy well-educated woman requires emergency appendectomy at 26 weeks gestation. Based on information she obtained on the internet, she questions you about the effect of your general anesthetics on her fetus' developing brain.

ANIMAL STUDIES

In a simulated clinical scenario:

- 7-day old rats (0-6 months in humans) received 6 hours of general anesthesia: midazolam, nitrous oxide, isoflurane.
- Animals had memory/learning impairments, apoptotic neurodegeneration, hippocampal synaptic function deficits.

J Neuroscience 2003;23:876

ANIMAL STUDIES

Are the adverse effects attributable to the direct effects of anesthetics, or are they the result of factors we would not see clinically; eg. high doses over long periods, acidosis, hypoxia, starvation?

Problems:

- Inter-species differences
- Simulating normal O.R. conditions
- Adequate monitoring

PRIMATE STUDIES

Are non-human primates also susceptible to anesthetic toxicity?

- Rhesus macaques received 5 hours of 1 MAC isoflurane while ventilated.
- There was a 13-fold increase in neuro-apoptosis in exposed animals, largely concentrated in the cerebral cortex.

Anesthesiology 2010;112:834

ANIMAL STUDIES

What are the fetal effects of maternal anesthesia?

- Pregnant rats were exposed to isoflurane for 4 hours in mid-gestation, equivalent to 2nd trimester in humans.
- Offspring had memory and behavioral abnormalities.

Anesthesiology 2011;114:521

ANIMAL STUDIES

From an accompanying editorial:

“...it is not clear which anesthetic technique might be least toxic, nor has any general anesthetic been convincingly shown to be more toxic...certainly non-urgent surgery should continue to be postponed until after pregnancy. Considerations should be made to using regional anesthesia when possible.”

Anesthesiology 2011;114:479

IS REGIONAL BETTER?

A retrospective study of adnexal mass surgery during pregnancy compared 137 women having general anesthesia with 71 having regional anesthesia.

The incidence of preterm labor was higher in the regional (30%) than the general (6%) anesthetic group. Both were higher than the non-surgical group (3%).

Int J Obstet Gynecol 2006;15:212

ANESTHETIC MANAGEMENT OF THE PREGNANT SURGICAL PATIENT

COMMON SURGERIES

The most common indications for surgery unrelated to pregnancy:

1. Appendicitis, 1:2000 pregnancies
2. Cholecystitis, 1:6000 pregnancies
3. Maternal trauma
4. Maternal malignancies

PREOP ASSESSMENT

- Is my patient pregnant?
Document LMP on record.
Offer pregnancy testing.
- Operate during second trimester if possible.
Less risk of early spontaneous miscarriage.
Theoretical risks of teratogenicity are avoided.
3rd trimester ↓ introp visibility, ↑ preterm labor
- Reassure her about risks to fetus or pregnancy.
- Educate about uterine displacement, symptoms of preterm labor.

PREOP MEDICATIONS

- Sedation
Narcotics
Benzodiazepines
- Aspiration Prophylaxis
Antacid
Metoclopramide
H-2 receptor blocker

MAGNESIUM Tocolysis

Usual dose: 4-6 gm loading, then 2 gm/hr

Implications: Neuromuscular blockade
Attenuated vascular responses
Vasodilation

INDOMETHACIN Tocolysis

Usual dose	50 mg loading, 25 mg q 6 hours PO or PR	
Implications	<i>Maternal</i>	<i>Fetal</i>
	Platelet function	Necrotizing enterocolitis
	GI symptoms	Oligohydramnios
	Renal insufficiency	Closure of fetal ductus

CHOICE OF ANESTHETIC

- There is no evidence in humans (yet) that any drug or anesthetic technique is dangerous to the fetus.
- Choose the safest anesthetic for the mother's condition, and modify for the physiologic changes of pregnancy.
- Avoid hypoxia and hypotension!

GENERAL ANESTHESIA

- Full preoxygenation/denitrogenation
- Rapid sequence induction, smaller ETT
- First trimester: use tried and true drugs
- Nitrous oxide versus FIO₂
- ET CO₂ 28-32; avoid hyperventilation
- Inhalational agents < 2.0 MAC
- Slow or no reversal of relaxants
- Compression stockings

REGIONAL ANESTHESIA

- Advantage of minimizing drug exposure
 - First trimester
 - Fetal monitoring
- Prevent hypotension
 - Adequate fluid replacement
 - Uterine displacement
- Decrease neuraxial local anesthetic dose by 30%
- Choose ephedrine vs. phenylephrine based on maternal heart rate
- Continue to provide postoperative pain control

POSTOPERATIVE CARE

- Continue monitoring fetal heart rate and uterine activity. Provide L&D nursing expertise.
- Maintain maternal oxygenation and LUD.
- Notify Pediatrics if the fetus is a viable gestational age \geq 24 weeks.
- Use neuraxial narcotics or regional blocks for pain management if possible to encourage early ambulation.



SPECIFIC SITUATIONS

TRAUMA

- A leading cause of maternal death, especially MVA without use of seat belts.
- Fetal loss is due to maternal death or placental abruption.
- Need early ultrasound in E.R. to determine gestational age and viability.
- Perform all necessary diagnostic tests on the mother with shielding as necessary.
- Maternal \uparrow blood volume may mask blood loss.

Obstet Gynecol 2009;114:147

TRAUMA

What are the risks of radiation exposure?

- ACOG has stated: “no single diagnostic x-ray procedure results in radiation exposure to a degree that would threaten the well-being of the developing fetus.”
- Teratogenic risks are not increased with < 5 rad exposure (eg. a head CT < 1 rad).
- Ultrasound and MRI are safe alternatives.

Anesth Analg 2010;110:863

TRAUMA

Indications for emergent C/S:

- Stable mother, viable fetus in distress
- Uterine rupture
- Gravid uterus interfering with repairs
- Mother unsalvageable, fetus viable

If the fetus is pre-viable or dead, focus on optimizing the mother. She will tolerate vaginal delivery at a later time better than an emergent laparotomy.

NEUROSURGERY

- Intracranial aneurysms or AVM may require repair in this age group.
- Usual anesthetic techniques can be used.
- Fetal monitoring is remote from the field and may be beneficial in some cases, eg. aggressive diuresis, hyperventilation, bleeding and fluid shifts.

Anesth Analg 2008;107:193

NEUROSURGERY

Successful endovascular treatment of acutely ruptured intracranial aneurysms in pregnancy:

- 32 wks gestation with HA and vomiting. CT and MRI show SAH and aneurysm: C/S → angio → embolization with coils.
- 22 wks gestation with HA, vomiting, LOC. CT shows SAH: GETA → angio → occlusion with coils using fetal shielding → SVD at term.

Am J Obstet Gynecol 2001;185:1261

CARDIOPULMONARY BYPASS

Pregnant patients who had cardiopulmonary bypass procedures were reviewed:

- Fetal prematurity or death were associated with emergent procedures, maternal comorbidities, and early gestational age.
- Recommendations: normothermic, high-flow bypass, postponing until 2nd trimester.
- Elective delivery before CPB should be considered if the fetus is viable.

Ann Thorac Surg 2011;91:1191

GOALS DURING CPB

- High pump flows (>2.5 L/min/m²)
- High MAP > 65 mmHg
- Hematocrit > 28%
- Normothermic CPB (limit < 32°C)
- Pulsatile flow ?
- Optimize CO₂, acid-base, glucose
- Continuous fetal HR monitoring

LAPAROSCOPY

Symptomatic cholelithiasis during pregnancy is not rare. Choice of medical versus surgical management has been controversial.

- Compared to medical management, surgery patients had less preterm labor, fewer premature deliveries, and fewer days in-hospital.
- 38% of medical patients had relapses. Each relapse accounted for additional 5 inpatient days.

Am J Surg 2004;188:755

LAPAROSCOPY

Is laparoscopy better for fetal outcome than an open procedure?

- There are no outcome differences between laparoscopy and laparotomy in maternal complications or fetal outcome.
- Laparoscopy patients (the mothers) had longer operative times but shorter hospital stays, less parenteral narcotics, and earlier resumption of regular diet.

Clin Obstet Gynecol 2009;52:557

LAPAROSCOPY

Following laparoscopy (n=2181) or laparotomy (n=1522) performed between the 4th and 20th weeks of gestation, there were **no differences** in:

- Infant survival to one year
- Rate of fetal malformations
- Birth weight
- Gestational duration
- Growth restriction

There *was* an increased risk of low birth weight < 2500 gm, delivery before 37 weeks, and growth restriction when comparing the operated groups to the general population.

Am J Obstet Gynecol 1997; 177:673

GOALS FOR LAPAROSCOPY

- Consider an open technique to enter abdomen
- Maintain normal end-tidal CO₂, consider blood gas monitoring
- Keep inflation pressure < 15 mmHg
- Can be used in any trimester of pregnancy
- Maintain uterine displacement and monitor the fetus if feasible
- Use compression devices for DVT prophylaxis

Surg Endosc 2008; 22: 849

SUMMARY

Approach the pregnant surgical patient with respect, rather than apprehension.

Recognize *her* fears related to her pregnancy.

Doing what is best for the mother will almost always be best for the fetus and the outcome of the pregnancy.

