Anesthesia in Pregnant Patients for Nonobstetric Surgery

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Epidemiology:

- Anesthesiologists in every subspecialty encounter, with varying regularity, patients presenting for surgery during the course of pregnancy. With the increasing sophistication of surgical and anesthetic techniques, increasingly complex surgeries are being undertaken.

- The frequency with which pregnancies are complicated by the need for nonobstetric surgical procedures is of the order of 0.75% to 2.0%.

- Of these procedures, approximately 42% are performed during the first trimester, 35% during the second, and 23% during the third
The frequency with which nonobstetric surgery is performed in pregnant patients may be considerably higher in the first trimester as pregnancy may be undetected at the time of surgical intervention.

The range and incidence of nonobstetric surgical conditions encountered in pregnant patients are similar to those in the general population.

Surgery during pregnancy: 1.5%-2% of all pregnancies in USA.

The operations include:
- Directly related to pregnancy;
- Indirectly related to pregnancy;
- Unrelated to gestation.
Suspected appendicitis is the most common indication for surgery for non-obstetric conditions during pregnancy, and occurs in approximately one in 635 to one in 500 pregnancies per year.

Appendicitis occurs more frequently in the second trimester than in the first or third trimester of pregnancy.

The physiologic and anatomic changes in pregnancy have been thought to obscure and thus delay the diagnosis of acute appendicitis, contributing to its increased risk in pregnancy.

Timely diagnosis of acute appendicitis in pregnancy can be difficult. In most cases a correct diagnosis can be arrived at on the basis of a history and physical examination with supportive routine laboratory tests. Urgent surgery is the treatment of choice but delay continues to be a common problem. Infective complications are well recognized in appendicitis; similarly this group of patients is at a higher risk of venous thrombosis and embolism, and routine prophylaxis should be considered in all.
- Fetal loss usually occurs in 3–15 per cent of women with complicated appendectomy during the first trimester.

- However, the rate may be as high as 20–30 % with a premature delivery rate of 15 – 45 %, and a significantly increased risk of spontaneous abortion, premature labor, and perinatal morbidity and mortality.

- Miscarriage and infant mortality occur more frequently in women with perforated appendicitis. However, the maternal mortality rate is very low as a result of the use of advanced antibiotics, close perioperative monitoring, cooperation between specialties and improvements in perioperative management.
Laparoscopic appendectomy in pregnancy is associated with a low rate of intra-operative complications in all trimesters. However, LA in pregnancy is associated with a significantly higher rate of fetal loss compared to open appendectomy. Rates of preterm delivery appear similar or slightly better following a laparoscopic approach. Open appendectomy would appear to be the safer option for pregnant women for whom surgical intervention is indicated.

Although guidelines for laparoscopic procedures during pregnancy have been established, concern remains over the safety of the procedure, with reports of an increased risk of intra-abdominal abscess, particularly in perforated appendicitis.
The major consideration in laparoscopic appendectomy in pregnancy is the effect of increased intra-abdominal pressure and fetal acidosis during carbon dioxide pneumoperitoneum.

Increasing abdominal pressure from the pneumoperitoneum can lead to decreased venous return, especially in women with impaired cardiac output, and result in maternal hypotension and hypoxia.

It has been reported that carbon dioxide is also absorbed across the peritoneum, which leads to fetal acidosis.
Cholecystectomy

- Cholecystectomy ranks as a second most commonly performed nonobstetric surgical procedure in pregnancy, with between 1 and 8 being performed per 10000 pregnancies.

- Pregnancy itself predisposes a patient to cholelithiasis. Increased bile lithogenicity and decreased gallbladder motility occur secondary to high circulating estrogen levels.

- However, whereas 3% of pregnant patients develop gallstones, only a limited number present with symptomatic biliary disease requiring surgery.
Laparoscopic cholecystectomy is the treatment of choice in the pregnant patient with gallbladder disease, regardless of trimester.

In the past non-operative management of symptomatic cholelithiasis in pregnancy has been recommended. At present early surgical management is the treatment of choice.

Early surgical management of gravid patients with symptomatic gallstones is supported by data showing recurrent symptoms in 92% of patients managed non-operatively who present in the first trimester, 64% who present in the second trimester, and 44% who present in the third trimester. This delay in surgical management results in increased rates of hospitalizations, spontaneous abortions, preterm labor, and preterm delivery compared to those undergoing cholecystectomy.
Altogether, nonoperative management of symptomatic gallstones in gravid patients results in recurrent symptoms in more than 50% of patients, and 23% of such patients develop acute cholecystitis or gallstone pancreatitis. Gallstone pancreatitis results in fetal loss in 10% to 60% of pregnant patients.

The significant morbidity and mortality associated with untreated gallbladder disease in the gravid patient favor surgical treatment.

Laparoscopic cholecystectomy is preferred because of the salutary outcomes and favorable side-effect profile. There have been no reports of fetal demise for laparoscopic cholecystectomy performed during the first and second trimesters. Furthermore, decreased rates of spontaneous abortion and preterm labor have been reported in laparoscopic cholecystectomy when compared to laparotomy.
Adnexal Pathologies

- Adnexal disease is not uncommon during pregnancy. Surgery may be required for diagnosis or treatment of ovarian pathology, and the laparoscopic approach is increasingly being used in this situation.

- Conservative management of adnexal pathology may allow disease progression.

- Between 1% and 8% of adnexal masses diagnosed in pregnancy are malignant.

- In addition, complications such as torsion and rupture of ovarian cysts are more common in pregnancy, often rendering surgical intervention unavoidable.
Guideline #19:

- Laparoscopy is safe and effective treatment in gravid patients with symptomatic ovarian cystic masses. Observation is acceptable for all other cystic lesions provided ultrasound is not concerning for malignancy and tumor markers are normal. Initial observation is warranted for most cystic lesions < 6 cm in size.

- The incidence of adnexal masses during pregnancy is 2%.

- In the event that surgery is indicated, various case reports support the use of laparoscopy in the management of adnexal masses in every trimester.
Guideline #20:

- Laparoscopy is recommended for both diagnosis and treatment of adnexal torsion unless clinical severity warrants laparotomy.

- Ten to 15% of adnexal masses undergo torsion.

- Laparoscopy is the preferred method of both diagnosis and treatment in the gravid patient with adnexal torsion.

- The gangrenous adnexa should be completely resected and progesterone therapy initiated after removal of the corpus luteum, if less than 12 weeks gestation. Laparotomy may be necessary as dictated by the patient’s clinical condition and operative findings.
The physiologic demands of pregnancy on the cardiovascular system may precipitate decompensation of cardiac valvular disease or aortic dissection in susceptible patients.

Similarly, lesions of the central nervous system may present during pregnancy and surgery may be required to alleviate dangerous elevations in intracranial pressure.

There are numerous reports in the literature of successful maternal and fetal outcomes after surgery for life-threatening cardiac and neurologic diseases.
OUTSIDE THE LABOR SUITE

- The maternal mortality rate in the United States has stagnated for the past 2 decades.

- Excessive concern as to medication, radiation, and litigation may render pregnant patients care neither safe, timely, efficient, effective, nor patient-centered.

- Diagnostic errors are made when pregnancy-related entities are not considered, or when more familiar diagnoses are clung to when contradicting information is present.

- Asking, “Are there known dangers to the fetus in effective treatment of the mother?” is not the same as asking, “Is effective treatment of the mother known to be safe for the fetus?”
Since very few diagnostic and therapeutic modalities are known to be completely risk-free for the fetus, steps maybe skipped, truncated, or replaced with less-effective options.

While professional guidelines, Web sites, and drug-labeling information are being reviewed, care for the pregnant woman is delayed. When the provider consults medical information resources, scientific information is often insufficient to support a risk-benefit analysis of therapy in the pregnant woman.

The specter of litigation hovers over this decision-making process: several highly publicized cases have demonstrated that, for success, the case against a physician does not have to have scientific merit; the plaintiff must simply be deserving of sympathy.
An approach to the pregnant patient

- Pregnant women die from the same causes that kill nonpregnant women, plus those directly related to pregnancy.

- The United Kingdom has one of the longest-standing and most complete databases in the Confidential Enquiries into Maternal Deaths (CEMD).

- In the most recent report (2000–2002), indirect causes accounted for the majority of maternal deaths: psychiatric illness was the number one cause of maternal death, followed by cardiac disease.
The top three causes are usually quoted as hemorrhage, hypertension, and thromboembolic disease. But those are the top three causes directly related to pregnancy, not the most common causes of maternal death.

Looking at all entities, the top five causes of maternal death were, in order, suicide, cardiac disease, thromboembolism, central nervous system hemorrhage, and obstetric hemorrhage.

The top five causes of death in all females of reproductive age are accident, suicide, homicide, cancer, and cardiovascular events.
Anesthesiologists tend to think of maternal mortality in terms of failure to intubate and pulmonary aspiration, complications of general anesthesia that account for most maternal deaths directly related to anesthesia.

However, direct anesthetic deaths are about as common as deaths from amniotic fluid embolism (six versus five cases, respectively).

There is evidence that anesthetic-related deaths may be shifting from the time of induction of anesthesia to emergence and the postoperative period, which has implications for systems of care, rather than individual practitioners.
Guidelines for clinical practice are intended to indicate preferable approaches to medical problems as established by experts in the field. These recommendations will be based on existing data or a consensus of expert opinion, when little or no data are available. Guidelines are applicable to all physicians who address the clinical problem(s) without regard to specialty training or interests, and are intended to indicate the preferable, but not necessarily the only, acceptable approaches due to the complexity of the healthcare environment.

Guidelines are intended to be flexible. Given the wide range of specifics in any health care problem, the surgeon must always choose the course best suited to the individual patient and the variables in existence at the moment of decision.
Guideline #1: Ultrasonographic imaging during pregnancy is safe and useful in identifying the etiology of acute abdominal pain in the pregnant patient.

Guideline #2: Expeditious and accurate diagnosis should take precedence over concerns for ionizing radiation. Cumulative radiation dosage should be limited to 5-10 rads during pregnancy.

Guideline 3: Contemporary multidetector CT protocols deliver a low radiation dose and may be used judiciously during pregnancy. (Computed tomography (CT) may be used in the evaluation of abdominal pain in the gravid patient [20]. Radiation exposure to the fetus may be as low as 2 rads for pelvic CT scans but can reach 5 rads when a full scan of the abdomen and pelvis is performed. This radiation dose is considered safe but may affect teratogenesis and increase the risk of developing childhood hematologic malignancies).
Guideline # 4: MR Imaging without the use of intravenous Gadolinium can be performed at any stage of pregnancy.

Guideline # 5: Administration of radionucleotides for diagnostic studies is generally safe for mother and fetus.

Guideline # 14: Intraoperative and postoperative pneumatic compression devices and early postoperative ambulation are recommended prophylaxis for deep venous thrombosis in the gravid patient.

Guideline # 21: Fetal heart monitoring should occur preoperatively and postoperatively in the setting of urgent abdominal surgery during pregnancy.
Guideline # 22: Obstetric consultation can be obtained pre– and/or postoperatively based on the severity of the patient’s disease, gestational age, and availability of the consultant.

Guideline # 23: Tocolytics should not be used prophylactically in pregnant women undergoing surgery but should be considered perioperatively when signs of preterm labor are present.
Physiologic changes in pregnancy

Respiratory system changes

- Under the influence of progesterone, there is an early (first trimester) 25% increase in alveolar minute ventilation (MV) caused by increases in both respiratory rate (15%) and tidal volume (40%). At full term, MV increases 45% to 70% higher than nonpregnant values.

- This produces a slight chronic respiratory alkalosis (Paco2 = 28-32 mm Hg; pH = 7.44), which shifts the maternal oxyhemoglobin dissociation curve to the right, promoting oxygen delivery to fetuses. The increase in the arterial pH level is limited by an increase in renal bicarbonate excretion. Despite the expected pregnancy-induced increase in metabolic demand, Pao2 remains normal or increases slightly during pregnancy.
Gravid uteri exert a restrictive effect on respiratory mechanics, with a reduction in functional residual capacity of 20% at term.

Airway management in pregnancy is further complicated by the anatomical changes related to both weight gain and edema of the upper airway and vocal cords, which occurs secondary to a generalized increase in capillary permeability.
Cardiovascular system and hematologic changes

- Cardiac output begins to increase early in the first trimester and peaks in the second trimester (up to 50% higher than the baseline value), at which time heart rate has increased by 25% and stroke volume has by 30%.

- The increased metabolic demands of fetuses and the presence of placenta as a low-pressure system in parallel with systemic circulation necessitate this increase in cardiac output. Systemic and pulmonary vascular resistances decrease in response to increased synthesis of vasodilators such as prostacyclin.
• Elevated hemidiaphragm shifts heart anteriorly and to left.

• S1 becomes louder with exaggerated splitting of mitral and tricuspid valve components.

• Grade I or II early or mid-systolic murmur heard at left sternal border likely due to tricuspid regurgitation.

• EKG – LVH seen by 12 weeks gestation.
Aortocaval compression in the supine position becomes clinically relevant. Supine hypotensive syndrome is associated with cardiac output reductions of up to 20%.

Blood volume expansion occurs in the first trimester and increases by 35% to 50% at term. The greater increase in plasma volume relative to red cell mass leads to dilutional anemia.

A benign leukocytosis up to 15000 during pregnancy and that up to 20000 during labor are commonly seen and can confound diagnosis of systemic infection.

Increased circulating levels of clotting factors VII, VIII, X, and XII; enhanced platelet turnover; clotting; and fibrinolysis produce a hypercoagulable state that leaves pregnant patients at high risk of experiencing thromboembolic events.
In early pregnancy, the effects of circulating progesterone include a reduction in lower esophageal sphincter tone and a slight increase in gastric acidity. Gastrointestinal smooth muscle demonstrates dysrhythmias leading to nausea and vomiting.

The angle of the anatomical gastroesophageal sphincter becomes less acute, exacerbating incompetence.

Parturient patients are at increased risk of developing aspiration pneumonitis after 16 weeks’ gestation.
Changes in central and peripheral nervous systems

- Pregnant patients demonstrate a 30% reduction in the minimum alveolar concentrations of volatile anesthetic agents. (Due to endorphins or progesterone).

- Similarly, neural tissue demonstrates increased sensitivity to the effects of local anesthetic drugs.

- The total volume of the epidural and subarachnoid spaces is reduced in pregnancy as inferior vena caval compression produces engorgement of the epidural venous plexus.
The response of the autonomic nervous system to hemodynamic changes is biphasic. In the first trimester, there is a shift toward increased vagal tone and decreased sympathetic activity in association with the increase in blood volume. A gradual transition in the second trimester leads to lower vagal tone and increased sympathetic activity by the third trimester, which helps overcome the mechanical effects of both aortocaval compression and low-resistance parallel placental circulation.
Renal

- RBF increases 75-85% and GFR increases 50%. By term, the normal Cr=0.5-0.6 mg/dl; BUN = 8-9 mg/dl.

- Glucosuria (1-10 gm/24 hours) due to increased GFR and altered tubular function.

- Proteinuria 0.3 g/day (normal 0.25 g/day)
ENDOCRINE

Diabetes Mellitus

Increased tissue sensitivity to insulin due to human chorionic somatomammotropin (human placental lactogen); glucose tolerance is impaired.

Thyroid

Size increases due to follicular hyperplasia and vascularity. Thyroid binding globulin (estrogen effect) causes an increase in T3 and T4 levels. (Free T3 and T4 unchanged).
Teratogenicity

- Significant postnatal change in function or form in offspring after prenatal treatment. Manifestations include death, structural anomalies, growth restriction, and functional abnormalities.

- Teratogenic potential of a drug or environmental exposure depends on species susceptibility, dose, duration, timing, and genetic predisposition.

- Period of organogenesis – approximately 15-55 days.
Data regarding anesthetics are obtained from 3 sources:
1) Animal studies;
2) Epidemiologic studies;
3) Studies of pregnancy outcome in women undergoing surgery during pregnancy;

Animal studies:
1) teratogenic effects, both structural and behavioral, have been demonstrated when anesthetics have been given at high doses for prolonged exposures.
2) Physiologic conditions – hypoxia, hypercarbia, and hyperthermia are all teratogenic in animals.

Human studies:
Teratogenecity – no increased incidence of congenital anomalies or behavioral teratogenecity from anesthesia or surgery.
FDA Classification System for Drug use during Pregnancy

- **A** – Controlled studies show no risk. Adequate, well-controlled studies in pregnant women failed to demonstrate risk to the fetus.

- **B** - No evidence of risk in humans. Either animal findings show risk, but human findings do not, or, if no adequate human studies have been done, animal findings are negative.

- **C** – Risk cannot be ruled-out. Human studies are lacking, and animal studies are either positive for fetal risk or lacking as well. However, potential benefits may justify the potential risk.
- **D** - Positive evidence of risk. Investigational or postmarketing data show no risk to the fetus. Nevertheless, potential benefits may outweigh the potential risk.

- **X** - Contraindicated in pregnancy. Studies in animals or humans or investigational or postmarketing reports have shown fetal risk that clearly outweighs any possible benefit to the patient.

Most anesthetics are class **C** or **B**, and fewer are class **D**. None are class **X**.
Anesthetic agents and teratogenesis

- IV agents – opioids, tricyclic antidepressants, phenothiazines, benzodiazepins, butyrophenones are teratogenic in animals at high doses. Behavioral teratogenesis is seen with barbiturates, phenothiazines, tricyclic antidepressants. No evidence for a teratogenic effect for any IV induction agent in humans, including barbiturates, ketamine, opiates, and benzodiazepines.

- Local anesthetics do not cause behavioral or morphologic teratogenecity in humans, with the possible exception cocaine.
Inhaled agents – halothane at subanesthetic concentrations causes growth restriction in rats and skeletal anomalies, or death with higher, more prolonged exposures. Isoflurane causes cleft palate in mice.

Nitrous oxide has been shown to be a weak teratogen in rodents after high concentrations are administered for prolonged periods. The required doses are extremely large, involving administration of 50% N₂O for more than 24 hours, and are not encountered in clinical practice. Current evidence does not support withholding nitrous oxide in clinical practice.

Muscle relaxants cause a malformations in rats but no defects were reported in humans.

If pregnancy continues for 1 week postop, premature labor is unlikely.
Any agent can be teratogenic in animals if sufficient exposure occurs at a sensitive developmental stage.

The impact of any administered drug depends on the dose and the gestational age at which it is administered. A small dose of a given drug may be catastrophic to the early embryo, yet a large dose of the same drug may have no effect on a fetus at an advanced stage of development.

Experimental models involving supraclinical drug doses do not necessarily indicate that a single short exposure would pose a significant risk in clinical practice.

Most iatrogenic structural abnormalities have resulted from drug exposure during the period of organogenesis (days 31-71). Functional abnormalities are associated with drug exposure during late pregnancy.
Large survey studies that considered outcomes in women who underwent surgery during pregnancy suggest no increase in congenital anomalies among their offspring but rather an increase in the risk for abortions, growth restriction, and increased frequency of low-birth-weight and very low-birth-weight neonates for reasons attributed to the requirement for surgery but not anesthetic administration.
With the establishment of robust databases and experimental animal models, researchers are beginning to address important epidemiological questions related to maternal use of medications and birth defects.

Extracting data from the National Birth Defect Prevention Study, it was determined that NSAID use during pregnancy was not a major factor for birth defects, but detected a small-to-moderately increased risk of specific categories of defects (anophtalmia/microphtalmia, neural tube defects, amniotic bands, transverse limb defects) with ibuprofen, aspirin, and naproxen exposure.

Researchers demonstrated that exposure to Ketamin was associated with more apoptotic neuronal cell death in the fetus (>2-fold) than in the neuronal period. This study provides the first proof-on-principal that fetuses are more vulnerable to developmental neurotoxicity of anesthetic agents than neonates.
“In addition to the pregnancy-related emergencies, pregnant women may be struck by any illness or injury affecting women who are not pregnant. When the acute onset of an illness that is not related to pregnancy strikes, the woman may require medical care in an area in which no obstetrics provider is available. It is important that all physicians grasp the principles of managing these women.”

The textbook Williams Obstetrics offers a rational approach: “A woman should never be penalized because she is pregnant. What therapy would be given if she was not pregnant? If a proposed medical or surgical regimen is altered because the woman is pregnant, can the alteration be justified?”

Although it is vitally important to be aware of changes due to pregnancy and the effects of the intervention on the mother and fetus, one cannot allow these concerns to result in substandard management of the other maternal problems.