Fetal Surgery: The Anesthesia Perspective

Laura B. Myers, MD
Assistant in Anesthesia
Harvard Medical School
Children's Hospital Boston

Introduction:
Fetal intervention was once thought to be a predominantly last-resort option for a few fetuses meeting specific disease criteria. Much has changed over the last decade. In fact, the National Institute of Child Health and Development predicted routine diagnosis and treatment of congenital malformations *in utero* prior to development of secondary morbidity by the year 2020.

Distinction:
Fetal intervention involves two or three patients simultaneously, the mother and fetus or fetuses. The mother receives no direct benefit from the intervention itself other than psychological assurance of fetal well being after a successful procedure. The mother is a bystander while the fetus or fetuses are active recipients of fetal therapy.

Physiologic Alterations of Pregnancy:
Pregnancy is associated with significant physiologic alterations as early as the first trimester that place the mother at increased risk for significant adverse outcome during anesthesia. A major concern in the pregnant patient is the risk of maternal aspiration of gastric contents during anesthesia. Pregnancy is associated with a shift in the position of the stomach caused by the gravid uterus, changing the angle of the gastroesophageal junction. This may result in incompetence of the gastroesophageal junction, making the pregnant patient prone to aspiration during general anesthesia or impaired consciousness from any cause. In addition, alveolar and minute ventilation increase during and after the first trimester of pregnancy while functional residual capacity decreases. These alterations result in less maternal oxygen reserve and place the mother at greater risk for hypoxemia during induction of anesthesia compared to the non-gravid female. While epidural anesthesia reduces these risks, they are not eliminated. As progesterone levels are increased in pregnancy and may also have sedating qualities, the addition of intravenous sedation to those patients with epidural anesthesia may suppress airway reflexes, making them at even greater risk of pulmonary aspiration. The use of supplemental sedative drugs may increase the risks of respiratory depression during epidural anesthesia.

In addition to maternal aspiration risk, pregnant patients are also at increased risk of failed endotracheal intubation. Factors including weight gain, breast engorgement, and capillary engorgement throughout the respiratory tract (nasal and oral pharynx, larynx, and trachea) with increased risk of rapid airway obstruction make careful pre-operative maternal airway assessment of utmost importance. Preparation for the potential loss of maternal airway in every case should be made with additional help and equipment immediately available if needed.

Fetal Stress Response:
Fetal pain is a controversial issue that must be addressed and considered during every fetal intervention. As the concept of "pain" is itself a subjective phenomenon, fetal pain is more accurately defined as the ability of the fetus to mount a stress response to noxious stimuli.

The fetal hypothalamic-pituitary-adrenal axis develops early in gestation. By 16 weeks gestation, the fetus is able to mount a "central sparing response" and is able to mount a rapid norepinephrine response by 18 weeks. Slower cortisol and beta-endorphin responses are demonstrated by 20 weeks. Neuroanatomic development also occurs early in gestation. Touch and pain sensation are among the first functional entities to develop. By 7 weeks gestation nociceptors appear around the mouth and by 20 weeks are distributed throughout the entire body. Peripheral afferent nerves develop from 10 weeks gestation but pain modulating descending pathways in the spinal cord mature very late in gestation. These data suggest that an exaggerated fetal endocrine response to a nonspecific stimulus may occur during fetal intervention.

Fisk et al. demonstrated increased cortisol, beta-endorphins, and the "central sparing response" in a 23 week old human fetus needled in the hepatic (innervated) vein. This same group demonstrated 10ug/kg fentanyl suppressed the beta-endorphin and cortisol responses but not the central sparing response to this noxious stimulus. This was the first data to demonstrate that the human fetal stress response was attenuated by the administration of a narcotic. Long- term effects of fetal stress have also been described. Independent groups have implicated fetal stress to exaggerated pain responses in eight week-old infants and have also implicated the fetal stress response as a contributor to pre-term labor.

Fetoscopic Surgery:
Fetoscopic intervention involves minimal insult to the uterus while obtaining access to the fetus or fetuses through surgical trocar insertion. At present, fetoscopic intervention is most commonly used to treat twin syndromes, namely twin-twin transfusion syndrome and twin reversed arterial perfusion sequence. Anesthesia for these procedures can be performed in a variety of ways; the ultimate decision is based on surgical factors and maternal medical history and physical examination. Please refer to the suggested readings below for full discussion of these factors.

Open Fetal Surgery:
Open fetal surgery is performed today in that subset of fetuses in which post-natal survival is considered to be unlikely or in those fetuses in which in utero fetal demise is almost certain. This includes hydropic fetuses with sacrococcygeal teratomas, congenital cystic adenomatoid malformation of the lung, bronchogenic cyst, and pulmonary sequestrations. In addition, an NIH funded trial to evaluate the long-term outcomes of in utero repair of myelomeningocele is currently underway at the participating institutions UCSF, CHOP, and Vanderbilt.

Anesthesia for open fetal surgery involves maintenance of uteroplacental perfusion to maximize chances of a favorable outcome. This involves deep uterine relaxation with 2 MAC anesthesia, invasive maternal monitoring, and additional intramuscular drug administration to the fetus. These will be discussed in detail during the lecture. Alternatively, please refer to the suggested readings listed below.

EXIT Procedure:
The EXIT procedure, or ex-utero intrapartum treatment procedure, was initially devised to reverse in utero applied tracheal clips in diaphragmatic hernia patients. By only partially delivering the fetus, uterine volume and hence perfusion and oxygenation are maintained, allowing time to perform direct laryngoscopy, bronchoscopy, intubation, and tracheotomy if needed. This procedure is now used clinically to deliver term or near term infants who will almost certainly sustain a hypoxic event immediately after delivery. Examples include fetuses with cervical teratomas, cystic hygromas, goiter, laryngeal webs, and other lesions involving the fetal airway. The EXIT procedure is also used to allow time to place ECMO cannulae, again avoiding life-threatening hypoxia during delivery.

Anesthesia for the EXIT procedure requires several differences from the other previously mentioned fetal interventions. Like open fetal surgery, complete uterine relaxation is necessary to expose the operative fetal anatomy but also maintain most of the fetus within the uterus. Unlike open fetal surgery, however, the fetus will be delivered at the end of the fetal intervention, resulting in a completely flaccid uterus that must immediately involute or extensive maternal hemorrhage will occur. This requires communication and coordination between the entire surgical and anesthesiology teams. Details of these issues will be addressed during the lecture and are also described in the readings below.

Suggested Readings:

1. Myers LB, Cohen D, Galinkin J, Kurth D. Anesthesia for fetal surgery. *Paediatric Anaesthesia* 2002; 12: 569-578.
2. Myers LB, Bulich LA, Editors. Anesthesia for Fetal Intervention and Surgery. BC Decker, Inc. In press.
3. Strumper D, Durieux M, Gogarten W, et al. Fetal plasma concentrations after intraamniotic sufentanil in chronically instrumented pregnant sheep. *Anesthesiology* 2003; 98: 1400-6.
4. Myers L, Watcha M. Epidural versus general anesthesia for twin-twin transfusion syndrome requiring fetal surgery. *Fetal Diagnosis and Therapy*. In press.
5. Fisk N, Gitau R, Tiexeira J, et al. Effect of direct opioid analgesia on fetal hormonal and hemodynamic stress response to intrauterine needling. *Anesthesiology* 2001; 95:828-35.
6. Rosen M. Anesthesia for fetal procedures and surgery. In: Schnider SM, Levinson G, eds. Anesthesia for Obstetrics, 3rd ed. Baltimore: Williams & Wilkins, 1993:281-295.
7. Gaiser RR, Kurth CD. Anesthetic considerations for fetal surgery. *Semin Perinatol* 1999; 23: 507-514.
8. Palahniuk RJ, Schnider SM. Maternal and fetal cardiovascular and acid-base changes during halothane and isoflurane anesthesia in the pregnant ewe. *Anesthesiology* 1974; 41: 462-472.
9. Tame JD, Abrams LM, et al. Level of post-operative analgesia is a critical factor in regulation of myometrial contractility after laparotomy in the pregnant baboon: implications for human fetal surgery. *Am J Obstet Gynecol* 1999; 180: 1196-1201.