Yonsei Medical Journal
Vol. 42, No. 6, pp. 669 - 680, 2001

Review Article

Anesthesia for Fetal Procedures and Surgery

Mark A. Rosen

Department of Anesthesia and Perioperative Care, University of California San Francisco, San Francisco, California, USA.

Many of the anesthetic considerations for fetal procedures and surgery are identical to those for nonobstetric surgery during pregnancy, including concern for maternal safety, avoidance of both teratogenic drugs and fetal asphyxia, and the prevention of preterm labor and delivery. Anesthesia is required for the mother and quite often the fetus to perform many fetal procedures.

Fetal procedures and surgery can be divided into subgroups according to their anesthetic requirements. For example: procedures that only require a needle insertion into the uterus but not into the fetus, such as intrauterine infusions; laser surgical photocoagulation of the communicating placental circulation for twin-twin transfusion syndrome (TTTS) and radio-frequency umbilical cord ablation for managing twin reversed arterial perfusion (TRAP), which are not really fetal procedures, rather they are placental or cord procedures; surgical procedures performed directly on the fetus; and the EX-utero Intrapartum Treatment (EXIT) procedure. Anesthetic considerations also depend on other factors, such as the location of the placenta.

Unlike maternal surgery, for fetal procedures, the fetus is not an innocent bystander for whom the least anesthetic interference is used. Instead, the fetus can be the primary patient and may benefit from anesthesia, with close monitoring of the anesthetic effects to ensure well-being. Fetal asphyxia, hypoxia, or distress can be most effectively recognized, predicted, and avoided by fetal monitoring. Monitoring is also crucial for assessing the fetal response to corrective maneuvers.

Key Words: Fetal surgery, anesthesia, in utero surgery, EXIT procedure, fetal anesthesia

Many of the anesthetic considerations for fetal procedures and surgery are identical to those for nonobstetric surgery during pregnancy. These include concern for maternal safety, avoidance of teratogenic drugs and fetal asphyxia, and the prevention of preterm delivery. The anesthesiologist must be familiar with the alterations in physiology induced by pregnancy and their clinical anesthetic implications. These basic considerations are extremely important, and have been reviewed previously.[1] Fetal surgery is distinguished from other nonobstetric surgeries performed during pregnancy by concern for fetal anesthesia, increased concern for fetal monitoring, concern for the greater likelihood of intra- or postoperative preterm labor, and concern for the protection of uteroplacental circulation to avoid fetal asphyxia. Providing anesthesia for a hysterotomy and fetal intervention poses interesting challenges since care needs to be provided to two patients simultaneously, mother and fetus. Additionally, intense intraopertive uterine relaxation ('surgical tocolysis') is crucial.

Anesthesia is required for mother and often the fetus to perform many of these procedures. Fetal procedures and surgery can be divided into subgroups according to their anesthetic requirements Procedures that only require needle insertion into the uterus but not into the fetus, such as amniotic fluid sampling, umbilical blood sampling, or intrauterine infusions are the least complicated fetal procedures and require the least amount of anesthesia. Local anesthetic infiltration at the needle insertion site on the maternal abdomen is usually adequate, which can be supplemented with light conscious sedation for an anxious mother. Laser surgical photocoagulation of communicating placental circulation for twin-twin transfusion syndrome (TTTS) and radio-frequency umbilical cord ablation for managing twin reversed

Received October 31, 2001

Correspondence address: requests to Dr. Mark A. Rosen, Department of Anesthesia and Perioperative Care, 513 Parnassus Avenue, Box 0648, University of California San Francisco, San Francisco, California 94143-0648, USA. Tel: 415-476-3234, Fax: 415-514- 0185, E-mail: RosenM@anesthesia.ucsf.edu

arterial perfusion (TRAP) are not fetal procedures, rather they are placental or cord procedures, and often require maternal anesthesia. Our experience suggests regional (spinal or epidural) anesthesia is sufficient if the placenta is posterior and access can be achieved by a percutaneous approach. In fact, this has been performed with local infiltration and intravenous sedation. However, if the placenta is anterior, access typically involves a laparotomy and a manipulation of the uterus to access its posterior wall. In these circumstances, we have found general anesthesia more ideal, a finding with which others agree.[2]

Surgical procedures performed directly on the fetus range from the deployment of pig-tail catheters to procedures that require a hysterotomy, such as an excision of a congenital cystic adenoma malformation (CCAM) or meningomyelocele repair. All of these procedures require anesthesia for both mother and fetus, and intraoperative tocolytic management. For the EX-utero Intrapartum Treatment (EXIT) procedure, maternal anesthesia and uterine relaxation are paramount for success. For the minimally invasive fetoscopic procedures, particularly those that do not involve surgery on the fetus itself, such as those involving surgery on the placenta (e.g. twin-twin transfusion syndrome), the goals and anesthetic requirements are more basic. From primate experiments, preterm labor and subsequent delivery is known to be minimal for those animals that underwent procedures with minimal uterine manipulation compared with those that underwent a hysterotomy. Furthermore, halogenated anesthetic agents were quite effective in halting the uterine electromyographic activity associated with increases in intraamniotic pressure observed on emergence from anesthesia, whereas ritodrine infusions or indomethacin were not effective.[3]

Unlike maternal surgery, during fetal procedures, the fetus is not an innocent bystander for whom we attempt the least anesthetic interference. Instead, the fetus can be the primary patient and may benefit from anesthesia, with close monitoring of anesthetic effects to ensure well-being.

For many percutaneous procedures, such as fetal blood sampling, or intrauterine blood transfusions, local anesthetic infiltration of the maternal abdominal wall or regional anesthesia can be sufficient. When intravenous sedation and anxiolysis are required, opioids and benzodiazepines can be safely administered. Supplemental oxygen is routinely administered during procedures involving intravenous sedation and "stand-by" readiness for rapid intervention is always available for fetal distress (i.e., induction of general anesthesia for emergency cesarean section) if the fetus is at a viable gestational age. Mothers fast overnight, receive an oral antacid before the procedure, and are monitored in a fashion suitable for general anesthetic administration. Incremental doses of intravenous midazolam (0.5 mg) and/or fentanyl (25 mcg) and/or low-dose propofol infusions are used to achieve the desired level of conscious sedation.

More invasive fetal treatments that do not involve a hysterotomy, such as minimally invasive fetoscopy, placement of vesicoamniotic or thoracoamniotic shunt catheters, or percutaneous endoscopic laser ablation of the placental vessels involve procedures similar to those for intrauterine blood transfusions.[4,5] However, despite sonographic guidance, larger sized needles or catheters and multiple placement attempts may be required. Adequate maternal anesthesia can be obtained with local anesthetic infiltration of the maternal abdomen, and the fetus may be sedated via the placental transfer of drugs administered to the mother (including opioids and benzodiazepines). However, infiltration of the maternal abdomen with local anesthetic may be unsatisfactory for maternal comfort when the needle placement requires multiple attempts. We have successfully used spinal, epidural, or general anesthetic techniques as alternatives. In addition, it is important to consider the potential for fetal analgesic requirements and immobility.

Fetal sedation by placental transfer of maternally administered medication does not ensure an anesthetized or immobile fetus. Excessive fetal activity may render the procedure technically difficult, infeasible or unsafe for the fetus. Fetal movement can be dangerous to the fetus because displacement of a needle or catheter may lead to bleeding, trauma, or compromise umbilical circulation. When placental transfer of maternally administered intravenous medication does not

control fetal movement and/or analgesia, general anesthesia can be used which will anesthetize both mother and fetus. Additionally, fetal anesthesia and control of fetal movement can be safely achieved by direct intramuscular or intravascular administration of opioids and/or neuromuscular blocking agents to the fetus. Pancuronium (0.05 to 0.1 mg/kg IV or 0.3 mg/kg IM) has been used for fetal paralysis during intravascular transfusions.[6-12] We have used either IV or IM pancuronium (0.1-0.25 mg/kg) due to its longer duration and vagolytic properties, which help maintain fetal heart rate, or vecuronium, in comparable doses, to achieve paralysis of a shorter duration; approximately 1 to 2 hours.[13] If regional anesthesia has been used for the mother, parenteral opioid (fentanyl) is also administered to the fetus in relatively large doses (25 mcg/kg) to provide analgesia and attenuate or abolish the autonomic and stress responses for potentially painful procedures on the fetus.

A variety of benefits and risks characterize the techniques for anesthesia during fetal procedures. The subjective phenomenon of pain, and the necessity or benefit of fetal 'amnesia' for surgical intervention has not been adequately assessed in a human fetus. The question at what stage of gestation is it possible for the human fetus to be aware of its surroundings and, in particular to be aware of pain remains unanswered. The answer involves a knowledge of neural development and integration of the sensory system in the developing brain and its structures and functions necessary for awareness. There was widespread belief that the human neonate and fetus were not capable of perceiving pain and that they possessed higher thresholds for nociceptive stimuli. Some theorized that this higher threshold would be adaptive for the pain associated with birth.

Evidence of the memories of pain in human neonates is only anecdotal. However, detailed hormonal studies in preterm neonates undergoing surgery under minimal anesthesia revealed a marked release of catecholamines, growth hormone, glucagon, cortisol, aldosterone, and other corticosteroids and the suppression of insulin secretion.[14-16] Furthermore, these endocrine and metabolic responses to stress are abolished by administering anesthetics to preterm neonates.[17] In addition, surgical manipulation of an non-anesthetized fetus results in varying degrees of autonomic nervous system stimulation, variations in the heart rate, increased hormonal activity,[18] and increased motor activity, which can be ablated by anesthesia. Later in gestation, a fetus will respond to environmental stimuli such as noises, light, music, pressure, touch, and cold.[19,20] Information regarding the development of perceptual mechanisms of pain and the response of human preterm neonates to pain provide a physiologic rationale to support the philosophic rationale of providing fetal anesthesia.[21] Pediatricians are well aware that preterm babies respond to heel sticks, perhaps with a level of response that is less than that of full-term babies.

The fetal response to noxious stimuli may represent reflex, rather than a conscious response at earlier gestational ages. Before thalamic connections exist to the cortex (beginning at about 22 weeks), it is doubtful that physiologic or pharmacological responses to noxious stimuli by the fetus involve consciousness. Further, in terms of development, feedback mechanisms to dampen the response to noxious stimuli are not fully developed until after 40 weeks of gestation, and some of the ways in which fetal nerve cells work and the spinal cord pathways used may be quite different than in adults. However, even a reflex response to noxious stimuli may affect sensory development. Perhaps the effect of trauma to the developing nervous system should be avoided. Consequently, along with the requirement for fetal immobility during some procedures, fetal 'amnesia' may be an important goal of fetal anesthesia.

For procedures involving a hysterotomy or endoscopy (e.g., repair of congenital cystic adenomatoid malformations, diaphragmatic hernia repair or tracheal balloon placement, selective termination of an anencephalic, acardiac, monochorionic twin, or treatment of twin-twin transfusion syndromes) halogentated inhalation anesthetics are used to both produce maternal and fetal anesthesia, as well as to provide the necessary uterine relaxation for surgery. Prior to inducing general anesthesia, we typically place a lumbar epidural catheter. Except for non-particulate oral antacids, premedication or adjuvant

anesthetic agents are routinely avoided for supplementation of the inhalation agent. This facilitates administration of the maximum doses of the halogenated agent, which may be required for uterine relaxation. The dose of the halogenated agent is limited by the stability of the maternal cardiovascular system.

Avoidance of fetal asphyxia is best accomplished by assuring maternal oxygenation and organ perfusion. During fetal surgery, along with high concentrations of the inspired halogenated agent, a maximal FIO2 is administered, and adequate maternal blood pressure is maintained, sometimes utilizing the appropriate vasopressors, to ensure adequate uterine blood flow. Maintaining a normal fetal temperature is also important. With fetal exposure, hypothermia can develop quickly. Therefore, we expose as little of the fetus as possible, and use a system of continuous irrigation with warmed lactated Ringer's solution to prevent fetal hypothermia. For endoscopic techniques, a continuous infusion of a warmed lactated Ringer's solution not only provides thermal stability for the fetus, but also improves visibility for the surgeons. High volume infusate must be comprised of lactated Ringer's solution (not normal saline), because there may be maternal absorption of fluids and electrolytes. Furthermore, the volumes infused and withdrawn, and intra-amniotic pressures must be carefully monitored to avoid uterine overdistention.

The hysterotomy is made with a stapling devise, to ensure uterine hemostatsis and seal the membranes. The hysterotomy is closed using fibrin glue to a create water tight seal. Amniotic fluid is restored with warm lactated Ringer's solution with a volume assessed by ultrasonography.

During closure of the hysterotomy, magnesium sulfate therapy is administered, initially as a bolus-loading dose (4 - 6 g over 20 min), which is then sustained as a continuous infusion (2 g/hr). After the initial bolus dose of magnesium sulfate is administered, the halogenated agent is discontinued and the epidural catheter is tested and incrementally dosed with local anesthetics in concentrations and volumes appropriate for surgery, and parenteral opioids and nitrous oxide in oxygen are administered. This regimen facilitates a tracheal extubation when the patient is fully awake, capable of protecting her airway, comfortable, and avoids the coughing or straining with extubation that may jeopardize the integrity of the watertight uterine closure.

We provide postoperative analgesia with low concentrations of epidural local anesthetic infusions (with or without opioids) or use intravenous patient-controlled analgesia (PCA) devices to administer opioids. This may have an additional benefit by reducing maternal stress. In the non-human primate experiments, stress was a significant factor in increasing the risk of uterine activity after a hysterotomy and fetal surgery.[3]

The danger of teratogenic effects from anesthetic drugs poses a potential risk. In genetically susceptible animal species, many of the commonly used anesthetic drugs induce teratogenic effects at specific stages of gestational development. However, in humans, no anesthetic agent appears to be safer or more teratogenic. However, there have been too few human studies to confirm that anesthetic agents are non-teratogenic, and it is unlikely that such studies could ever be conducted to provide statistically significant results.

Various procedures and techniques may affect fetal physiologic functions. The relationship between these procedures and altered fetal physiology is not precisely understood. For example, uterine incision, fetal manipulation, and anesthetic management each may affect fetal and placental circulation by several mechanisms, sometimes producing fetal compromise. Increased uterine activity, maternal hypotension, maternal hypocarbia, or hyperventilation may interfere with uterine and umbilical blood flow. Fetal manipulation may affect the umbilical blood flow by direct compression or by inducing responses that affect fetal circulation.

The fetal cardiovascular circulation is adapted for use of the placenta as the organ for oxygen uptake and carbon dioxide elimination. Therefore it has a large placental blood flow and very small pulmonary blood flow. It is also adapted for existence in a low-oxygen environment and provides the cerebral circulation with blood that has greater oxygen content than that perfusing the lower body. Fetal cardiovascular circulation allows for the mixing of blood between the right

and left sides of the heart. Approximately one-third of the relatively well-oxygenated inferior vena caval blood (which includes the blood returning from the placenta) is deflected by the christa dividens in the right atrium and shunted through the foramen ovale into the left atrium. Two-thirds of the inferior vena caval blood passes from the right atrium to the right ventricle. Almost all poorly oxygenated superior vena caval blood also passes from the right atrium to the right ventricle. A conduit between the main pulmonary artery and the aorta, the ductus arteriosus, shunts approximately 90% of the right ventricular output ejected into the pulmonary artery. The left ventricular output, which includes the relatively well oxygenated inferior vena caval blood (deflected through the foramen ovale) and a small amount of blood that perfuses the pulmonary circulation, is ejected into the aorta and perfuses the head and upper extremities.

Cardiac output has two main determinants: heart rate and stroke volume. Fetal cardiac output, measured in terms of the combined left and right ventricular output, is directly related to the heart rate,[22] which is probably the most important determinant of fetal cardiac output. Stroke volume is a function of preload, afterload and myocardial contractility. Fetal myocardial contractility is probably maximally stimulated, with a limited capacity to increase stroke volume. Fetal myocardial muscle strips are less compliant than those of adult hearts and have a greater resting tension, but a diminished response for increasing myocardial tension when stimulated.[23] In fetal lambs, augmentation of a preload has little effect on increasing the cardiac output. Volume loading increases the cardiac output by only 15 to 20%.[24]

To function properly, the fetal circulation depends on a high venous return.[25] Because the heart rate is predominant in regulating the fetal cardiac output, baroreceptor and chemoreceptor responsiveness have important regulatory roles. Baroreflex activity exists by midgestation and increases in sensitivity as gestation advances.[26] The chemoreflex activity from the aortic and carotid chemoreceptors in fetal lambs has been elicited and studied in utero.[27-30] However, most of the information on the chemoreceptor role in regulating circulation has been obtained from anesthetized or short-term studies in fetal animals. A method for selectively denervating the aortic and carotid chemoreceptor and baroreceptor in fetal lambs in utero was developed, which facilitates an investigation of their roles in both normal fetal cardiovascular regulation and fetal response to stress.[31]

Because the fetus has a limited capacity to increase cardiac output in response to stress, oxygen delivery to the vital organs must be maintained by redistributing the blood flow. Cerebral blood flow in fetal lambs is twice that in the adults, although both cerebral metabolic rates are similar.[32,33] These characteristics of fetal blood flow may represent a protective advantage for the fetus.

Among the factors that may modulate cerebral blood flow are cerebral metabolic rate, arterial carbon dioxide tension ($PaCO_2$), arterial oxygen content, blood pressure, and autoregulation.[34-36] In fetal lambs, increases in cerebral metabolic rate or $PaCO_2$ and decreases in arterial oxygen content are associated with increased cerebral blood flow. Cerebral blood flow autoregulation has been demonstrated to preserve the cerebral blood flow in the normoxic fetal lamb when the systemic blood pressures range 20% above or below the normal values. However, autoregulation in response to hypotension may be incomplete, and the mechanism of autoregulation may depend on the arterial oxygen concentration.[37]

The effects of inhalation anesthetic agents on the cardiovascular system of the fetus have been investigated, yet much remains to be understood. In fetal lambs, the concentration of halothane required to prevent movement in response to painful stimuli is much lower than that for adult sheep or newborn lambs.[38] Although placental transfer of inhaled agents occurs rapidly, fetal levels of the halogenated agents remain lower than the maternal levels for a significant period after administering these agents to the mother. Reports conflict on the fetal effects when the mother has received halothane or isoflurane. In one study, maternal anesthesia with 0.7% halothane or 1% isoflurane (1 minimum alveolar concentration [MAC] for sheep) caused a mild decrease in the fetal blood pressure with no change in the fetal pulse rate, oxygen level, or acid-base status. However, anesthesia with halo-

thane 1.5% or isoflurane 2% (i.e., 'deep anesthesia') caused decreases in fetal blood pressure, heart rate, oxygen saturation, and base access, with progressive fetal acidosis.[39] Other studies reported that maternal anesthesia with 1.5% halothane caused a decrease in fetal arterial pressure after a few minutes (primarily because of a decrease in peripheral vascular resistance), with no change in the pulse rate, cardiac output, oxygen, acid-base status, or blood flow to the fetal brain or other major fetal organs.[40-41] Yet, another study demonstrated that maternal anesthesia with 2.0% isoflurane produced no significant decline in the fetal blood pressure, but did produce a decrease in the fetal cardiac index and progressive fetal acidosis.[42]

Deep inhalation anesthesia (2 MAC) may result in progressive fetal acidosis, whereas light anesthesia (1 MAC), or brief fetal exposure to deep anesthesia appears safe. Whether the adverse responses result from direct impairment of fetal myocardial contractility, redistribution of fetal blood flow or changes in uterine perfusion is uncertain. Furthermore, the applicability of these studies is limited because the combined impact of fetal anesthesia, intrauterine manipulation, and fetal stress on maternal and fetal cardiovascular stability and regional blood flow remains unknown. Progressive fetal hypoxia may have resulted from failure to maintain uterine blood flow with administration of halogenated agents by increasing the preload and providing appropriate vasopressors. In fact, uterine perfusion may increase with the administration of halogenated agents if the blood pressure is maintained, as a result of uterine vessel vasodilation.[39]

In non-anesthetized experimental animals, fetal asphyxia induced by occlusion of the umbilical circulation results in fetal bradycardia and hypertension, with decreased cardiac output and increased cerebral blood flow mediated partially by the fetal alpha and beta-adrenergic systems.[43-47,68-72] There are conflicting reports on the effects of maternal halothane administration on the asphyxiated fetus. In one study, maternal halothane administration did not further compromise fetal well-being. The blood pressure of the anesthetized fetus declined to values that were normal compared with those of the awake, asphyxiated fetus. However, because the pulse rate increased, the cardiac output remained unchanged. Oxygenation did not deteriorate and the cerebral blood flow remained elevated.[48] In another study, halothane administered to the mother of a severely acidotic fetus caused further aggravation of fetal acidosis and oxygen desaturation.[49] Cerebral blood flow decreased as fetal blood pressure decreased.

Fetal asphyxia, hypoxia, or distress can be most effectively recognized, predicted, and avoided by fetal monitoring. Monitoring is also important to assess the fetal response to corrective maneuvers. Methods for monitoring fetal well being include fetal blood gas, pH, glucose, and electrolyte determinations and measurements of the fetal heart rate, blood pressure, and umbilical blood flow. Invasive methods and vascular access used in experimental fetal preparations require indwelling catheters that currently have limited application for clinical fetal surgery. However, capillary blood samples can be obtained for blood gas determinations, and vascular access can be achieved for fluid, blood, or drug administration during prolonged procedures involving a hysterotomy. On several occasions at UCSF, we have established vascular access in fetuses undergoing surgery and administered fluid or blood for resuscitation. Experimental techniques for accessing the fetal blood vessels on the surface of the placenta in rhesus monkeys for reliable, long-term vascular access have been successful.[50,51] Perhaps in the future, more information may be used from detailed waveform analysis of the fetal electrocardiogram (ECG). New devices will become available for monitoring the myometrial electrical activity and mechanical contractility and the fetal electroencephalogram. Additionally, devices will become available for the continuous monitoring of the fetal arterial oxygen saturation, such as the fetal pulse oximeter for labor (Nellcor N-400, Tyco Healthcare, Nellcor, Pleasanton, California, USA), PO2 and PCO2, and for monitoring fetal cerebral oxygenation, blood volume, and blood flow by near infrared spectroscopy.[52] We have experimented with the use of an implantable radiotelemeter for monitoring uterine activity and fetal heart rate.[53]

The author has used fetal heart rate monitoring,

pulse oximetry, and intermittent blood gas determinations as relatively noninvasive methods for assessing fetal well-being during fetal surgery. The fetal heart rate can be monitored with a standard internal fetal electrode and a reference electrode on the maternal abdomen, both connected to a maternal ground plate and processed by a fetal heart rate cardiotachometer.[54] However, the signal obtained is of low amplitude and is overwhelmed by movement artifacts, rendering the conventional display of the beat-to-beat heart rate unreliable. The author has found that direct monitoring of the fetus by ECG is more reliable than the standard internal fetal electrode. Modified insulated atrial pacing wires are used as ECG leads. The bare wire at the distal end is sutured subcutaneously onto the fetal thorax for diaphragmatic hernia repair using the attached curved needles. The proximal end of the insulated wire is attached to a coaxial shielded cable, connecting the three leads to a cardiotachometer. The cardiotachometer was modified by increasing the gain to allow for signal amplification and by adding a fixed low-pass frequency filter and variable high-pass frequency filter, which substantially reduce motion artifacts. The ECG lead wires are stabilized to minimize capacitive coupling and the changes in voltage offset between the fetal skin and the ECG lead wire. This allows for a more reliable display of the fetal ECG with visible P and QRS complexes.

Plethysmography combined with spectrophotometric oximetry (pulse oximetry) has also proved extremely useful. A noninvasive sensor contains two low-voltage, low-intensity, light-emitting diodes as light sources and a photodiode as a light receiver. Changes in the absorption of red light, relative to a change in the absorption of infrared light, indicate the arterial hemoglobin oxygen saturation.[55] For open fetal surgical procedures and EXIT procedures, neonatal digital sensors wrapped around the fetal arm, leg, or (preferably) palmer arch are used. This is held in place with sterile, adhesive plastic and covered with sterile aluminum foil to prevent artifacts from the intense ambient surgical lighting. Alternatively, in the early 1980's, we developed a flat sensor for placement over any exposed fetal part so light can be measured predominantly by reflectance rather than transmission. This has become the foundation for fetal pulse oximetry in labor.[56-58] Intraoperative fetal pulse oximetry with the Nellcor N-400 monitor has been demonstrated to be a very reliable monitoring parameter in the fetal lamb model.[59]

The use of readily available, conventional pediatric sensors and conventional oximetric instruments calibrated for higher saturation can be valuable for heart rate monitoring if the waveform is analyzed for data reliability. Although relative trends in oxygen-related quantities may be inferred from the data provided by conventional oximeters, they may not be precise. The influence of fetal hemoglobin is insignificant, and the neonatal monitors used for pulse oximetry in the range 75% to 100% saturation are reasonably reliable. However, oximeters calibrated for adults underestimate the arterial oxygen saturation at the 25% level. At lower saturation, numerical modeling suggests that sensors with two different wavelengths than are currently available provide a better performance. These different wavelengths are incorporated into the Nellcor N-400 fetal oximeter.

Additionally, intraoperative sonography using a sterile sleeve on the sonographic probe is important for monitoring the fetus, particularly for endoscopic procedures for which other monitors cannot be applied to the fetus. The fetal heart rate, ventricular volume and contractility can be determined by visualization of the heart, or heart rate can be ascertained by a Doppler assessment of the blood flow through the umbilical cord. However, in many circumstances, the sterile transducer cannot be positioned continuously because it interferes with the surgical field.

The human uterine wall has a thick, muscular layer that is sensitive to stimulation or manipulation. Because uterine stimulation increases the likelihood of inducing uterine contractions, the risk of preterm labor accompanies invasive fetal intervention. After incision, strong uterine contractions can occur, and these have resulted in high incidences of postoperative abortion in experimental preparations using non-human primate fetuses. Strong uterine contractions may impede uterine blood flow or induce partial placental separation, which interferes with umbili-

cal-placental blood flow, both of which compromise fetal well being. A uterine contraction can displace a percutaneous intrauterine needle placed for intrauterine transfusion or shunt catheter placement. Prevention and treatment of preterm labor is critically important for managing patients undergoing fetal intervention

Tocolytic therapy includes a variety of drugs. The agents most commonly used for tocolysis are beta-adrenergic agonists and magnesium sulfate, which prevent or inhibit preterm labor. Tocolysis is usually not necessary after simple percutaneous umbilical blood sampling or intrauterine transfusions. However, for more invasive percutaneous procedures (such as shunt catheter placement), magnesium or low-dose beta adrenergic agonist tocolytic agents can be administered intravenously for prophylactic control of uterine irritability.

For procedures involving hysterotomy and endoscopy, halogenated agents are used intraoperatively to inhibit uterine contractility and to provide the uterine relaxation necessary for surgery.[60] A regimen of tocolysis is normally used, which includes preoperative administration of indomethacin by suppository, intraoperative anesthetic by the inhalation of a halogenated agent (end tidal concentrations of approximately 3 MAC), supplemented, when necessary by bolus doses of nitroglycerin (50-100 mcg),[61-63] and postoperative tocolysis by magnesium, supplemented by terbutaline (a beta-adrenergic agonist), if necessary. After a several days, tocolytic therapy is shifted to a continuous subcutaneous infusion or oral administration of terbutaline, which the patient continues after hospital discharge. Depending on uterine activity, the postoperative regimen is supplemented by the use of indomethacin or calcium channel blocking agents.

At times, the halogenated agent alone does not provide the complete uterine relaxation required intraoperatively. Furthermore, there is some concern as to whether the fetus was inadequately anesthetized to block the autonomic response to stress or the halogenated agent adversely affected fetal myocardial contractility during the prolonged procedures.[64] For several years we tried using an alternative anesthetic and tocolytic technique during the repair of fetal diaphragmatic hernias. For maternal anesthesia, nitrous oxide, fentanyl, and a 0.25% inspired concentration of isoflurane were administered. The patient was paralyzed, her lungs mechanically ventilated, and fluids were administered to maintain a normal central venous pressure. We achieved intraoperative and postoperative uterine relaxation by administration of nitroglycerin at doses up to 20 μg/kg/min, and the mean arterial pressure was maintained above 60 mm Hg, using ephedrine when needed. Before the uterine incision, 50 μg fentanyl and 0.3 μg pancuronium were administered intramuscularly to the fetus by ultrasound guidance. Although successful, it did not appear that this technique offered any advantages, and as a result,[65] this technique is no longer used.

Once closure of the uterus is begun, a bolus loading dose of magnesium sulfate (4 gm) followed by a continuous infusion (2 gm/hr) is used during the transition between the intra- and postoperative tocolyis. The magnesium can be administered earlier. The continuous intravenous magnesium sulfate infusion is maintained for postoperative tocolysis, supplemented by beta-adrenergic agonists when necessary. Intraoperatively, intravenous fluids are restricted to minimize the risk of postoperative pulmonary edema associated with the administration of magnesium sulfate and beta-adrenergic agonists.

The 'surgical tocolysis' provided by deep inhalation anesthesia, and sometimes supplemented by nitroglycerin could significantly increase the risk of maternal hemorrhage with uterine incision. To reduce such risk, surgical techniques have been developed that employ a stapling device for hemostasis and to seal of the membranes during a hysterotomy. This same stapling device is used for EXIT procedures as well.

Magnesium sulfate infusions, supplemented by terbutaline are the mainstay of our postoperative tocolytic management. Indomethacin (a prostaglandin synthetase inhibitor) is used pre- and postoperatively for the more invasive fetal surgical procedures. Although there have been case reports of prenatal closure of the ductus arteriosus and persistent fetal circulation associated with the use of prostaglandin synthetase inhibitors for tocolysis, these effects are rare when used to treat mothers before 34 weeks' gestation for a limited duration. Fetal echocardiography is utilized

postoperatively to detect early evidence of adverse cardiovascular changes due to indomethacin, at which time this agent is discontinued. Indomethacin use has also been associated with decreased fetal urine output caused by potentiation of the peripheral effects of antidiuretic hormones. In addition, neonatal bleeding and renal impairment could result from prolonged indomethacin therapy.

EXIT PROCEDURE

At birth, tracheal occlusion poses an obvious problem for the fetus. The occluding device must be removed before the tracheoscopy and bronchoscopy are performed to inspect the trachea and before resuscitation can proceed. Endotracheal intubation is performed under controlled circumstances, and often surfactants are administered. To allow the time that these procedures require while uteroplacental gas exchange is preserved a surgical and anesthetic modification of a general anesthetic approach to a cesarean section was adopted for the ex utero intrapartum treatment (EXIT) procedure.[66,67]

A hysterotomy is made with a stapling devise developed at UCSF, to ensure uterine hemostasis during fetal manipulation (U.S. Surgical Corporation, Norwalk, Conn.).[68] The deep inhaled halogenated anesthetic technique provides the necessary uterine relaxation, despite the uterine incision and partial or full delivery of the fetus. This is crucial for preventing placental disruption from the endometrium, maintaining placental perfusion and oxygenation of the fetus while the surgeon secures the fetal airway. Unlike a typical cesarean delivery, there is no attempt to limit induction of anesthesia to the delivery time; rather, anesthesia is induced well in advance to ensure adequate concentrations of inhalation anesthetic for surgical tocolysis. Careful maintenance of the maternal mean arterial pressure with fluids and ephedrine is necessary to avoid fetal compromise.

Nitroglycerin boluses (50 - 100 ug) are used if supplemental uterine relaxation is required. Nitric oxide donor agents have long been known to provide uterine relaxation.[69] Obstetrical anesthesiologists previously used inhaled amyl nitrate for acute relaxation. Nitric oxide donor agents similar to nitroglycerin provide potent tocolysis in non-human primates.[70] More recently, obstetrical anesthesiologists rediscovered nitric oxide donor agents. Nitroglycerin has been reported to provide uterine relaxation in clinical cases of a delivery of an entrapped fetal head during a vaginal breech delivery, at cesarean section, for breech extraction, for manual removal of a retained placenta, for a reduction of a prolapsed (inverted) uterus, and for an external version, among others.[1,61,62,71-73] Despite the compelling clinical experience, the mechanism of action for uterine relaxation is unclear (increased uterine compliance vs. decrease in uterine contractile force), and the mechanism actually may be independent of nitric oxide.[74] For other obstetric indications such as uterine hyperstimulation in labor (not fetal surgery) a sublingual spray is used as a readily available, convenient method of nitroglycerin administration.

IM pancuronium and fentanyl (or morphine) is administered to the fetus, and the fetus is monitored by the placement of a pulse oximeter probe on the fetal hand. Subsequently, after the fetal airway is secured with an endotracheal tube, surfactant is administered (when indicated), and after ventilation through the tracheal tube results in an increasing oxygen saturation, the umbilical cord is clamped. After the cord is clamped, oxytocin is administered, a preoperatively placed epidural catheter is activated and an opioid/nitrous oxide anesthetic administered. This regimen facilitates the increased uterine tone and the anesthetic does not contribute to potential postpartum hemorrhage. The average blood loss for the EXIT procedures do not exceeded the average blood loss for routine cesarean sections at UCSF. The previously placed epidural catheter is used to provide postoperative epidural analgesia.

The EXIT procedure has also been employed by our group and others for fetuses that have a predictably compromised airway, such as an obstructing mass (cystic hygroma, cervical teratoma, hemangioma, large thyroid goiter), that would benefit from careful inspection and tracheal intubation or tracheostomy at the time of birth.[75-82] This technique has now been used for the removal of tracheal clips by other groups who have previously consulted with the author.[81] We have used

the EXIT procedure to perform an intrapartum fetal thoracotomy and removal of a large chest mass (congenital cystic adenomatoid malformation). Using this technique, we've safely maintained fetal well being and the operating conditions for 2 hours. The fetal safety of this technique is apparent by monitoring the fetal oxygen saturation and heart rate, and by obtaining normal cord blood gases immediately after the cord is clamped. Another group reported an improved outcome from 'fetal stabilization' for antenatal diagnosed diaphragmatic hernia patients, with fetal anesthetization before airway management thereby decreasing the incidence of persistent pulmonary hypertension and improving the survival rate of patients with severe CDH.[83]

REFERENCES

1. Rosen MA. Management of Anesthesia for the Pregnant Surgical Patient. Anesthesiology 1999;91:1159-63.
2. Myers L, Galinkin J, Gaiser R. Regional versus general anesthesia for twin-twin transfusion syndrome requiring fetal surgery. Anesthesiology 2001;95:A1260.
3. Rosen MA. Anesthesia for Fetal Surgery. In: Hughes SC, Levinson G, Rosen MA, editors. Anesthesia for Obstetrics. Philadelphia: Lippincott, Williams and Wilkins; 2002.
4. Manning F, Harrison MR, Rodeck C, and the members of the International Fetal Medicine and Surgery Society. Report of the International Fetal Surgery Registry: catheter shunts for fetal hydronephrosis and hydrocephalus. N Engl J Med 1986;315:336-40.
5. Spielman FJ, Seeds JW, Corke BC. Anaesthesia for fetal surgery. Anaesthesia 1984;39:756-9.
6. Seeds JW, Corke BC, Spielman FJ. Prevention of fetal movement during invasive procedures with pancuronium bromide. Am J Obstet Gynecol 1986;155:818-9.
7. Moise KJ, Carpenter RJ, Deter RL, Kirshon B. The use of fetal neuromuscular blockade during intrauterine transfusions. Am J Obstet Gynecol 1987;157:874-9.
8. Copel JA, Grannum PA, Harrison D, Hobbins JC. The use of intravenous pancuronium bromide to produce fetal paralysis during intravascular transfusion. Am J Obstet Gynecol 1988;158:170-1.
9. Byers JW, Aubry RH, Feinstein SJ, Lodeiro JG, McLaren RA, Srinivasan JP, et al. Intravascular neuromuscular blockade for fetal transfusion. Am J Obstet Gynecol 1988;158:677.
10. Pielet BW, Socol ML, MacGregor SN, Dooley SL, Minogue J. Fetal heart rate changes after fetal intravascular treatment with pancuronium bromide. Am J Obstet Gynecol 1988;159:640-3.
11. Moise KJ, Deter RL, Kirshon B. Intravenous pancuronium bromide for fetal neuromuscular blockade during intrauterine transfusion for red-cell alloimmunization. Obstet Gynecol 1989;74:905-8.
12. Chestnut DH, Weiner CP, Thompson CS, McLaughlin GL. Intravenous administration of d-tubocurarine and pancuronium in fetal lambs. Am J Obstet Gynecol 1989;160:510-3.
13. Leveque C, Murat I, Toubas F. Fetal neuromuscular blockade with vecuronium bromide: studies during intravascular intrauterine transfusion in isoimmunized pregnancies. Anesthesiology 1992;76:642-4.
14. Anand KJS, Brown MJ, Bloom SR, Aynsley-Green A. Studies on the hormonal regulation of fuel metabolism in the human newborn infant undergoing anaesthesia and surgery. Horm Res 1985;22:115-28.
15. Anand KJS, Brownk MJ, Causon RC. Can the human neonate mount an endocrine and metabolic response to surgery? J Pediatr Surg 1985;20:41-8.
16. Anand KJS. Hormonal and metabolic function of neonates and infants undergoing surgery. Curr Opin Cardiol 1986;1:681-9.
17. Anand KJS, Sippell WG, Aynsley-Green A. Randomized trial of fentanyl anaesthesia in preterm neonates undergoing surgery: Effects on the stress response. Lancet 1987;1:243-8.
18. Rose JC, Macdonald AA, Heymann MA, Rudolph AM. Developmental aspects of the pituitary-adrenal axis response to hemorrhagic stress in lamb fetuses in utero. J Clin Invest 1978;61:424-32.
19. Liley AW. The foetus as a personality. Aust N Z J Psychiatry 1972;6:99-105.
20. Smyth CN. Exploratory methods for testing the integrity of the foetus and neonate. J Obstet Gynaecol Br Commonw 1965;72:920-35.
21. Anand KJS, Hickey PR. Pain and its effects in the human neonate and fetus. N Engl J Med 1987;317:1321-9.
22. Rudolph AM, Heymann MA. Cardiac output in the fetal lamb: The effects of spontaneous and induced changes of heart rate on right and left ventricular output. Am J Obstet Gynecol 1976;124:183-92.
23. Friedman WF. The intrinsic physiologic properties of the developing heart. Prog Cardiovasc Dis 1972;15: 87-111.
24. Gilbert RD. Control of fetal cardiac output during changes in blood volume. Am J Physiol 1980;238:H80-6.
25. Gilbert RD. Determinants of venous return in the fetal lamb. Gynecol Invest 1977;8:233-45.
26. Shinebourne EA, Vapaavuori EK, Williams RL, Heymann MA, Rudolph AM. Development of baroreflex activity in unanesthetized fetal and neonatal lambs. Circ Res 1972;31:710-8.
27. Dawes GS, Duncan SLB, Lewis BV, Merlet CL, Owen-Thomas JB, Reeves JT. Hypoxaemia and aortic chemoreceptor function in foetal lambs. J Physiol 1969; 201:105-16.
28. Dawes GS, Duncan SLB, Lewis BV, Merlet CL, Owen-Thomas JB, Reeves JT. Cyanide stimulation of the

systemic arterial chemoreceptors in foetal lambs. J Physiol 1969;201:117-28.
29. Dawes GS, Lewis BV, Milligan JE, Roach MR, Talner NS. Vasomotor responses in the hind limbs of foetal and newborn lambs to asphyxia and aortic chemoreceptor stimulation. J Physiol 1968;195:55-81.
30. Goodwin JW, Milligan JE, Thomas B, Taylor JR. The effect of aortic chemoreceptor stimulation on cardiac output and umbilical bloodflow in the fetal lamb. Am J Obstet Gynecol 1973;116:48-56.
31. Itskovitz J, LaGamma EF, Rudolph AM. Baroreflex control of the circulation in chronically instrumented fetal lambs. Circ Res 1983;52:589-96.
32. Jones MD, Rosenberg AA, Simmons MA, Molteni RA, Koehler RC, Traystman RJ. Oxygen delivery to the brain before and after birth. Science 1982;216:324-5.
33. Makowski EL, Schneider JM, Tsoulos NG, Colwill JR, Battaglia FC, Meschia G. Cerebral blood flow, oxygen consumption and glucose utilization of fetal lambs in utero. Am J Obstet 1972;114:292-303.
34. Jones MD Jr, Sheldon RE, Peeters LL, Meschia G, Battaglia FC, Makowski EL. Fetal cerebral oxygen consumption at different levels of oxygenation. J Appl Physiol 1977;43:1080-4.
35. Rosenberg AA, Jones MD, Traystman RJ, Simmons MA, Molteni RA. Response of cerebral blood flow to changes in PCO2 in fetal, newborn and adult sheep. Am J Physiol 1982;242:H862-6.
36. Tweed WA, Cote J, Wade JG, Gregory G, Mills A. Preservation of fetal brain blood flow relative to other organs during hypovolemic hypotension. Pediatr Res 1982;16:137-40.
37. Tweed WA, Cote J, Pash M, Lou H. Arterial oxygenation determines autoregulation of cerebral blood flow in the fetal lamb. Pediatr Res 1983;17:246-9.
38. Gregory GA, Wade JG, Biehl DR. Fetal anesthetic requirement (MAC) for halothane. Anesth Analg 1983;62: 9-14.
39. Palahniuk RJ, Shnider SM. Maternal and fetal cardiovascular and acid-base changes during halothane and isoflurane anesthesia in the pregnant ewe. Anesthesiology 1974;41:462-72.
40. Biehl DR, Cote J, Wade JG. Uptake of halothane by the foetal lamb in utero. Can Anaesth Soc J 1983;30:24-7.
41. Biehl DR, Tweed WA, Cote J. Effect of halothane on cardiac output and regional flow in the fetal lamb in utero. Anesth Analg 1983;62:489-92.
42. Biehl DR, Yarnell R, Wade JG, Sitar D. The uptake of isoflurane by the foetal lamb in utero: effect on regional blood flow. Can Anaesth Soc J 1983;30:581-6.
43. Cohn HE, Sacks EJ, Heymann MA, Rudolph AM. Cardiovascular responses to hypoxemia and acidemia in fetal lambs. Am J Obstet Gynecol 1974;120:817-24.
44. Peeters LLH, Sheldon RE, Jones MD, Makowski EL, Meschia G. Blood flow to fetal organs as a function of arterial oxygen content. Am J Obstet Gynecol 1979;35: 637-46.
45. Reuss ML, Parer JT, Harris JL, Krueger TR. Hemodynamic effects of alpha-adrenergic blockade during hypoxia in fetal sheep. Am J Obstet Gynecol 1982;142: 410-5.
46. Court DJ, Parer JT, Block BSB, Llanos AJ. Effects of beta-adrenergic blockade on blood flow distribution during hypoxaemia in fetal sheep. J Dev Physiol 1984;6: 349-58.
47. Johnson GN, Palahniuk RJ, Tweed WA, Jones MV, Wade JG. Regional cerebral blood flow changes during severe fetal asphyxia produced by slow partial umbilical cord compression. Am J Obstet Gynecol 1979;135: 48-52.
48. Yarnell R, Biehl DR, Tweed WA, Gregory GA, Sitar D. The effect of halothane anaesthesia on the asphyxiated foetal lamb in utero. Can Anaesth Soc J 1983;30:474-9.
49. Palahniuk RJ, Doig GA, Johnson GN, Pash MP. Maternal halothane anesthesia reduces cerebral blood flow in the acidotic sheep fetus. Anesth Analg 1980;59: 35-9.
50. Hedrick MH, Jennings RW, MacGillivray TE. Endoscopic placental vessel catheterization for chronic fetal vascular access. Surg Forum 1992;43:504-5.
51. Hedrick MH, Jennings RW, MacGillivray TE. Chronic fetal vascular access. Lancet 1993;342:1086-7.
52. Rosen MA. International Symposium on Intrapartum Surveillance. Nottingham, England: Nottingham press; 1990.
53. Jennings RW, Adzick NS, Longaker MT. Radiotelemetric fetal monitoring during and after open fetal operation. Surg Gynecol Obstet 1993;176:59-64.
54. Harrison MR, Anderson J, Rosen MA. Fetal surgery in the primate. I. Anesthetic, surgical, and tocolytic management to maximize fetal-neonatal survival. J Pediatr Surg 1982;17:115-22.
55. Yelderman M, New W. Evaluation of pulse oximetry. Anesthesiology 1983;59:349-52.
56. Gardosi JO, Schram CM, Symonds EM. Adaptation of pulse oximetry for fetal monitoring during labour. Lancet 1991;1:1265-7.
57. Johnson N, Johnson VA, Fisher J, Jobbings B, Bannister J, Lilford RJ. Fetal monitoring with pulse oximetry. Br J Obstet Gynaecol 1991;98:36-41.
58. Nijland R, Nierlich S, Jogsma HW. Validation of reflectance pulse oximetry: An evaluation of a new sensor in piglets. J Clin Monit 1997;13:43-9.
59. Luks FI, Johnson BD, Papadakis K. Predictive value of monitoring parameters in fetal surgery. J Pediatr Surg 1998;33:1297-301.
60. Harrison MR, Golbus MS, Filly RA, Callen P, Katz M, deLorimier AA. Fetal surgery for congenital hydronephrosis. N Engl J Med 1982;306:591-3.
61. Peng ATC, Gorman RS, Shulman SM. Intravenous nitroglycerine for uterine relaxation in the postpartum patient with retained placenta. Anesthesiology 1989;71: 172-3.
62. Altabef KM, Spencer JT, Zinberg S. Intravenous nitroglycerin for uterine relaxation of an inverted uteru. Am J Obstet Gynecol 1992;166:1237-8.

63. Segal S, Csavoy AN, Datta S. Placental tissue enhances uterine relaxation by nitroglycerin. Anesth Analg 1998; 86:304-9.
64. Harrison MR, Adzick NS, Flake AW. Correction of congenital diaphragmatic hernia in utero: VI. Hard-earned lessons. J Pediatr Surg 1993;28:1411-8.
65. Cauldwell CB, Rosen MA, Harrison MR. The use of nitroglycerin for uterine relaxation during fetal surgery. Anesthesiology 1995:A929.
66. Schulman SR, Jones BR, Slotnick N, Schwartz MZ. Fetal tracheal intubation with intact uteroplacental circulation. Anesth Analg 1993;76:197-9.
67. Mychaliska GB, Bealer JF, Rosen MA. Operating on placental support: The Ex Utero Intrapartum treatment procedure. J Pediatr Surg 1997;32:227-31.
68. Bond SJ, Harrison MR, Slotnick RN, Anderson J, Flake AW, Adzick NS. Cesarean delivery and hysterotomy using an absorbable stapling deviced. Obstet Gynecol 1989;74:25-8.
69. Kumar D, Zourlas PA, Barnes AC. In vivo effect of amyl nitrate on human pregnant uterine contractility. Am J Obstet Gynecol 1965;91:1061-8.
70. Jennings RW, MacGillvray TE, Harrison MR. Nitric oxide inhibits preterm labor in the rhesus monkey. J Maternal-Fetal Med 1993;2:170-5.
71. DeSimone CA, Norris MC, Leighton BL. Intravenous nitroglycerin for uterine relaxation aids manual extraction of a retained placenta [letter]. Anesthesiology 1990; 73:787.
72. Greenspoon JS, Kovacic A. Breech extraction facilitated by glyceryl trinitrate sublingual spray [letter]. Lancet 1991;338:124-5.
73. Mayer DC, Weeks SK. Antepartum uterine relaxation with nitroglycerin at Cesarean delivery. Can J Anaesth 1992;39:166-9.
74. Langevin PB, Katovich MJ, Wood CE, James CF, Langevin SO. The effect of nitroglycerin on the gravid uterus in sheep and rabbits. Anesth Analg 2000;90: 337-43.
75. Catalano PJ, Urken ML, Alvarez M, Norton K, Wedgewood J, Holzman I. New approach to the management of airway obstruction in "high risk" neonates. Arch Otolaryngol Head Neck Surg 1992;118:306-9.
76. Langer JC, Tabb T, Thompson P, Paes BA, Caco CC. Management of prenatally diagnosed tracheal obstruction: access to the airway in utero prior to delivery. Fetal Diagn Ther 1992;7:12-6.
77. Schwartz MZ, Silver H, Schulman S. Maintenance of the placental circulation to evaluate and treat an infant with massive head and neck hemangioma. J Pediatr Surg 1993;28:520-2.
78. Tanaka M, Sato S, Naito H, Nakayama H. Anesthetic management of a neonate with prenatally diagnosed cervical tumour and upper airway obstruction. Can J Anaesth 1994;41:236-40.
79. Skarsgard ED, Chitkara U, Krane EJ, Riley ET, Halamek LP, Dedo HH. The OOPS procedure (operation on placental support): in utero airway management of the fetus with prenatally diagnosed tracheal obstruction. J Peditar Surg 1996;31:826-8.
80. Liechty KW, Crumbleholme TM, Flake AW, Morgan MA, Kurth D, Hubbard AM, et al. Intrapartum airway managment for giant fetal neck masses: The EXIT (ex utero intrapartum treatment) procedure. Am J Obstet Gynecol 1997;177:870-4.
81. Gaiser RR, Cheek TG, Kurth CD. Anesthetic management of cesarean delivery complicated by ex utero intrapartum treatment of the fetus. Anesth Analg 1997; 84:1150-3.
82. Waldman JD, Chilton L, Golmes G, Plowden JJW. Placenta-dependent systemic oxygenation; a case report of transposition with no septal defects. Prenat Neonat Med 1997;2:152-5.
83. Sachiyo S, Tomoaki T, Yamanouchi T. Fetal stabilization for antenatally diagnosed diaphragmatic hernia. J Pediatr Surg 1999;34:1652-7.