ANESTHESIA FOR REPRODUCTIVE DISORDERS

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Important considerations for anesthetizing pregnant patients will be discussed. More information is available by consulting the references noted below.
Goals upon completion of this lecture include:

- -understand the physiologic changes occurring in the pregnant animal
- -know the effects of anesthetic agents on the developing fetus
- -be familiar with the effects of anesthesia on the mother and fetus
- -formulate at least two methods of effectively anesthetizing a small and a large animal for C-section with minimal morbidity/ mortality
- -know the basic steps and drugs utilized in neonatal resuscitation

Selected references:

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Moon PF, Erb HN, Ludders JW, Gleed RD, Pascoe PJ. "Perioperative Management and Mortality Rates of Dogs Undergoing Cesarean Section in the United States and Canada"; JAVMA. 2133; 365-370; 1998

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INTRODUCTION

Pregnant animals present a unique anesthetic challenge to the veterinarian. Pregnancy is a general **hypermetabolic state.** The physiologic changes of pregnancy lead to **alterations in the cardiovascular, pulmonary, central nervous and gastrointestinal systems.** The normal parturient compensates for these changes; uncompensated imbalances can be life threatening to the mother and/or fetus.

Most common anesthetics cross the placenta and affect the fetus to various degrees. Whether preparing to anesthetize a pregnant animal for C-section or for non-obstetrical surgery, the veterinarian must have a thorough understanding of the effects of the physiologic changes and the anesthetic technique(s) in order to minimize risks to the mother and fetus.

Although little research is available concerning anesthetic drugs and viability, studies show a **reduction in maternal mortality rates** with the advancement of newer anesthetic drugs

and improved perianesthetic care. A recent study showed a 1% mortality rate among dogs undergoing c-sections (reduced from 14% in 1966). Puppy viability hasn't changed much however; estimates still show about a 15% mortality rate for post c-section neonates.

Whether the surgery to be performed is **obstetrical** (i.e. a c section) or **non-obstetrical** (i.e. colic), considerations for the mother and the baby are very similar. General recommendations include:

- **-Postpone elective surgery** until after delivery
- -Necessary (but non-emergency procedures) should be **postponed until the second or third trimester**
- **-Avoid** drugs with **teratogenic potential** and drugs that cause extreme shifts in uterine tone
- **-Combine agents** to achieve analgesia, muscle relaxation, and light levels of general anesthesia while **minimizing the side effects** of any one agent
- -Use **reversible agents** such as narcotics or use **local/regional anesthesia** when possible
- **-Minimize maternal stress and pain**
- -Ensure adequate **maternal oxygenation** to prevent uterine/fetal hypoxia
- **-Avoid** excessive **depression and hypotension** secondary to drug administration
- -Promote **rapid recovery**

In addition, in the event of a c-section:

- **-Remove the neonate(s)** from the uterus **QUICKLY**
- -Make sure **adequate assistance** is available for neonatal care

MATERNAL PHYSIOLOGIC CHANGES OCCURRING WITH PREGNANCY

As fetal development progresses, most of these changes become more profound.

Cardiovascular system

-Increased oxygen consumption

- -Hypermetabolic state of pregnancy and demands of the **(multiple) fetus(es)**

-Cardiac output (CO) increases approximately 30-40%, rising most during the second trimester

- -Achieved by an increased heart rate (CO = HR x SV)
- -Occurs as a response to increased oxygen demands of pregnancy
- **-Uterine blood flow increases** until, by term, it accounts for 10-20% of total CO
- -CO returns to pre-pregnancy levels within 3-4 weeks after partuition

-Total blood volume increases about 25-40% during gestation

- -Secondary to peripheral hormonal changes **(prostaglandins, progesterone)** causing **vasodilation,** and placental arterio-venous shunting leading to volume expansion via sodium and water retention
- -Plasma volume increases more than packed cell volume often leading to a **dilutional anemia**
- -Despite decreased oxygen content (a result of anemia), the increased CO keeps **oxygen delivery normal**

-Electrolyte values remain unchanged (normal) because plasma volume expansion is accompanied by electrolyte retention
-Increased blood volume and decreased SVR may cause patients with pre-existing cardiovascular disease to decompensate

-**Blood pressure falls** slightly
-Secondary to generalized vasodilation resulting in a fall in systemic vascular resistance (SVR) and decreased afterload
-Mechanical compression by the gravid uterus (positional) adds to hypotension

-**Platelet count and coagulation factors** (1, VII, X, and XII) **increase** during pregnancy
-Resulting "hypercoagulable state" predisposes pregnant women to venous thrombosis. Veterinary correlation is unknown.

Pulmonary system

-**Functional residual capacity (FRC) decreases**
-Caused by the uterus impinging on the diaphragm
-Normally of little concern unless patient has other factors to aggravate hypoxia (i.e. obesity, airway disease)
-FRC returns to normal levels within 2-3 weeks after partuition

-**Respiratory rate (RR) and tidal volume (TV) increase**
-Compensation for increased the oxygen demand
-Hyperoxygenation results since the increase in alveolar ventilation exceeds oxygen demands

-**Mild respiratory alkalosis**
-Increased respiratory rate rids the body of excess $C0_2$ (an acid)

Central nervous system

-**Increased pain threshold** related to increased **progesterone** and **endogenous endorphin** levels lead to:
-Reductions in inhalant anesthetic requirements **(decrease MAC** up to 40%)
-Reduced opioid requirements (to achieve analgesia)
-Decreased enzymatic breakdown of opiates also reduces opioid requirements

-Doses of **local anesthetics** required for **epidural anesthesia** are **decreased** due to:
-Venous engorgement of the epidural space
-Increased spread secondary to increased epidural pressure (related to the vascular engorgement)

Gastrointestinal system

-**Increased risk of gastric reflux and aspiration pneumonia**
-Gastric emptying is prolonged
-Esophageal sphincter tone is decreased
-Gastric motility is decreased
-Gastric contents become more acidic

-Pretreatment with **metoclopramide and H2 blockers** may help reduce the risks of lung damage if aspiration occurs

-Function returns to normal within 2-3 days post-partum

-Hepatic function tests (alkaline phosphatase, ALT, LDH, and BSP retention time) are increased. Significance is unknown.

Renal system

-Renal blood flow increases markedly during gestation (up to 80% increase)
-Glomerular filtration rate (GFR) increases 50%
-Despite respiratory alkalosis, renal compensation maintains normal pH by increasing bicarbonate excretion in the kidneys.
-**Post-partum diuresis** is responsible for returning plasma volumes to normal levels (therefore, the dilutional anemia also resolves) within 2-3 weeks

FETAL PHYSIOLOGIC CONSIDERATIONS

Maintain adequate placental blood flow

-**Placental blood flow is directly related to maternal blood flow** and blood pressure
  -Decreased maternal blood pressure can lead to poor placental perfusion and subsequent fetal hypoxia, morbidity and mortality
  -**Hypotension is best avoided** by
    -adequate fluid therapy
    -avoiding excessive anesthetic depth
    -prevention of positional impedance to blood flow

Prevent fetal hypoxia

-**Maternal hypoxemia = fetal hypoxemia** cause by:
  -Inadequate ventilation
  -Hypotension
  -Anemia
  -Acid-base imbalances

Avoid teratogenesis

-Cell line differentiation occurs during the **first trimester** (greatest potential for teratogenesis)
-A number of agents have been incriminated as having teratogenic or fetotoxic effects. Although absolute proof is lacking, experimental evidence suggests a number of anesthetic agents may have **teratogenic potential:**
    -injectables
    -benzodiazepines
    -pentobarbital
    -chloropromazine
  -inhalants
    -nitrous oxide (long exposure)
    -halothane (long exposure to high doses)
    -methoxyflurane
    -diethyl ether (long exposure)

Protect against spontaneous abortion/fetal resorption

-Certain agents tend to **increase or decrease uterine pressure** leading to alterations in blood flow and resulting in fetal mortality
  -injectables
    -glucocorticoids cause abortion in some species
    -**xylazine** has been shown to increase uterine pressure in pregnant cattle and may lead to pressures high enough to cause abortion
  -inhalants
    -nitrous oxide (N_20) and halothane have been reported to cause increased incidence of fetal resorption in rats

CLINICAL IMPLICATIONS OF PERINATAL CHANGES

Preanesthetic recommendations

-Use **mild tranquilization** with narcotics (reversible, with relatively few adverse cv effects) **only if necessary** (i.e. if the dam is highly stressed or intractable). Avoid use of drugs that can cause cardiovascular imbalances (such as acepromazine, xylazine).
  -if opioids are used, it may be **advantageous to use atropine**, since it will cross the placental barrier and prevent fetal bradycardia

-Place an **IV catheter** and administer balanced electrolyte fluids
  -*Many mothers presenting for emergency c-sections are dehydrated; remember that most expectant mothers are mildly anemic; therefore, a "normal" (non-pregnant) PCV in a near-term mother probably indicates dehydration*

-**Clip** the surgical area **prior to induction** if the animal is amenable

-**Preoxygenate** for 3-5 minutes prior to induction

-Avoid placing the animal in dorsal recumbency until necessary

Induction recommendations

-Use a **rapid induction** and intubation technique to minimize maternal hypoxia
  -*Increased oxygen consumption means hypoxemia occurs rapidly during apnea*

-**Support ventilation** if adequate assistance is available
  -*The pregnant animal cannot adequately ventilate spontaneously due to physical compression on the diaphragm*

-**Combine different agents** to minimize effects of each agent

Maintenance recommendations

-**Work quickly!**

-Avoid excessive doses of inhalant anesthetics
  -*Remember **MAC requirements are reduced** in the pregnant animal*

-Monitor blood loss
  -*Preexisting anemia means moderate surgical blood loss can be significant*

-Work quickly!

-Avoid positional exacerbation of hypotension
  -Do not position the animal with the head down

-Avoid dorsal recumbency except when necessary
-Avoid excessive exteriorization of the uterus (can decrease **venous return)**
-Work quickly!

Neonatal resuscitation during a c-section

As with **any resuscitation, the ABCD's** are key to remembering what to do:

-Airway
-Clear material from airways immediately
-Gently suction the oropharyngeal area with a suction device or large-bore IV catheter and syringe if material is present

-Breathing
-Stimulate the neonate to **breathe/move** by briskly (but carefully!) rubbing with a towel
-Check **mucous membrane color** and provide gentle positive pressure ventilation if cyanosis is present
-doxapram - 1 drop sublingual may help stimulate respiration

-Cardiac/Circulation
-Check the **heart rate**; if the neonate is bradycardic (<100 bpm) give an anticholinergic; if the neonate is asystolic give epinephrine
-atropine - 1 drop sublingual
-epinephrine - 1 drop sublingual

-Drugs
-**Reverse** any **narcotics** given to the mother and give a **respiratory stimulant** (doxapram) if needed
-naloxone - 1 drop sublingual

-Don't worry about the umbilical cord until AFTER ventilation has been ensured
-If the neonate is active and breathing on its own, the cord can then be ligated/cut
-Ligate at least 1 inch from the umbilicus
-Check each neonate thoroughly for **congenital abnormalities** such as limb deformities, spinal deformities and cleft palate
-Keep the neonates **warm** until they can be placed with the mother
-Recommended room temperature is 85 F. However, do NOT place them directly on a heating pad or close to a heat lamp (severe burns can occur-baby skin is fragile)

Recovery of the dam

-Reverse narcotics if necessary
-Make sure the **mother** is **alert** before putting with neonates
-Make sure mother is kept warm and **mammary area is clean** and dry

SPECIFIC ANESTHETIC DRUGS FOR C-SECTION DELIVERY

Most of the properties making injectable agents desirable for production of analgesia/ anesthesia (high lipid solubility, low molecular weight, low ionization) also promote placental transfer and make them undesirable for use in pregnant animals. It then becomes

necessary to choose those agents (or combinations) with the least effects on the fetus.

Anticholinergics

atropine

-crosses the placenta rapidly and may cause fetal tachycardia.

-significance of fetal effects has not been studied

-recommended to be used if an opioid is used in the mother to prevent maternal and fetal bradycardia; not always necessary

glycopyrrolate - large molecular weight prevents rapid placental transfer

Alpha-2 agonists

xylazine, detomidine, medetomidine

-rapid placental transfer occurs

-not recommended in small animals due to potential for cardiac arrhythmias and respiratory depression

-proven abortogenic in cattle; **use with caution** in pregnant mares

Major tranquilizers (phenothiazines)

acepromazine, promazine, chlorpromazine

-rapid placental transfer

-hypotension potential in mother can adversely affect fetus

-long lasting effects and non-reversible

-generally not recommended; if used, use LOW doses

Minor tranquilizers (benzodiazepines)

diazepam, midazolam, zolazelpam (in Telazol®)

-potential for teratogenesis in early pregnancy

-placental transfer does occur (fetal concentration twice that of maternal levels)

-minimal maternal cardiovascular depression; fetal depression may occur

-reversible; effects are less dramatic and shorter acting (compare to major tranq)

-despite side effects, nice to use in low doses combined with opioids

Opioids

-readily cross placenta

-fetal depression occurs, but may be minimized with low doses

-easily reversible (except buprenorphine which binds tightly to the receptor)

-most frequently used agents for premed /induction in small animals for C-section at UMVMC

butorphanol - can be given as a premed IM (if premedication is necessary); effects last 1-2 hours so it may be necessary to repeat the reversal the neonates. Useful in both dogs and cats, but tranquilization (with a benzodiazepine) may be necessary, especially in cats.

oxymorphone/hydromorphone - can be given as a premed IM (if premedication is necessary), or as an IV induction agent; effects last 2-4 hours so it will be

necessary to repeatedly reverse the neonates. Useful in both dogs and cats, but tranquilization (with a benzodiazepine) *is necessary, especially* in cats.

fentanyl - used as an induction agent (with a benzodiazepine) given IV in dogs. Maternal effects last 20-30 minutes (short); neonates should be reversed.

morphine and buprenorphine - although excellent analgesics, the possible respiratory depressant and bradycardic effects are too long lasting with these drugs. Not recommended for use during c-sections.

Barbiturates

-rapidly cross placenta and directly affect fetus

pentobarbital - **not recommended** due to high degree of respiratory depression and fetal mortality

thiobarbiturates (thiopental)- reach equilibrium in the fetus within 2-5 min. Redistribution occurs rapidly and the fetal liver is capable of some metabolism. Therefore, **low induction doses** (<3mg/kg) **cause minimal fetal** depression if **not repeated.**

Non-barbiturate sedative hypnotics

propofol - rapid placental transfer occurs; fetal effects are similar to thiobarbiturates; may be **useful in low doses** (1-2 mg/kg)

etomidate - useful but very expensive; good for patients with cardiovascular disease

Dissociative agents

ketamine and tiletamine (in Telazol®)

-readily crosses placenta and high doses may cause fetal depression/ hypoxia secondary uterine vasoconstriction

-not reversible

-minimal analgesia

-muscle relaxation minimal for (injectable) abdominal procedures

-useful in **low doses for induction** (NOT maintenance), especially in cats & horses

Muscle relaxants

Guiaifenesin (GG)

-will cross placenta

-commonly used here as part of induction regime with minimal side effects noted; helps to **decrease induction dose of ketamine or thiopental** in horses

Neuromuscular blocking agents(pancuronium, (cis)atracurium, succinyl-choline)

-**NOT analgesic**; patient is paralyzed, unable to respond if feeling pain

-not practical for practicing veterinarian as ventilatory support is mandatory

-large molecular weight of most of these agents prevents rapid placental transfer and fetal effects are minimal

Inhalants

-all cross the placenta rapidly

-degree of fetal depression is dose-dependent

Sevoflurane

-rapid placental transfer; effects on **developing fetuses unknown**

-most **ideal agent** of all modern inhalants

-approved for use in dogs

-insoluable, therefore **rapid** effect and rapid recovery

Isoflurane

-rapid placental transfer; effects on **developing fetuses unknown**

-preferred over other agents (i.e. halothane, methoxyflurane) for C-sections

Halothane

-decreases myometrial tone and may prolong involution

-may cause uterine vasodilation and increase bleeding

-experimental studies in rats show increased incidence of fetal resorption

Methoxyflurane

-little change noted in uterine tone or motility

-high solubility and associated slow induction time make it a poor choice

Nitrous oxide

-long-term exposure to high levels (>70%) may lead to fetal impairment if used during early pregnancy

->70% may also lead to fetal hypoxia secondary to maternal hypoxia

-monitor mom using a pulse oximeter to notice early desaturation and hypoxemia

-use of ***50 - 60% allows reduction of dose of more potent inhalants***

Miscellaneous agents associated with C-section

oxytocin - do not give IV intraoperatively as **maternal hypotension** can occur

calcium gluconate - often given to strengthen uterine contractility; if given, monitor heart rate and rhythm closely for arrhythmias; **do not give during anesthesia unless hypocalcemia** has been documented

SUGGESTED TECHNIQUES for different species

Regional analgesia (**line block, epidural**) with local anesthetic agent (lidocaine, bupivacaine) will decrease doses of all the following agents

Dog

-Opioid /tranquilizer premed + low dose thiobarbiturate/propofol induction + inhalant maintenance

OR

-Opiold/ tranquilizer induction + inhalant maintenance

OR

-Low dose thiobarbiturate/propofol induction + inhalant maintenance + line/epidural block for analgesia

OR

-Mask inhalant induction + inhalant maintenance + line block/epidural for analgesia

Cat

-Opioid /tranquilizer premed + low dose thiobarbiturate/propofol induction + inhalant maintenance

OR

-Low dose keta mine /benzodiazepine induction + inhalant maintenance + line block/epidural for analgesia

OR

-Low dose thiobarbiturate or propofol induction + inhalant maintenance + line block/epidural for analgesia

OR

-Chamber/mask induction + inhalant maintenance + line block/epidural for analgesia

Horse

-Guiaifenesin/ketamine induction + inhalant maintenance + post-op NSAIDS for analgesia

OR

- Guiaifenesin / thiobarbiturate induction + inhalant maintenance + post-op NSAIDS for analgesia

Cow

-Epidural or paravertebral regional anesthesia (lidocaine) most commonly used

Swine

-Lidocaine epidural (may be difficult to perform)

OR

Xylazine / ketamine premed +/- inhalant (depending on situation)

OR

-Telazol® premed + low-dose thiobarbiturate induction + inhalant maintenance