Commentary

Prevention of fetal suffering during ovariohysterectomy of pregnant animals

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Veterinarians who neuter cats and dogs sometimes find, for a variety of reasons, that they are required to spay pregnant animals. Ovariohysterectomy of pregnant animals in animal shelters and humane societies, for example, is commonly recommended to help reduce the overpopulation of unwanted dogs and cats and because shelters have a limited capacity to care for neonatal animals and neonatal animals often fare poorly in shelter environments.1,2 For feral cat control programs, ovariohysterectomy of pregnant females furthers the mission of population control and allows all animals brought to the clinic to be spayed the same day, eliminating the need for re trapping or extensive foster care. In the case of owned animals, owners may request pregnancy termination, and ovariohysterectomy is considered the best alternative for termination of unwanted pregnancies in cats and dogs not intended for breeding.3

Many veterinarians performing ovariohysterectomy in dogs and cats in the middle to later stages of pregnancy question the most appropriate way to ensure a humane death for in utero fetuses removed from the dam. Unfortunately, little guidance is available from published veterinary sources. For example, the 2007 AVMA guidelines on euthanasia,4 in the section on prenatal and neonatal euthanasia, simply state that “When ovarian hysterectomies are performed, euthanasia of feti should be accomplished as soon as possible after removal from the dam. Neonatal animals are relatively resistant to hypoxia.” However, the guidelines do not cite any research on whether chemical or physical means of euthanasia are recommended for in utero fetuses. In addition, the guidelines do not state the developmental stage at which fetuses might require euthanasia, nor do they recommend effective methods for euthanasia of fetuses or methods for determination of successful euthanasia. Similarly, no mention of fetal disposition is made in the Association of Shelter Veterinarians veterinary medical care guidelines for spay-neuter programs,5 nor is the topic discussed in other veterinary publications aimed at practitioners in the United States, including journals, textbooks, published guidelines, and trade magazines. The 2011 revision to the AVMA guidelines on euthanasia cites recent reviews indicating that euthanasia of fetuses is unnecessary, but this section is brief and may not provide sufficient information to assuage veterinarians’ concerns about fetal sensory awareness and suffering or provide veterinarians with an understanding of the various factors that influence fetal consciousness.

In lieu of published guidelines, veterinarians’ protocols for whether or how to euthanize fetuses are diverse and conflicting, driven by concerns that the fetuses are sentient and may be suffering or experiencing pain or distress at the time of maternal ovariohysterectomy. During discussions at conferences and on the electronic mailing list of the Association of Shelter Veterinarians, for instance, I have heard a variety of protocols for euthanasia of fetuses following removal of the uterus in pregnant female dogs and cats, including palpation of the fetuses through the uterus followed by injection of sodium pentobarbital into the abdomens of the fetuses, or injection of sodium pentobarbital into the maternal uterine blood vessels following detachment from the dam. In addition, some veterinarians report that they do not use any active procedures for euthanasia of in utero fetuses, simply disposing of the intact, unopened uterus, and others refuse to perform ovariohysterectomy of pregnant animals in the advanced stages of gestation because of a perceived inevitability of fetal suffering.

Normal Fetal Activity in Utero

Concerns about fetal suffering during ovariohysterectomy of pregnant animals may arise, at least in part, because of observation of fetal body and respiratory movements. However, these movements are a part of normal fetal physiology in utero and should not on their own be a cause for welfare concerns. Fetal movement first appears in cats at 23 to 25 days of gestation6–8 and in dogs at 34 to 36 days after the preovulatory luteinizing hormone surge.9 Fetal movement becomes more frequent and varied as the fetus matures and may be spontaneous or a reaction to stimuli such as amniotic sac compression.6–8 Fetal respiratory movements normally occur in all mammalian fetuses in utero,10 progressing from sporadic diaphragmatic movements in early gestation to intermittent bouts of regular, rhythmic breathing motions later in pregnancy.11,12 In cats, regular respiratory movements are seen throughout the final trimester of pregnancy and may be observed sporadically before this time.11 These respiratory movements are vital for lung growth and maturation10 and create a regular exchange of fetal lung fluid with the surrounding amniotic fluid.12,13 In addition to these respiratory movements, fetuses swallow amniotic fluid, especially during the second half of gestation, and this is thought to play a role in amniotic fluid volume regulation.13

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Fetal Distress

Welfare concerns during ovariohysterectomy of pregnant animals may also arise because of the use of the term fetal distress to describe physiologic compromise of fetuses. In this term, however, the word distress is used to describe a physiologic state and is not meant to indicate or imply conscious emotional distress, awareness, or conscious suffering. Fetal distress is defined as a “compromise of the fetus during the antepartum period or intrapartum period.” The term has been used to describe fetal hypoxia, but its use has fallen out of favor because it is imprecise and nonspecific, and the American College of Obstetricians and Gynecologists Committee on Obstetric Practice recommends using the term nonreassuring fetal status in conjunction with a description of the specific, physiologic findings that are raising concerns.13

Fetal Consciousness

Despite the apparent lack of information available to the veterinary community regarding fetal awareness and ability to suffer, research published elsewhere on fetal consciousness sheds light on this subject. In an extensive review of fetal physiology and pain perception, Mellor and Diesch14 assert that “an animal must be both sentient and conscious for suffering to occur.” In other words, the animal must have adequate neural development for sensory perception or sentience and must also be in a waking, conscious state. The in utero environment, the process of ovariohysterectomy, and several characteristics of dog, cat, and rabbit fetuses prevent attainment of one or both of these requirements for suffering and thus effectively preclude fetal suffering during ovariohysterectomy.

General Anesthesia

Patients undergoing ovariohysterectomy are typically under general anesthesia. Any drug that must readily pass through the blood-brain barrier to have an effect on the dam will also pass through the placenta.15-19 Many injectable and inhalant drugs equilibrate rapidly across the placenta, particularly those with high lipid solubility and low molecular weight. In humans, for example, morphine equilibrates across the placenta within approximately 5 minutes20; following IV administration, ketamine concentrations in the fetus are higher than those in the maternal circulation within approximately 1.5 minutes21; and fetal diazepam concentrations may be twice as high as those in the maternal circulation.22 In goats, medetomidine, an α-2-adrenoceptor agonist, crosses the placenta, directly affecting the fetus, and decreases uterine blood flow, reducing fetal oxygenation.23 Inhalant anesthetic agents such as isoflurane also readily pass to the fetus.15-19 The steady rate of administration of inhalant anesthetic agents leads to less rapid equilibration than bolus injections22; however, in sheep, the fetal minimum alveolar concentration for isoflurane is less than half the maternal minimum alveolar concentration.23 Thus, the fetus can be anesthetized at concentrations sufficient to anesthetize its dam.

Many of the mechanisms that postnatal animals use to eliminate anesthetic medications do not function in fetuses. Fetal hepatic metabolism may not be mature enough to transform or eliminate many drugs,19,24 and inhalant anesthetic agents cannot be eliminated by respiration. Once the uterus is removed from the dam, placental transfer of drugs back to the dam for elimination is no longer a possibility.

Despite adequate maternal anesthesia and analgesia during ovariohysterectomy, fetal movement can be occasionally observed through the exteriorized uterus. However, such movement does not necessarily indicate fetal consciousness or inadequate distribution of anesthetic medications to the fetus, considering that studies in adult humans and other animals show that memory and awareness are ablated at anesthetic concentrations < 50% of those needed to abolish movement.25

Fetal Neurodevelopment

Mammalian fetal neurodevelopment occurs in a predictable sequence regardless of species; however, the timing of birth within this developmental progression differs greatly among mammalian species.26 Neuroanatomic development progresses from rudimentary to complex, behavioral movements increase in coordination, and the neurophysiologic development of the electroencephalogram (EEG) parallels these neuroanatomic and behavioral changes. The capabilities for sensory perception and conscious awareness appear with the development of differentiated cortical electrical activity.26 The differentiation between rapid eye motion and non–rapid eye motion sleep patterns in fetuses or neonates is thought to correlate with the development of the capacity for conscious awareness.26-28

Dogs, cats, rabbits, and rats are all born at a stage of moderate neurologic immaturity.29 At birth, the EEG of these species exhibits electrical silence or very low voltage, intermittent or continuous activity; and no differentiation between rapid eye motion and non–rapid eye motion sleep.26,29 Neonatal rats 3 to 7 days after birth have no EEG response to a painful stimulus,27 and neonatal cats 1 day after birth have no distinguishable EEG changes during vocalization or handling.29 As early as the second day after birth, an EEG response to pain is detectable in dogs, cats, and rabbits.28,30 Dogs appear to have greater variability in neonatal EEG findings, and in some neonatal puppies, wakefulness and sleep may be distinguished 1 day after birth,29 although generally this differentiation appears most often between 4 and 10 days after birth in dogs.30,31 Rabbits have EEG activity 1 day after birth, but sleep pattern differentiation does not appear until 4 days after birth.29 Thus, in dogs and cats, fetal neurologic development is at an inadequate stage to support conscious awareness in near-term and probably even full-term fetuses.26,27

Neuroinhibition of Fetuses

Even in fetuses that have attained adequate neurologic maturity to have differentiation of rapid eye motion and non–rapid eye motion sleep patterns, substantial evidence exists that fetuses remain in a state of unconsciousness throughout pregnancy.26,31 and fetal EEG patterns and behavior demonstrate continuous sleep-like states of unconsciousness. These fetuses are
not arousable to conscious wakefulness even with potentially noxious stimulation. A collection of fetal, placental, and uterine factors with inhibitory effects on fetal EEG activity operate throughout the latter part of pregnancy, including adenosine, allopregnenolone, pregnenolone, prostaglandin D₂, and at least one placental neuroinhibitory peptide. In addition, intratruean warmth, cushioned tactile stimulation, and buoyancy act together with hypoxic inhibition of cerebrocortical activity to further suppress fetal stimulation and EEG activity.

At birth or delivery or if the uterus is opened after spaying, fetuses (essentially neonates) are exposed for the first time to air. Neonates are subjected to a variety of physical stimuli such as cutaneous and thermal changes. Oxygen tension increases dramatically with the first few breaths, from 15 to 23 mm Hg in fetuses to 60 to 90 mm Hg in newborns. The placently derived inhibitory hormones are withdrawn, and their concentrations in the fetal circulation rapidly decrease, to be replaced by the neuroactivators 17β-estradiol and noradrenaline. In fetuses with nervous systems that are mature enough to support consciousness, this marked change in the neonate’s environment leads to a rapid progression into conscious wakefulness. In the case of cat and dog fetuses, adequate neurologic maturity to support consciousness is unlikely to be attained before the end of gestation.

Fetal Response to Hypoxia

Fetuses are physiologically tolerant of hypoxia. This is especially true of fetuses born in an intermediate state of maturity such as cats, dogs, rabbits, and rats. In the second trimester, rat fetuses may survive as much as 90 minutes of hypoxia resulting from uterine vessel occlusion and sheep may survive > 30 minutes of hypoxia resulting from umbilical cord compression. In the third trimester, fetal mice may survive in utero for > 20 minutes after euthanasia of their dam, regardless of the maternal euthanasia method, and full-term neonatal dogs and rabbits may survive > 30 minutes of hypoxia. This fetal tolerance to hypoxia results from physiologic adaptation to the normally low-oxygen intrauterine environment as well as several oxygen-sparing mechanisms present in acutely hypoxic fetuses and allows fetuses to survive transient hypoxic insults during gestation and labor.

Oxygen-sparing mechanisms that occur in hypoxic later-term fetuses include a decrease in fetal breathing movements, which account for approximately 30% of all oxygen consumption in fetal lambs. Most interestingly, fetal heart rate decreases immediately at the onset of hypoxia, and cerebral heat production decreases within the first minute of hypoxia. Most interestingly, fetal EEG activity becomes isoelectric within 60 to 90 seconds after the onset of hypoxia. These responses to hypoxia appear to be mediated by adenosine. Adenosine concentrations in the fetal brain rise quickly during hypoxia and more than double during prolonged hypoxia. Adenosine leads to a decrease in fetal breathing movements and actively mediates the suppression of EEG activity and the decrease in cerebral heat production that indicates suppressed cerebral metabolism.

This adenosine-mediated fetal metabolic and neurologic suppression further deepens the already unconscious state in hypoxic fetuses. The isoelectric EEG activity of hypoxic fetuses is incompatible with consciousness. Thus, despite prolonged survival of hypoxic in utero fetuses after pregnant ovariohysterectomy, fetal consciousness and thus fetal suffering cannot occur.

During midgestation, fetuses may respond to hypoxia with a transient increase in motor activity, whereas in full-term fetuses, this motor response is decreased or absent. Transiently increased fetal motor activity may be a mechanism to remove mechanical or positional umbilical cord compression. This increased activity occurs despite the EEG transition to an isoelectric state, indicating that the movement is not controlled by the cortex and is not indicative of a conscious state. This unconscious fetal movement may be observed by surgeons during ovariohysterectomy.

Summary and Conclusions

Compelling scientific evidence supports the conclusion that fetuses remain unconscious when retained in utero after maternal ovariohysterectomy. Maternal general anesthesia results in equilibration of most common anesthetic drugs across the placenta, subjecting the fetus to circulating drug concentrations comparable to those of the dam. Furthermore, many fetal mechanisms for drug elimination are either undeveloped or are prevented by the ovariohysterectomy procedure. Dogs, cats, and rabbits are born with a moderately immature state of neurophysiologic development that appears to be inadequate to support consciousness throughout most or all of gestation. Neuroinhibitors lead to a continuous sleep state, even in fetuses that are neurophysiologically developed enough to support a conscious state. Hypoxemia suppresses fetal EEG activity, making consciousness impossible once the maternal uterine blood supply has been occluded or transected.

Thus, for veterinarians performing ovariohysterectomy in pregnant animals, appropriate procedures for fetal disposition should include the retention of the fetuses in the closed uterus after uterine removal from the dam. Once the uterus is removed from the dam, fetal death will occur without fetal suffering or fetal consciousness without any further action on the part of the veterinarian. The closed uterus may be simply set aside and the fetuses left undisturbed. The veterinarian may elect to inject a sodium pentobarbital euthanasia solution through the wall of the closed uterus into the fetal abdominal cavity to hasten fetal death. Although this procedure is not necessary for the prevention of fetal suffering, it has no detrimental welfare effects and may speed the cessation of the spontaneous in utero fetal movements that some veterinarians and staff find troubling.

If the pregnant uterus is to be opened after ovariohysterectomy, I recommend, on the basis of the evidence cited in this commentary, that the uterus be left unopened and the fetuses undisturbed for a minimum of 1 hour after removal from the dam to prevent inadvertent fetal resuscitation. Fetal exposure to air prior to fetal death may lead to the stimulation of respiration,
loss of neuroinhibition, exhalation of inhalant anesthetic drugs, and perhaps even the potential for fetal consciousness and suffering prior to euthanasia. Injection of sodium pentobarbital into the uterine vasculature after ovariohysterectomy is unlikely to result in any appreciable concentration of the drug entering the fetal circulation owing to the lack of maternal blood pressure and circulation in the detached uterus and the reversed pressure gradient between the fetal and maternal sides of the placental unit. Although this practice would have no detrimental welfare effects, it is unlikely to result in any effect on the fetuses and thus provides no benefit.

References

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