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# Clinical Approach to Abortion, Stillbirth, and Neonatal Death in Dogs and Cats

Catherine G. Lamm, DVM, MRCVS<sup>a,\*</sup>, Bradley L. Njaa, DVM, MVSc<sup>b</sup>

## KEYWORDS

• Abortion • Diagnostics • Neonatal • Stillbirth

The normal gestational period for the dog is 57 to 72 days and that for the cat is between 52 and 74 days.<sup>1,2</sup> Fetal death during gestation can result in resorption, expulsion (abortion), or fetal retention and mummification.<sup>3</sup> If the neonate is born dead at full term, it is stillborn. Neonatal death is considered to be death within the first 3 weeks after birth. Diagnostic procedures to determine the cause of abortion, stillbirth, or neonatal death in dogs and cats are relatively similar in terms of sample collection and submission. For diagnosis, it is critical to collect the appropriate samples, including representative fetal tissues, fetal and maternal blood samples as well as placenta, for further ancillary testing.

When initially presented with an aborted, stillborn, or dead neonatal puppy or kitten, contact the local veterinary diagnostic laboratory prior to sample collection and submission. As all diagnostic laboratories vary, your local diagnostic laboratory will be able to advise you on their preferred sample types and methods of submission. Regional diagnostic laboratories often have abortion panels with discount rates and occasionally have abortion kits available to assist you in sample collection. This information may be useful as you work through the case.

The purpose of this article is to provide a guide to the investigation of abortion, stillbirth, and neonatal death in dogs and cats. It focuses on diagnostic procedures, differentials, and ancillary testing in these species.

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The authors have nothing to disclose.

<sup>a</sup> School of Veterinary Medicine, University of Glasgow, Bearsden, Glasgow, G61 1QH, UK

<sup>b</sup> Department of Pathobiology, Oklahoma State University, Stillwater, OK 74076, USA

\* Corresponding author.

*E-mail address:* [Catherine.Lamm@glasgow.ac.uk](mailto:Catherine.Lamm@glasgow.ac.uk)

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## DIAGNOSTIC PROCEDURES FOR ABORTION, STILLBIRTH, AND NEONATAL DEATH IN DOGS AND CATS

One of the greatest challenges of the diagnostic procedure is obtaining appropriate samples. Dogs and cats frequently eat the placenta and will occasionally consume dead fetuses as well. The placenta is the most critical tissue to obtain and can have more diagnostic value than the fetus itself.<sup>4</sup> Submission of fetuses/deceased neonates, placenta, and serum from the dam is ideal. Early submission and proper storage and transport of samples are critical to prevent tissue autolysis, which can inhibit both histopathologic interpretation and ancillary testing.<sup>4</sup> In outbreak situations within kennels or catteries, submission of acute and convalescent serum samples from affected and unaffected bitches or queens is extremely useful in tracking infections as they progress through the population.

The procedure outlined later for evaluation of fetal or neonatal death is a guideline. Please contact your local diagnostic laboratory for their preferred samples and testing methods. **Fig. 1** provides a check-off list to help you through the work-up of abortion or stillbirth cases.

A complete history is integral in determining the cause of abortion or neonatal death. Submissions should be accompanied by a complete history, which includes:

- Is the bitch/queen primiparous or multiparous?
- What is the size of the litter and number of littermates affected?
- Has the bitch or queen had problems with previous litters? If so, what diagnostic testing was completed?
- Are there other animals in the household? Are they used for breeding?
- Have other bitches/queens in the household experienced any other reproductive problems including infertility, abortion, or stillbirths? If so, what were they and were any diagnostic procedures performed?
- Do any other animals in the home have upper respiratory disease, diarrhea, or other clinical signs?
- What is the vaccination history of bitch/queen?
- What is the health status of the dam and surviving littermates?
- What is the breeding history of the bitch/queen and stud/tom?
- Has any genetic testing been completed?
- Have there been new additions to the household or kennel/cattery? Have any dogs/cats in the household travelled and returned recently? What quarantine protocols are implemented?

With this information, the diagnostician can target diagnostic testing and make further suggestions as needed if the standard diagnostic tests results are negative.

When presented with a dead fetus or neonate, the animal may be forwarded as a whole carcass to the diagnostic laboratory. Alternatively, the submitting veterinarian can perform a necropsy with appropriate samples collected and shipped. When submitting samples, record any gross abnormalities observed on the general accession form and, ideally, capture a few gross images as part of the submission. However, rarely will gross lesions be observed even when infectious causes are suspected. Because of this it is critical to collect samples for histopathology, serology, bacteriology, and virology in order to attempt to identify a cause. If a fungal disease is suspected, fungal cultures usually need to be specifically requested on the submission form as not all fungal organisms will grow on routine aerobic cultures. Definitive diagnosis is not always achieved but this testing scheme will help rule out infectious causes.

**Check-off List for Feline and Canine Abortion, Stillbirth, and Neonatal Death****1. Completed Submission Form**

- Complete history including any lesions noted

**2. In Blood Tube for Serology**

- Dam serum
- Serum or fetal fluid

**3. In Formalin for Histopathology**

Thin (less than 0.5 cm wide) sections of the following:

- Placenta
- Liver
- Kidney
- Lung
- Heart
- Brain
- Any lesions, specify on form

**4. Fresh for Virology and Bacteriology**

- Placenta
- Lung (fetuses only)
- Liver
- Kidney
- Spleen (neonates only)
- Any lesions, specify on form

**5. In Blood Tube for Culture**

- Stomach contents (fetuses only)

**Fig. 1.** Check-off list to assist in sample collection on cases of fetal or neonatal death.

**Necropsy**

Assemble necessary tools for a necropsy prior to starting, including a scalpel, scissors, forceps, needles, syringes, blood tubes with no additives, and collection



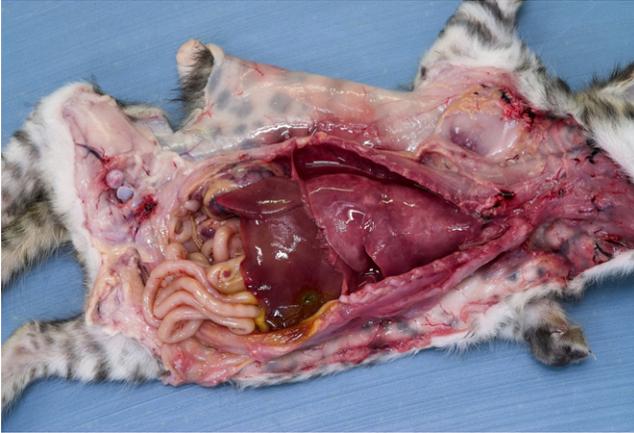
**Fig. 2.** Minimum supplies needed for a complete postmortem examination of a puppy or kitten.

containers for both histopathology and microbiological testing (**Fig. 2**). Measure and record the animal's weight. If a fetus or other animal that has died within 24 to 48 hours of birth, measure the crown-to-rump length. Document amount of hair growth present and whether it is soft or coarse. Toward the end of gestation, teeth should erupt through the gums. In aggregate, weight, crown-to-rump length, level of hair growth and its texture, and the presence or absence of erupted teeth will help define gestational age.

Rinse any fecal or other material from the fetus and fetal membranes and place on a wet table to begin the examination. Carefully perform a detailed external examination looking for abnormalities, including congenital defects, such as palatoschisis, spina bifida, and limb abnormalities or skull abnormalities. Examine the head and limbs for any evidence of redness, swelling, or improper mobility that may indicate a fracture or other musculoskeletal disease. Examine the umbilicus for evidence of swelling or redness that may indicate inflammation or bulging that may indicate an umbilical hernia.

Use a scalpel to reflect the limbs and open the thoracic and abdominal cavities (**Fig. 3**). With the cavities opened and prior to more thoroughly examining the internal organs, aseptically collect samples for bacteriology and virology testing as outlined in **Fig. 1**. Clean scissors, forceps, and a new scalpel blade should be used for collection. If possible, dip the instruments in alcohol and allow to air dry or flame prior to collection of samples. Do not touch the samples with your gloves or allow the sample to come in contact with anything other than your collection tools and the inside of the collection jar. The samples should be at least 1 cm<sup>3</sup> for bacteriology and virology. Collect heart blood and stomach contents using separate sterile syringes with needles and inject directly into separate blood collection tubes without additives. If heart blood cannot be aspirated, collect any free fluid within the abdominal or thoracic cavity (fetal fluid) and submit that for serology as an alternative. Samples for histopathology will be collected later.

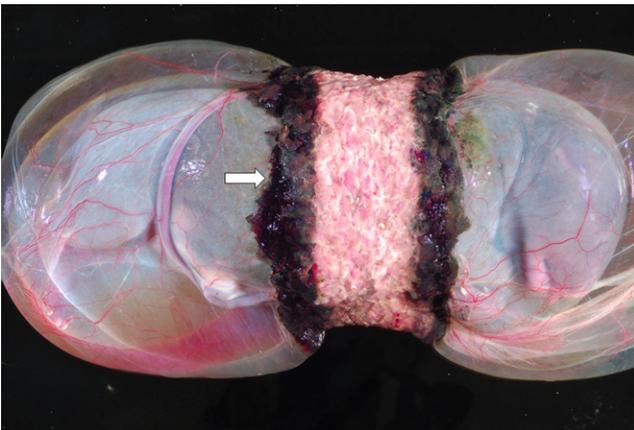
Once all of the cavities have been opened and aseptic samples have been collected, examine the carcass for evidence of any gross lesions. Pay particular



**Fig. 3.** Abdominal and thoracic cavities of a neonatal kitten opened for postmortem examination. (Photograph taken by and courtesy of Richard Irvine.)

attention to hemorrhages, both internal and external, as well as congenital defects such as a ventricular septal defect within the heart. Representative samples should be taken from all organs examined for histopathology and should be less than 0.5 cm in width for proper fixation. Samples should be placed in 10% neutral buffered formalin in a sealable container with a 1:10 ratio of tissue to formalin to ensure proper fixation. Be aware that the pathologist will often only examine a fraction of the organs collected as they will target specific areas based on species, history, and gross findings.

To examine the placenta, rinse gently with tap water and spread the membranes out on a flat surface. Dogs and cats have a zonary placenta. In dogs, the placenta is often bordered by dark red to dark green bands, which correspond to areas of hemorrhage (**Fig. 4**). This is a normal anatomic structure known as the marginal or



**Fig. 4.** Chorioallantois of a dog. Note the dark red to green bands representing the marginal hematomas on either side of the zonary placental attachment (arrow). The fetus can be seen within the fetal membranes.



**Fig. 5.** Mummified aborted fetal kitten and placenta. The fetus has a shrunken, wrinkled appearance. (Photograph taken by and courtesy of Richard Irvine.)

perizonal hematoma. This structure is much narrower and less distinct in cats and is pale brown. Any abnormalities in the placenta should be noted and a sample collected for histopathology. An impression smear of the chorioallantois should be obtained in order to examine for evidence of inflammatory cells and/or bacterial organisms. *Brucella* organisms are particularly evident within placental impression smears, allowing for rapid diagnosis. A section of placenta should also be collected for bacterial culture as earlier described.

### ***Assigning Significance to Gross Findings***

Some findings within the fetus may appear grossly striking but are incidental. It is common for fetuses to have a red tinge to their internal organs. Only when well-demarcated areas of obvious hemorrhage and/or edema are present is the lesion clinically relevant. Clear yellow or red fluid may be present within the body cavities as an incidental finding. The presence of clotted blood within the cavities is not normal, however, and may indicate trauma.

Fetal mummification occurs when the fetus dies in utero and is then retained for an extended period of time. The fetus will appear dry and shrunken and have wrinkled skin (**Fig. 5**). This is a nonspecific change that can be seen with viral infection as well as many other causes of in utero death. This change is in stark contrast to fetal maceration, which commonly occurs with bacterial infections, as the bacteria continue to replicate within the dead fetus, resulting in gas production and quick degradation of the fetal tissues. The end result is typically fetal bones mixed with reddish brown uterine fluid.

Congenital defects, such as those mentioned earlier, can be seen at necropsy and gross examination is often the only way to diagnose abnormalities such as heart defects. Congenital defects can cause fetal or neonatal death, such as hydrancephaly, or can be incidental, such as with unilateral renal agenesis. If you are unsure if a lesion is related to the death of the animal, take a photograph, write a detailed description, and send it to a pathologist for consultation.

### ***Preparing Your Submission***

Package the formalin container in a separate plastic bag from the fresh tissues and serum. Make sure absorbent material is present in this plastic bag to prevent leakage

and contamination. Fill out the appropriate paperwork for your diagnostic laboratory. On the submission form, be sure to include all findings on necropsy examination as well as the information required for a detailed history as mentioned earlier. Submission of digital or scanned images is encouraged.

Again, check whether the local diagnostic laboratory offers an abortion profile. If an abortion profile is not offered, request the following:

- Aerobic, *Campylobacter*, and *Salmonella* cultures of the lung and liver (pooled), stomach contents, and placenta
- Herpesvirus polymerase chain reaction (PCR) on the kidney if renal hemorrhages are noted grossly
- Serology for herpesvirus, brucellosis (dog only), and leptospirosis
- Histopathology of formalin fixed tissues.

Ship the samples overnight on ice packs. Call your regional diagnostic laboratory to see if they are open on Saturday before shipping overnight on a Friday. Fresh samples should be stored at 4°C until submission is possible. If samples must be stored for more than 3 days, freeze the fresh samples and store the formalin-fixed tissues at room temperature until the samples can be shipped. When concerned about anaerobic bacterial infections, make sure to use appropriate swabs and store them in anaerobic storage containers at room temperature until shipment. Never freeze tissues for histopathology as this causes severe artifactual tissue destruction.

If concerned about a genetic disease, there are numerous referral laboratories that offer different genetic tests. One example is the Veterinary Genetics Laboratory at the University of California, Davis, which offers a wide variety of test options in the dog and cat. Most testing is done from blood samples. However, contact the referral laboratory directly to discuss required samples and shipping requirements for the particular test requested.

Maternal causes of abortion and neonatal death are broad and require an extensive work-up by the veterinarian. In addition to routine testing, hormone levels, endometrial biopsies, and other diagnostic procedures in the bitch and queen are available. More information on evaluation of the bitch, is available in detail in article by Wilborn and Maxwell elsewhere in this issue.

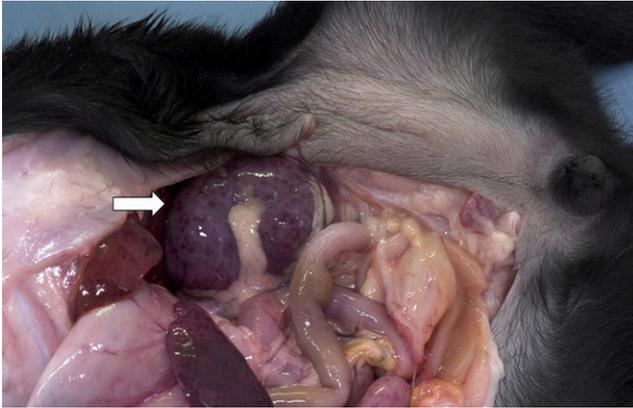
### ***Interpretation of Results***

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Each diagnostic test offered by a laboratory has the potential for both false-positive and false-negative results. As with diagnostic testing in the live animal, each result should be interpreted within the context of the clinical findings and gross or histologic abnormalities. Interpretation of serology results is particularly precarious as a positive result may only indicate exposure or vaccination rather than true infection and cause of abortion or neonatal death. If you have questions about interpretation of results, contact the specialists at the diagnostic laboratory for further explanation.

## **DIFFERENTIALS FOR ABORTION, STILLBIRTH, AND NEONATAL DEATH IN DOGS AND CATS**

The causes of fetal and neonatal loss can be broadly separated into infectious and noninfectious etiologies.<sup>3-5</sup> The main purpose of diagnostic evaluations in the fetus and neonate is to rule out infectious disease and significant congenital defects as causes of abortion. Infectious disease is particularly critical to rule out as this may affect other litters within large-scale breeding operations. Trauma either from delivery or following birth can also result in death in dogs and cats. Other noninfectious



**Fig. 6.** Neonatal puppy with herpesvirus infection. There are hemorrhages within the kidney (arrow). (Photograph taken by and courtesy of Richard Irvine.)

causes, including genetic disease and maternal factors, are much more difficult to diagnose.<sup>4,5</sup> Once infectious diseases, trauma, and congenital defects have been ruled out, the possibility of maternal factors as a cause should be explored clinically. For additional information on infertility in the bitch, please see article by Wilborn and Maxwell elsewhere in this issue.

### ***Infectious Causes***

Infectious causes of abortion in dogs and cats can be broadly grouped into viral, bacterial, fungal, and protozoal diseases. The diagnostic protocol proposed in this chapter attempts to identify infection with a particular organism, targeting the most common causes of fetal and neonatal death in the United States. This protocol does not include testing for less common etiologies, such as *Leishmania* spp and bluetongue virus (BTV).<sup>6,7</sup>

The most common cause of viral abortion and neonatal death in dogs is herpesviral infection.<sup>8-11</sup> Puppies can be infected in utero or at the time of parturition and death can occur in utero or up to 3 weeks following birth.<sup>12</sup> Body temperature plays an important role in neonatal herpesviral mortality, with viral replication optimized at lower temperatures.<sup>12</sup> Clinical presentations include sudden death, lethargy, and excessive crying.<sup>12</sup> Herpesviral infection in dogs is usually easy to diagnose on postmortem examination and is characterized by multiorgan haemorrhages, the most notable of which are seen in the kidney, lung, and liver (**Fig. 6**).<sup>12</sup> Herpesviral infection can be confirmed with histopathology and polymerase chain reaction. In cats, herpesviral infection as a cause of abortion is extremely rare and is most often associated with respiratory disease in the queen rather than direct infection of the fetus.<sup>13</sup> As in dogs, neonatal death due to herpesvirus can be seen in kittens.<sup>10</sup> For more information on herpesviral infection in dogs, please see article by Decaro and colleagues elsewhere in this issue.

Other viral infections known to cause sporadic abortions and neonatal death in dogs include BTV, canine parvovirus-1 (canine minute virus), canine distemper virus (CDV), and canine adenovirus-1 (CAV1).<sup>10,14</sup> Fetal and/or neonatal death may be secondary to maternal morbidity or due to direct infection.<sup>10</sup> BTV and canine parvovirus-1 infection are covered in detail in article by Decaro and colleagues

elsewhere in this issue. Abortions associated with CDV are rare and most often associated with maternal morbidity. In a small percentage of cases, the virus can cross the placenta and result in direct fetal infection.<sup>15</sup> CAV1 is not typically associated with abortion; however, CAV1 infection has been associated with fatal pneumonia in pups less than 4 weeks of age.<sup>16</sup>

Causes of sporadic viral abortion and neonatal death in cats include feline leukemia virus, feline parvovirus (feline panleukopenia virus), feline immunodeficiency virus, feline coronavirus, and feline calicivirus (FCaV).<sup>10,13,16–20</sup> Most of these viral infections are covered in detail in article by Decaro and colleagues elsewhere in this issue. FCaV infection in the queen can result in abortion secondary to maternal morbidity. Rarely, FCaV can cross the placenta, resulting in fetal infection, widespread cutaneous hemorrhages within the fetus, and subsequent abortion.<sup>18</sup>

The two most common causes of bacterial abortion and neonatal death in dogs are *Brucella canis* and *Streptococcus* spp infection.<sup>3,21–24</sup> Additional information on these organisms is provided in article by Graham and Taylor elsewhere in this issue. Infection with other bacterial organisms, such as *Escherichia coli*, *Campylobacter* spp, *Leptospira* spp, and *Salmonella* spp can occur sporadically.<sup>3,25–27</sup> Most bacterial causes of abortion and neonatal death will be isolated during routine aerobic cultures.<sup>26</sup> Although *Brucella* spp will grow on routine blood agar plates, colonies often take several days to become visible. Because of this, routine cultures that are reported as “no growth” at 48 hours have not ruled out brucellosis. Other exceptions include *Salmonella* spp and *Campylobacter* spp, both of which require special culture techniques. *Leptospira* spp are extremely difficult to culture, and growth can take several weeks. Paired serology on blood from the bitch or queen is a rapid diagnostic tool for leptospirosis. It is important to remember that recent vaccination of the dam may interfere with serologic interpretation. Histopathology is recommended to confirm that the organisms isolated from routine bacterial cultures are indeed associated with an infectious process and not a contaminant. This is particularly true concerning isolates from the placentas it is often contaminated by feces and other material that may be present in the birthing area. Bacterial causes of abortion in cats are similar to those in dogs, with the exception of brucellosis.<sup>13,17,28,29</sup> Abortions due to fungal infection are rare in dogs and cats.

Although protozoal infections may result in abortion, stillbirth, or neonatal death in dogs and cats, it is extremely rare. Cats and dogs are the definitive hosts for the protozoa *Toxoplasma gondii* and *Neospora caninum*, respectively.<sup>3,30</sup> Cats and dogs can serve as a source of infection in other animals with these organisms, which can result in abortion in other species, particularly ruminants and people.<sup>30</sup> Cats harboring *T gondii* are typically asymptomatic, although immune-suppressed cats can develop systemic toxoplasmosis particularly when infected with virulent strains, which can result in significant morbidity and mortality.<sup>13,31</sup> If the queen has systemic toxoplasmosis, she may abort due to systemic illness rather than direct fetal infection.<sup>3,13,32</sup> Transplacental transmission and fetal infection with *T gondii* have been shown in cats and dogs experimentally and associated fetal death has been reported.<sup>3,31,33</sup> Abortion or stillbirth related to neosporosis in dogs and cats has not been reported.<sup>3,34</sup>

### **Traumatic Causes**

Traumatic causes of abortion in dogs and cats can be further subdivided into trauma during parturition, such as with dystocia, and trauma occurring after birth.<sup>35</sup> Dystocia is often noted by the owner during parturition. Affected puppies or kittens often have regionally extensive hemorrhage and/or edema. Location of the lesions varies and is



**Fig. 7.** Three neonatal puppies from the same litter. There is extensive hemorrhage around and within the skull, typical of infanticide. (Photograph taken by and courtesy of Richard Irvine.)

dependent upon where the fetus was lodged within the birth canal and for how long. Other puppies or kittens within the litter may or may not be affected. Following cases of dystocia, the mother should be evaluated for possible causes of dystocia and cesarean section delivery may be considered in future pregnancies.

Neonatal trauma is often characterized by regionally extensive hemorrhage that may be accompanied by fractures of bones within the affected area. Infanticide is often caused by skull crushing and results in hemorrhage and fractures of the skull (Fig. 7). In cases of infanticide, typically more than one puppy or kitten in the litter may be affected. Dams that commit infanticide in one litter are at increased risk of committing infanticide in future litters.

### ***Congenital Defects and Genetic Disorders***

Congenital defects can be sporadic and without direct cause, can be a phenotypic reflection of a genetic disease, or can be related to toxin ingestion.<sup>5,13,35</sup> If similar congenital defects are present in more than one animal in the litter, further workup is required to rule out the 2 latter causes. Chromosomal defects typically result in early embryonic death and resorption.<sup>10,13</sup> As mentioned previously, referral laboratories are your best resources for confirming genetic disorders and should be contacted directly for submission guidelines.

### ***Noninfectious Causes and Maternal Factors***

The potential for abortion and stillbirth always exists if the bitch or queen is systemically ill, is excessively stressed, has received severe trauma, is administered certain drugs, ingests certain toxins, etc.<sup>5,10,35,36</sup> Once infectious and traumatic causes of abortion, stillbirth, and neonatal death have been ruled out, the possibility of maternal morbidity as the cause for fetal or neonatal death should be explored.

Abnormalities in metabolism or nutrition, such as diabetes mellitus, hypothyroidism, eclampsia, and pregnancy toxemia, can result in fetal or neonatal loss in the bitch and queen.<sup>13,21,32,37</sup> Diabetes mellitus in the bitch has been associated with fetal loss and stillbirths.<sup>21</sup> Due to persistent hyperglycemia, puppies born to bitches with diabetes are often large and dystocia can occur.<sup>21</sup> Pregnancy toxemia occurs secondary to a negative energy balance related to large litter sizes and/or inadequate

food intake.<sup>21</sup> Eclampsia is characterized by low serum calcium, which can result in fetal loss in the bitch and the queen.<sup>13,32</sup> Clinical chemistries and urinalysis are helpful in diagnosing diabetes, pregnancy toxemia, and eclampsia.<sup>21</sup>

Hypoluteinization occurs when the corpora lutei secrete insufficient progesterone to maintain pregnancy and has been reported in dogs.<sup>3,10,38–41</sup> Typically, these dogs appear clinically infertile due to recurrent early embryonic loss and resorption.<sup>41</sup> Hypoluteinization can be a treatable disease that is diagnosed by measurement of serum progesterone levels.<sup>3,41</sup>

### ***Other Causes of Neonatal Death***

Following birth, some kittens and puppies fail to thrive and are often lumped together using the phrase “fading syndrome.”<sup>42</sup> As the name implies, fading syndrome is used to simply describe a clinical presentation rather than a specific etiology.<sup>42</sup> This syndrome can be caused by a wide variety of infectious, toxic, traumatic, metabolic, and genetic diseases.<sup>42</sup> Maternal factors, such as mastitis, may also play a role. The cause for the fading syndrome may be readily evident, such as with a cleft palate and inability to effectively nurse, or may be much more obscure, such as idiopathic hypoglycemia resulting in hepatic lipidosis.<sup>26</sup> A complete postmortem examination of the affected neonate and thorough physical examination of the dam and littermates are required to determine the cause of failure to thrive.

### **SUMMARY**

Diagnosis of the cause of abortion, stillbirth, and neonatal death in the dog and cat can be challenging. The purpose of the diagnostic procedures outlined in this article is to provide the practitioner with a protocol for collection of quality samples and a guide to the recommended ancillary testing. The purpose of this procedure is to explore potential infectious causes of abortion and limit the spread of disease within a kennel population. Other sporadic causes of death may be more difficult to diagnose. Ultimately, it is important that the regional diagnostic laboratory be contacted prior to sample collection to ensure optimal results.

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