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## Approaches to Reducing Neonatal Mortality in Dogs (19-Mar-2003)

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### Introduction

The rate of stillbirth and neonatal death (to 4 weeks of age) is highly variable, and related to many factors, including the quality of labor, congenital abnormalities and acquired disorders. The average incidence of stillbirths during both complicated and uncomplicated vaginal deliveries is reported to range from 5.55 - 33.0% [1,2]. The stillbirth rate reported in one study for puppies delivered by cesarean section was 6 - 11% [3]. Reported neonatal mortality rates range from 9.23 - 26.0% subsequent to complicated and uncomplicated whelpings. Mortality is greatest during the first week of life. Prudent veterinary intervention in the perinatal period can increase neonatal survival by controlling or eliminating factors contributing to puppy morbidity and mortality. Poor prepartum condition of the dam, dystocia, congenital malformations, genetic defects, injury, environmental exposure, malnutrition, parasitism and infectious diseases all contribute to neonatal morbidity and mortality. Optimal husbandry impacts neonatal survival favorably and involves managing labor and delivery to reduce stillbirths, controlling parasitism and reducing infectious diseases, preventing injury and environmental exposure, and optimizing nutrition of the dam and neonates. Proper genetic screening for selection of breeders minimizes inherited congenital defects. Many definitions of the perinatal period exist. For purposes of this discussion, the perinatal period will be defined as the time from the last two weeks of gestation until weaning, and can be divided into the prepartum (prenatal) period, parturition, and the postpartum (neonatal) period.

### Prenatal Care

Management of the Bitch - Optimally, veterinary counsel prior to the pregnancy should involve proper genetic screening, bitch health assessment, adequate immunization and parasite control, selection of an optimal stud dog, ovulation timing to enhance conception and define gestational length, and good breeding management. A complete physical examination and counseling about parturition and neonatal husbandry should be part of any clinical pregnancy evaluation. The physical examination should include evaluation of the bitch's general status and give special attention to the mammary glands and nipples (for normal development of lactation, and normal anatomy) and the birth canal (for adequate size, and detection of any strictures). Routine anthelmintic treatment of bitches will not decrease transplacental and transmammary migration of *Toxocara canis*, or transplacental migration of *Uncinaria stenocephala*, thus puppies will require treatment as neonates (see below).

Nutrition - Proper perinatal nutrition and body condition for the bitch should be addressed at the time of pregnancy diagnosis. Minimally, a change from an adult diet to a diet formulated for pregnancy and lactation labeled "nutritionally complete for all life stages" or "complete nutrition for growth, pregnancy and lactation" should occur at the fourth week of gestation and continue through weaning. Recently, a change to such a diet at the time of breeding rather than mid gestation has been advocated to improve litter size and neonatal viability [4]. The amount fed must be managed so as to maintain proper body condition, as obesity negatively impacts labor. Supplements should be discouraged because they generally unbalance the nutrition provided by a commercially prepared diet. The pregnancy and lactation diet should be one previously tested and found to be adequate by the Association of American Feed Control Officials (AAFCO) standards, and not one simply "formulated to meet AAFCO standards" (or European equivalent). A protein level of 27 - 34% (preferably animal-based sources), at least 18% fat with a balanced supply of both n-6 and n-3 fatty acids, and 20 - 30% carbohydrates along with optimum vitamins and minerals (for avoiding mineral deficiencies or excesses) is advisable. Exercise should continue through pregnancy in progressive moderation, to maintain the bitch's body condition.

Disease Exposure - During the last 3 - 4 weeks of gestation, the bitch should be housed in familiar surroundings minimizing

exposure to pathogens (including those from other dogs or humans acting as fomites after travel to dog events). Late gestational abortion and neonatal death can be associated with numerous viral, bacterial and parasitic infections (Table 1) [2,5]. Exposure of an immunologically innocent bitch to canine herpesvirus during the last 3 weeks of gestation can result in late term abortion or neonatal death within the first 3 weeks of life [6]. Canine minute virus (parvovirus type-1) can infect puppies in utero if a bitch is infected between 20 and 35 days of gestation, and can result in resorption or acute neonatal death from 1 to 3 weeks post partum. Experimentally, in utero infection with type 2 canine parvovirus (CPV-2) has been associated with myocarditis in neonates, although this is an uncommon diagnosis under natural conditions. Canine distemper virus can cross the placenta and cause congenital infections. *Campylobacter* spp. have been reported to cause abortion, stillbirths and sick neonates. Several bacterial organisms (e.g., *Escherichia coli*, beta-hemolytic streptococci) as well as mycoplasma and ureaplasma, all part of the normal vaginal flora, can be associated with septicemia if established in the neonate. The natural incidence of transplacentally acquired *Toxoplasma gondii* infection in the dog is thought to be uncommon, experimental infection resulted in neonatal death. Similarly, although the incidence of natural transplacental transmission of the protozoal *Neospora caninum* is unknown, experimental infection resulted in stillbirth with evidence of myocarditis. Evaluation of neonatal mortality with these infectious diseases in mind can be important clinically.

**Table 1. Infections reported to cause late-gestational abortion, stillbirth or neonatal mortality in dogs.**

**VIRAL**

- Canine herpesvirus
- Canine minute virus (parvovirus type-1)
- Canine parvovirus type 2 (CPV-2)
- Canine distemper virus

**BACTERIAL**

- *Campylobacter* spp.
- *Escherichia coli*
- Beta-hemolytic Streptococci
- Mycoplasma
- Ureaplasma
- *Brucella canis*

**PROTOZOAL**

- *Toxoplasma gondii*
- *Neospora caninum*

Late-gestation - A quiet, draft free, warm environment with a proper whelping box should be made available to the bitch during the last 7 - 10 days of gestation. Optimally, the whelping box should have an impervious surface that is readily disinfected and walls which preclude crushing of pups. This can be accomplished by the inclusion of a "pig" rail or by graduated sides such as found in plastic childrens' swimming pools (Fig. 1a, Fig. 1b, Fig. 1c).



Figure 1a. Plastic children's pool used as a whelping box. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 1b. Manufactured cardboard lined whelping box with guard rails. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 1c. Manufactured plastic whelping box with molded guard rails. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Proper bedding in the whelping box should be absorbent, readily exchanged, and not likely to suffocate or bury puppies. It can be shredded newspaper (Fig. 2), high-quality low-dust pine shavings, corrugated paper, or a fitted, textured fabric with adhesive backing.



Figure 2. Shredded newspapers used as bedding in whelping stall. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

## Parturition

Monitoring Parturition - Clients should be educated about the normal events in canine parturition, and be prepared to recognize early signs of dystocia. The active, early management of labor is accepted in human obstetrics as a method of reducing dystocia and improving neonatal survival. The quality (appropriate length) of labor in women correlates closely with neonatal viability [17]. At the author's facility, the overall stillbirth rate declined from 9.2% to 2.5% with incorporation of uterine and fetal monitoring into the whelping process. The use of uterine and fetal monitoring systems greatly enhances the ability to assess the quality of labor and the viability of unborn puppies, making the diagnosis of dystocia more timely and accurate. Recently, systems for monitoring labor and delivery in the bitch have become commercially available and affordable (Veterinary Perinatal Services, Inc., Wheatridge, CO, USA). These systems are intended for use by veterinarians in the clinical setting when evaluating a bitch in labor, or by breeders at home with veterinary guidance (Fig. 3). Their design is based on labor monitoring systems utilized routinely in human obstetrics; they include a uterine tocodynamometer and fetal doppler (Fig. 4, Fig. 5).



Figure 3. Uterine monitor in use on a bitch in stage I labor. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 4. Uterine monitoring equipment (monitor, recorder, modem) and hand held doppler. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 5. Hand held doppler in use. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Monitoring Dystocia - The use of uterine and fetal monitors allows the veterinarian to detect and monitor labor, as well as manage dystocia medically or surgically with insight. The administration of calcium gluconate and oxytocin to treat dystocia can be directed and tailored based on the results of monitoring. Generally, the administration of calcium increases the strength of myometrial activity, and oxytocin increases the frequency of myometrial contractions. When ineffective, weak uterine contractions are detected calcium gluconate (Fujisawa Inc., USA), 10% solution (0.465 mEq Ca<sup>++</sup>/ml) can be given subcutaneously at a rate of 1 ml per 4.5 kg/10 lb body weight. Subcutaneous administration is effective and without concern

about arrhythmias. Subcutaneous administration of calcium solutions presents a small risk for granuloma formation at the injection site, volumes above 6 ml should be split into multiple sites. Oxytocin, 10 USP u/ml, (American Pharmaceutical Partners, Inc., CA, USA) is administered when uterine contractions are less frequent than expected for the stage of labor, and fetal heart rates are normal (170 - 220 beats per minute, or at least twice the maternal heart rate). Doses of oxytocin that are substantially lower than those traditionally given (0.5 - 2.0 units per dog by subcutaneous or intramuscular injection), are effective in improving the quality of myometrial contractions. The presence of fetal distress is reflected by sustained deceleration of the heart rates. Decelerations associated with uterine contractions suggest mismatch of the fetus (too large) and dam (birth canal too small or obstructed), or fetal malposition, malpresentation or malposture.

Cesarian Sections - If fetal stress is evident, and response to calcium and oxytocin is poor, surgical intervention (cesarean section) is indicated to improve outcome. The decision to intervene surgically is hastened if fetal heart rates are persistently decelerating. Optimal anesthetic protocols improve neonatal survival. Premedication of bitches with an anticholinergic glycopyrrolate (Robinul, Fort Dodge), induction with the short acting injectable anesthetic Propofol (PropoFlo, Abbott) or by mask inhalation of isoflurane or sevoflurane, and maintenance with isoflurane or sevoflurane is optimal, whereas methoxyflurane, ketamine, thiamylal, thiopental and xylazine are not advised [3]. A local block of the region of the ventral abdominal incision with lidocaine permits a more rapid approach. After removal of the puppies, the administration of a short acting narcotic analgesic such as buprenorphine (Buprenex, Norwich Eaton) or butorphanol tartrate (Torbugesic, Fort Dodge) to the bitch is advised. Post-operative sedation of the bitch may predispose to clumsiness with the puppies and a lack of appropriate maternal behavior for 12 - 24 hours, close monitoring is advised.

### **Postpartum Care**

Neonatal Resuscitation - Optimal neonatal resuscitation following cesarean section includes prompt clearing of airways by gentle suction with a bulb syringe, and drying and stimulation of the puppies to promote ventilation and avoid chilling (Fig. 6).



Figure 6. Suctioning a neonate's airways with a small bulb syringe. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Puppies should not be swung to clear airways as described in the veterinary literature, because of the potential for cerebral hemorrhage from concussion. Avoidance of phenothiazine, barbiturate, dissociative and narcotic pre-medications and anesthetic agents in the dam contributes to improved neonatal vigor and negates the need for the use of reversal agents in the neonates. The use of the respiratory stimulant doxapram in neonatal resuscitation has no conclusive support in the veterinary literature, and is not mentioned in human infant resuscitation literature. Doxapram acts as a central stimulant and its effect is diminished by brain hypoxemia [1]. Rubbing the puppy thorax with a soft towel and applying gentle positive pressure oxygen ventilation via a small, well fitting face mask and rebreathing bag are effective methods of stimulating ventilation. Spontaneous breathing and vocalization at birth are positively associated with survival through 7 days of age [7]. Similar intervention for resuscitation of puppies following vaginal delivery should take place if the dam's actions fail to stimulate respiration, vocalization and movement within one minute of birth.



Figure 7. Neonatal resuscitation kit. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Neonatal Clinical Parameters - Neonatal critical care is challenging due to the fragility and small size of the patient, making diagnostics and therapeutics difficult. Some variations in the blood chemistry profile exist in neonatal and pediatric patients including elevated alkaline phosphatase and phosphorus, and decreased albumin, globulins, cholesterol and BUN as compared to adult normals. Neonatal changes in the hemogram as compared to adult normals have been described, including

lower RBC parameters. Urine of neonates is normally dilute and glucosuria is a frequent occurrence. Sample collection can be facilitated in the neonate by gently swabbing the prepuce or vulva with a cotton ball to stimulate urination.

Neonatal puppies are highly susceptible to environmental stress, infection, and malnutrition. Puppies lack thermoregulatory mechanisms until four weeks of age, and thus the ambient temperature must be high enough, between 80 - 90 degrees F (27 - 32 degrees C), to facilitate maintenance of a body temperature of at least 97 degrees F (36 degrees C). Hypothermia negatively impacts immunity, nursing and digestion. Puppies with body temperatures less than 95 degrees F (35 degrees C) should be warmed slowly before feeding.

Resuscitation Guidelines - Updated neonatal resuscitation guidelines exist in the literature [1]. Current recommendations include immediate assessment and support of body temperature by keeping the pups warm and dry, support of airway patency by positioning the pup with the head extended and suctioning the oropharyngeal area gently, support of breathing by stimulation of vocalization and support of circulation best monitored by evaluating for a normal (150 - 220 bpm) heart rate and mucous membrane color (pink with 1 - 2 second capillary refill). Ventilatory support should include constant flow O<sub>2</sub> delivery by facemask. If this is ineffective after one minute, positive pressure with a snugly fitting mask or endotracheal intubation and rebreathing bag (using a 2-mm endotracheal tube or a 12 to 16-gauge intravenous catheter) is advised. Anecdotal success with Jen Chung acupuncture point stimulation has been claimed when a 25-gauge needle is inserted into the nasal philtrum at the base of the nares and rotated when bone is contacted. Cardiac stimulation should follow ventilation support, as myocardial hypoxemia is the most common cause of bradycardia or asystole. Direct trans-thoracic cardiac compressions are advised as the first step; epinephrine is the drug of choice for cardiac arrest (0.2 mg/kg administered best by the intravenous or intraosseous route). Atropine is currently not advised in neonatal resuscitation. The mechanism of bradycardia is hypoxemia-induced myocardial depression rather than vagal mediation, and anticholinergic induced tachycardia can actually exacerbate myocardial oxygen deficits. Doxapram is unlikely to be of any benefit in apneic hypoxic neonates. Venous access in the neonate is challenging, the single umbilical vein is one possibility. The proximal humerus, proximal femur and proximomedial tibia offer intraosseous sites for drug administration [18].

Compromised Immunity - Incompletely developed immune systems during the first 10 days of life make neonates vulnerable to systemic infection, both bacterial and viral. Adequate ingestion of colostrum must occur promptly postpartum for puppies to acquire passive immunity. The intestinal absorption of IgG generally ceases by 24 hours after parturition. Colostrum deprived kittens given adult cat serum at a dose of 150 ml/kg SC or IP developed serum IgG levels comparable with suckling littermates. However, colostrum deprived puppies given 40 ml/kg adult dog serum orally and parentally failed to match suckling littermate's IgG levels [8-10].

Neonatal Infections and Septicemia - The umbilicus of neonates should be treated with tincture of iodine immediately after birth to reduce contamination and prevent ascent of environmental bacteria into the peritoneal cavity (omphalitis-peritonitis) (Fig. 8).



Figure 8. Tincture of iodine treated umbilicus. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Neonatal bacterial septicemia can cause rapid deterioration resulting in death if not recognized and treated promptly. Factors that predispose a puppy to septicemia include endometritis in the bitch, a prolonged delivery or dystocia, feeding of replacement formulas (due to the association with poor neonatal health and the potential for aspiration), the use of ampicillin (predisposes for resistant bacteremia), stress, low birth weight (less than 350 g for average Labrador retriever size breeds), and chilling with body temperature < 96 degrees F (35.3 degrees C). The organisms most frequently associated with septicemia are *E.coli*, streptococci, staphylococci, and *Klebsiella* spp. Pre-mortem diagnosis can be challenging, and clinical signs may not be noted because death occurs suddenly. Indications that septicemia may be present include a decrease in weight gain, failure to suckle, hematuria, persistent diarrhea, unusual vocalization, abdominal distension and pain, and sloughing of the extremities. When septicemia is suspected, the clinician should consider prompt therapy with broad spectrum, bactericidal antibiotics, improved nutrition via supported nursing, tube-feeding or bottle-feeding, maintenance of body temperature, and appropriate fluid replacement. The third generation cephalosporin antibiotic ceftiofur sodium (Naxcel,

Pharmacia & Upjohn) is an appropriate choice for neonatal septicemia as it alters normal intestinal flora minimally and is usually effective against the causative organisms. More specific, narrow spectrum antimicrobial therapy can be selected once culture and sensitivity testing is concluded. Ceftiofur sodium should be administered at a dose of 2.5 mg/kg SC q 12 h for no longer than 5 days, and should be continued until 48 hours after symptoms have disappeared. Because puppies less than 48 hours old have reduced thrombin levels, presumptive therapy with vitamin K may be used (0.01 - 1.0 mg sc per puppy) [11].

Canine Herpesvirus - Exposure of an innocent bitch to canine herpesvirus during the last 3 weeks of gestation can result in late term abortion or neonatal death within the first 3 weeks of life because inadequate maternal antibodies exist to allow passive immunity to be acquired by the puppies. Transmission occurs subsequent to contact with infectious vaginal fluids or oronasal secretions. Signs in the neonate include anorexia (poor weight gain), dyspnea, abdominal pain, incoordination, diarrhea, serous to hemorrhagic nasal discharge and petechiation of the mucous membranes. The mortality rate in affected litters is commonly 100%, with deaths occurring over a few days to a week. Older (> 3 - 4 weeks of age) puppies exposed to herpes virus may have an inapparent infection but later central nervous signs including blindness and deafness have been observed. Therapy has generally been unrewarding, but recent experience suggests successful treatment with acyclovir and exogenous warming (unpublished observations, Davidson). The infected bitch is generally asymptomatic. Subsequent litters of the bitch are usually normal, having acquired maternal antibodies. Premortem diagnosis of canine herpesvirus infection in neonates can be challenging. Pathognomonic changes occurring in the kidneys include multifocal petechial hemorrhages. Intranuclear inclusion bodies can be difficult to find. Diagnosis by polymerase chain reaction (PCR) is confirmatory [6,12-14].

Neonatal Nutrition - Neonates have minimal body fat reserves and limited metabolic capacity to generate glucose from precursors. Glycogen stores are depleted shortly after birth, making adequate nourishment from nursing vital. Even minimal fasting can result in hypoglycemia. Hypoglycemia can also result from endotoxemia, septicemia, portosystemic shunts and glycogen storage abnormalities. Oral fluid and glucose replacement may be preferable if the puppy has an adequate swallowing reflex and is not clinically compromised. Clinical hypoglycemia involves blood glucose levels less than 30 to 40 mg/dl, and can be treated with dextrose solution intravenously, at a dose of 0.5 to 1.0 g/kg using a 5 to 10% solution; or a dose of 2 to 4 ml/kg of a 10% dextrose solution. Single administration of parenteral glucose is adequate if the puppy can then be fed or nurses. Fifty percent dextrose solution should only be applied to the mucous membranes because of the potential for phlebitis if administered intravenously; however, circulation must be adequate for absorption from the mucosa. Neonates administered dextrose should be monitored for hyperglycemia because of immature metabolic regulatory mechanisms. If a neonate is too weak to nurse or suckle, a mixture of a warmed, balanced crystalloid ( lactated ringer's solution or normosol solution and 5% dextrose may be administered subcutaneously at a dose of 1 ml per 30 g of body weight, until the pup can be fed or nurses. A balanced warmed nutrient-electrolyte solution can be administered orally by stomach tube every 15 - 30 minutes until the neonate is capable of suckling. The neonatal caloric requirement is 133 calories/kg/day during the first week of life, 155 calories/kg/day for the second, 175 - 198 calories/kg/day for the third and 220 calories/kg/day for the fourth [1]. Commercially manufactured puppy milk replacement formulas (Esbilac - Pet-Ag Inc, Elgin, IL; Puppy Milk Replacer Formula: Eukanuba, The Iams Co, Dayton OH; Veta-Lac Powder for Puppies: Vet-A-Mix, Shenandoah, IA) are usually superior to homemade versions. The use of milk obtained from the dam can be considered if available. An osmotic diarrhea (usually yellow, curdled stool appearance) can result from overfeeding formula, necessitating diluting the product 50% with water or a balanced crystalloid such as lactated ringer's solution. Pups should gain weight steadily from the first day after birth, however a transient mild loss from birth weight is acceptable on day 1; gaining 2 to 7 g (0.002 - 0.007 kg) per day for each kg of anticipated adult weight, i.e., 0.03 to 0.10 ounces per day for each pound of adult body weight. Weights of pups should be recorded daily for the first two weeks, then every 3 days until a month of age (Fig. 9). Pups should increase their body weight by 5 - 10% per day, doubling their birth weight by 10 - 12 days of age [15]. Healthy well nourished puppies are quiet and sleep when not nursing, although they may twitch while dreaming.



Figure 9. Monitoring weight gain in the neonate. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Preventative Health Care - Routine neonatal preventive health care should include broad spectrum anthelmintic therapy, started at 3 weeks of age, and repeated in 14 days. Subsequent fecal examinations for parasites can monitor efficacy of therapy. A broad spectrum non-toxic anthelmintic such as pyrantel pamoate (5 mg/kg PO) is advised. Routine deworming of the dam is not advised because parasites transmitted to fetus (across the placenta) or neonate (via the mammary gland) are

encysted in tissues and not residing in the gastrointestinal tract. In kennels with historically severely parasitized pups, deworming of dams from day 40 of gestation through 14 days of lactation with fenbendazole (Panacur) at a dose of 50 mg/kg/day PO can reduce dam to pup transmission, but is expensive. Immunization of puppies with appropriate vaccinations (canine distemper, parvovirus, adenovirus type II and parainfluenza minimally) can be initiated at 5 - 7 weeks of age, and repeated every 3 - 4 weeks until 16 weeks of age.

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