

Topics in canine neonatology and pediatrics

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Neonates

Puppy mortality can occur in utero, during whelping, after birth, in the first weeks of life, or after weaning and has been reported to be as high as 26%.¹ However, about half of all puppies that fail to survive to weaning are stillborn or die within the first three days of life. Factors implicated in these perinatal deaths include prematurity, in utero infection with viruses such as canine distemper and canine parvovirus, anatomic birth defects, birth trauma during difficult birth (dystocia), inadequate nutrition, maternal neglect, and environmental stresses. As a result, predisposing factors of perinatal death include factors such as difficult birth (dystocia), malformations from inherited disorders or congenital defects, low birth weight (15% or more lower than the average in the litter), maternal illness and lack of preventative health care (vaccination, parasite control, etc.), unfavorable environmental conditions, and infectious agents. A main focus point of intervention is prevention of predisposing factors as well as early identification and treatment of at risk neonates.² Prevention focuses on pre-breeding health and genetic screening of sire and dam, optimal husbandry, managing labor and delivery to reduce stillbirths, controlling parasitism, reducing infectious disease, preventing injury and environmental exposure, and optimizing nutrition of the dam and neonates.^{3,4}

Identifying at risk neonates

Table 1. An APGAR scoring system for routine assessment of newborn puppy viability and short-term survival prognosis⁵

Parameter	0 points	1 point	2 points
<i>Activity</i> , muscular tone	Flaccid	Moderate tone (flexion) in the extremities	Active movement, flexion
<i>Pulse</i> , cardiac rhythm	Absent to under 110/min	110-220/min	>220/min
<i>Grimace</i> , irritability reflex	Absent	Moderate movement	Responsive, easily irritable, vocalization
<i>Appearance</i> , mucous membrane color	Pallor, cyanosis	Moderate cyanosis	Pink
<i>Respiration</i> , respiratory pattern	Absent	Weak, irregular rhythm	>15/min, regular rhythmic

Table 2. Interpretation

Points	Stamina, Vitality
0-3	Weak
4-6	Average, moderate
7-10	Normal

Prompt identification of signs of neonatal distress can be extremely important for providing rapid treatment to less viable newborns. Time is certainly a critical factor and the earlier intervention is applied, the more effective and successful that intervention will be. The recent addition of a validated APGAR score system (above) for neonatal puppies aids in the identification of at risk neonates so that early intervention can be applied in an effort to reduce neonatal losses. The APGAR score system was originally devised in 1952 by Dr. Virginia Apgar as a simple and repeatable method to quickly assess the health of newborn children immediately after birth. It evaluates five criteria which are summarized using the acronym, APGAR (Appearance, Pulse, Grimace, Activity, and Respiration).⁵

It is also important to perform a complete physical examination on all newborns. Evaluation should include the oral cavity and mucous membranes which should be moist and bright pink to red/hyperemic from fetal hemoglobin. There should be no evidence of cleft palate with a strong suckle reflex present. The haircoat should be full and clean as missing hair on toes and muzzle may indicate prematurity and meconium staining indicates in utero distress. Evaluate the limbs, umbilicus, and urogenital structures for signs of congenital defects (i.e., patent urachus indicated by urine produced out of umbilicus).^{4,6} A normal neonate will squirm and vocalize when examined and then nurse and sleep quietly when returned to the dam.

In addition to the above, a low birth weight is a significant risk factor for neonatal puppy death. Birth weights of puppies are breed dependent. A puppy that is less than 15% of the average birth weight of littermates is at high risk. Puppies should gain about 5-10% of their birth weight per day so that they double their birth weight by approximately ten days. Puppies should also be approximately ten times their birth weight by six weeks of age. The cause of low birth weight or failure to thrive with poor growth is usually difficult to determine and may include factors such as prematurity, inborn errors of metabolism, congenital birth defects, infections, nutritional deficiencies, environmental stressors, and maternal neglect.^{2,7,8}

Neonatal and pediatric puppies are not little adults

Due to continued development following birth, there are significant differences in the physical findings of neonatal and pediatric puppies compared to adults. It is important to recognize these differences in both identifying normal from at risk puppies as well as in the plan for intervention, if needed.⁹

Respiratory rate in neonates is lower and more irregular than adults with the average of 10-18 breaths per minute. A respiratory reflex is present in the genital and umbilical area resulting in stimulation of respiration for the first three days after birth.⁶ In addition, respiratory control mechanisms in neonates are immature and surfactant production in the lungs is produced just prior to birth. This creates a high susceptibility to hypoxia (low oxygen) in the newborn, particularly those that are premature.

There are also significant differences with the cardiovascular system of the neonate. Neonatal bradycardia (low heart rate) is most commonly associated with hypothermia (low body temperature) and hypoxia (low oxygen often from poor respiration).^{4,8} This is a key factor to understand with intervention, making sure the neonate's body temperature and ventilation are addressed prior to administering medications to elevate heart rate. The cardiovascular system in the neonate is a lower pressure and volume system compared to adults. They have less peripheral vascular resistance and so are less able to react to environmental stressors. They also have a higher heart rate (160-200 beats/min) and cardiac output compared to adults. This elevated heart rate decreases as the puppy develops increased parasympathetic influences (vagal tone) at about four weeks of age. As a result, certain drugs such as atropine, isoproterenol, and dopamine have minimal effect on cardiac function until four to five weeks of age.¹⁰

Dehydration is always a major concern as newborns are extremely susceptible since they are composed of higher percentage (75%-80%) of water with a large body surface area compared to adults. In addition, immature kidneys have a limited ability to concentrate urine. As a result, water turnover is two to three times that of an adult. Unlike an adult, hydration status cannot be accurately assessed using skin turgor or tenting.¹¹ Estimates of the degree of dehydration must be determined by weight loss, dryness of the oral mucus membranes and eyes, as well urine specific gravity measurements (a rule of thumb that neonatal urine is a very pale yellow and the darker yellow it becomes, the more of a concern for dehydration).

Monitoring weight gain is a good indicator of health status. As mentioned above, on average, nursing puppies should double their weight in an average of ten days. In the first 24 hours following birth, it is not uncommon for puppies to not gain as rapidly or even maintain their birth weight while adjusting to life outside of the uterus. However, following the first 24 hours after birth, a normal puppy

should gain 5-10% of their body weight per day or the puppy should gain two grams per kilogram (kg) of the expected adult weight per day.¹² Puppies that do not gain after 24 hours of birth or lose weight at any time should be identified as neonates at risk since weight loss is generally one of the first signs of dehydration.

Thermoregulation is problematic in the neonate and a common cause for death. The shivering reflex and peripheral vasoconstriction responses are not fully developed until at least two to four weeks of age. Their relatively large body surface area and lack of insulating fat promotes rapid heat loss. They are very vulnerable to environmental stressors and rely on the ambient temperature, the dam's mothering instincts, and/or littermates for warmth. Environmental temperature exposure can be critical as a healthy newborn can only maintain a body temperature 12°F greater than that of the surrounding environment, and so the environmental temperature must be high enough to facilitate maintenance of a body temperature of at least 96-98°F.¹³ Hypothermia negatively impacts immunity, nursing, and digestion.¹⁴ The neonatal intestine slows in motility creating a dangerous ileus when body temperatures are below 96°F.¹⁵ Do not feed a cold puppy! An accurate rectal temperature in neonates requires a digital thermometer that reads to 95°F or lower. Humidity is also vital to prevent dehydration, especially at these high environmental temperatures. Generally, 55-65% humidity helps to prevent dehydration. Exogenous heat should be supplied as needed to prevent hypothermia. A note of caution with heating pads which run the risk of burning neonates incapable of moving away from excessively hot surfaces as well as variable heat, particularly with electric heating pads. Below is a chart of the recommended temperature adjacent to neonates.¹⁰ These are main considerations for orphaned pups. If the dam is present and has great maternal behavior be careful not to make the dam's environmental temperature too hot which may result in her discomfort or even neglect of the puppies thereby creating a serious problem. Please keep in mind that the recommended temperatures adjacent to neonates are often accomplished with a draft free whelping box in a comfortably warm room with a very attentive dam.

Table 3. Recommended environmental temperatures for neonates

Weeks of age	Normal rectal temperature of the newborn	Recommended environmental temperature immediately adjacent to neonate-major consideration if orphaned or hospitalized
First week	96-98°F	85-90°F
Second week	97-99°F	80°F
Third week	Low normal adult	75°F
Fourth week	Low normal adult	70-75°F
Fifth week	Low normal adult	70°F

Ninety to 95% of the neonate's passive maternal immunity is derived from colostrum ingestion within the first 24 hours of nursing.¹⁶ Incompletely developed immune systems during the first ten days of life make neonates vulnerable to systemic infection (most commonly bacterial and viral). Failure of passive transfer is a high risk for neonatal mortality. After 12-24 hours, the immunoglobulins are no longer absorbed through the intestinal tract. If failure of passive transfer is suspected, plasma or serum should be given, paying close attention to method of treatment as it should not be given by mouth 12-24 hours after birth and alternative route of administration must be utilized.¹⁷

The normal neonate will sleep quietly and suckle every two to four hours. While it has been shown that a healthy fasting puppy can potentially maintain adequate blood glucose for 12-24 hours through physiologic mechanisms (such as glycogenolysis and gluconeogenesis), this is often not the case with an at-risk neonate who has fewer reserves and is at high risk of hypoglycemia (low blood sugar) when they do not nurse for even short time frames (three to four hours). In addition, it is not recommended to fast pediatric puppies for long periods of time (more than six to eight hours) as their

physiologic mechanisms for glucose regulation are not completely matured compared to adults. Below is a chart with daily requirements for nutrition as well as fluids.⁶ Neonates should be able to take their daily requirements in five to six meals during the first weeks of life equating to feedings every two to four hours. During the first week of life, puppies can ingest 10-15% of their body weight in milk necessitating the potential for smaller more frequent feedings during this time frame. After the first week of life, they are able to ingest 20-25% of their body weight in milk allowing for a gradual increase in volume and time between feedings.⁴

Table 4. Daily nutritional and fluid requirements

Weeks of age	Canine neonatal caloric requirements	Fluids in mL/100 gram body weight per day
First week	133 Kcal/kg/day	18 mLs
Second week	155 Kcal/kg/day	13-22 mLs
Third week	175-198 Kcal/kg/day	13-22 mLs
Fourth week	220 Kcal/kg/day	13-22 mLs

The gastrointestinal tract is sterile at birth but is rapidly colonized by variety of bacteria from the dam and the environment. Neonates have altered intestinal permeability and higher gastric pH compared to adults. This creates different metabolism for oral therapies in neonates compared to adults. The soft, yellow brown meconium is passed within the first 48 hours. Then the normal neonatal feces are pasty yellowish to brownish tan, but they are usually not observed with a fastidious bitch. The stools should become formed at weaning. Overfeeding often produces a green or yellow watery stool; and white stools may be observed with lactose intolerance. Foamy bright yellow stools may be present with illness such as viral or bacterial diseases. Blood tinged stools may be seen in sepsis or with severe parasitism.⁷ Diagnostic testing can be performed on neonatal fecal samples after stimulation to defecate and will aid in the decision for the potential need for treatment.

Liver function is significantly decreased for the first four weeks which is related to the underdeveloped liver enzyme systems that are generally not equivalent to adult liver function until approximately six months of age. Due to immature liver metabolic functions, caution is advised in selection of drugs metabolized and/or excreted via the liver.⁶

While the numbers of functional nephrons in the kidneys are present at birth, physiological development, as measured by glomerular filtration rate and the ability to concentrate urine, is very immature until at least three weeks of age and not equaling adults until four to six months of age. In the neonate, the ano-genital reflex can be used to stimulate urination for collection and evaluation of urine. The normal specific gravity ranges from 1.006-1.017 (dilute and often very pale yellow in color) and is used to estimate hydration status and response to fluid therapy. Mild glucosuria and proteinuria is considered normal for up to six weeks of age.⁴

The central nervous system development is slow in the neonate. They sleep at least 90% of the time. Until four weeks of age, the majority of the sleep is deep, active sleep. Active sleep tones and strengthens those muscles necessary to allow the neonate to stand at approximately 14 days then walk by day 21. Active learning begins at three weeks followed by important socialization periods. Reflexes can be difficult to assess in the neonate because of variations in development and the technical difficulty associated with their small size. Puppies are born with a righting, withdrawal, and tactile anal and urinary reflexes. From birth to day three they demonstrate total flexor dominance but by day four extensor dominance predominates until three weeks of age. The suckling reflex is present until three weeks of age. The rooting reflex is present at birth. Cross extensor reflexes may be normally present at birth but should not be present after 14 days. Crossed extensor reflex after this time period is indicative of upper motor neuron pathology.^{10,18}

Neonates cannot voluntarily urinate or defecate. These functions are initially controlled by an ano-genital reflex associated with vigorous stimulation of the perineal area by the dam's tongue or a wet

swab. Although this reflex is present for up to 28 days in puppies, stimulation is only required for the first 18-21 days, thereafter the puppy is able to urinate and defecate on its own. Generally the eyelids open at ten to 14 days revealing a cloudy cornea which clears within 24 hours. For the first three weeks vision is poor. The corneal reflex is present as soon as the eyes open however the menace reflex is poor to absent for the first four to 12 weeks. Tear production begins when the eyelids open, which is an important consideration if there is a premature opening of the eyelids where lubrication will be needed to prevent eye trauma from dry eye and exposure. The true iris color is generally complete by approximately week eight (some breed variation noted). While the puppy can hear at birth, the external ear canals do not open until ten to 14 days at which time the startle response begins.¹⁹ The brain stem auditory response (BAER) is the best method of evaluating a puppy's hearing. Routine testing using this evaluation of specific breeds at risk for deafness is generally performed after six weeks of age.

Identification of those at risk and treatment considerations

The clinical approach to identifying disease in neonatal and pediatric puppies includes the need for collaborative efforts by the breeder, primary care veterinarian, and at times veterinary specialists. As with adults, the foundation is a thorough history and physical examination keeping in mind the physical and physiological differences of neonatal and pediatric puppies. Additional queries regarding littermates, relatives, and other animals in the environment will assist with the collection of genetic disease, infectious disease, toxin, nutritional, and other important data to be considered in the investigation of disease presentations. Diagnostic testing is generally required to further investigate the cause of illness in a diseased animal, and while there are some limitations as well as prioritization that may be needed due to the small size as well as physical differences in neonatal and pediatric puppies, many diagnostics can still be performed and are very beneficial in diagnosis of disease.²⁰ For example, routine tests such as a complete blood cell count, chemistry screen, and urinalysis may suggest specific hematologic or metabolic disorders, and they may help to rule out many acquired disorders. A general rule of thumb is to not exceed 1 mL of blood loss per 100 grams of body weight per week in neonates and pediatric patients. Radiology and other imaging techniques may reveal skeletal malformations, echocardiogram may reveal cardiac anomalies, and ophthalmologic examination may further define an inherited eye disease. Based on these findings, additional clinical function testing or evaluations for inborn errors of metabolism may be required for diagnosis.^{21,22} In the case of severe and life threatening illness, histopathology of a tissue biopsy or in some cases a necropsy evaluation from a deceased puppy may be required for a definitive diagnosis. The latter is particularly important when faced with a fading neonatal puppy as this may give information vital to surviving littermates as well as future planned matings; however this important diagnostic tool is all too often underutilized.

Drug therapy, including antibiotic therapy, should be used cautiously in neonatal and pediatric patients, taking into consideration the age, the drug properties, and the possible toxicities. For example, fluoroquinolones, such as enrofloxacin and ciprofloxacin, can result in cartilage defects in large breed, growing, puppies who are weight bearing. In consideration of drug properties, water soluble or lipid soluble properties of the drug are significant in the decision making process as neonatal and pediatric puppies have a higher body water composition and lower fat. As discussed above, neonatal and pediatric puppies also have reduced renal and hepatic clearance and lower total protein resulting in more available drug.⁴ A common indication for antibiotic therapy is in the prevention of sepsis from hypoxia-induced bacterial translocation, and so antibiotics are often one of the interventions considered in at-risk neonates. Interventions, particularly drug therapies, should only be performed at the instruction of the primary care veterinarian or veterinary specialist, as neonatal and pediatric puppies are more susceptible to side effects of these medications than are adults.

Summary

Neonatal and pediatric puppies are not "little" adults and the recognition of these differences is vital in addressing the identification, diagnosis, and management of at risk neonatal and pediatric puppies. Early identification and intervention is critical in an effort to reduce puppy mortality. Intervention

includes identifying at risk animals with the utilization of APGAR scoring mechanisms and physical examination, keeping in mind the important physical and physiological differences between neonatal and pediatric puppies compared with adults. Prevention focuses on pre-breeding health, optimal husbandry, managing labor and delivery, reducing infectious disease, and optimizing nutrition of both the dam and puppies. Diagnosis and treatment also needs to account for the physical and physiological differences present in neonatal and pediatric patients. The ultimate goal and secret for success is for breeders and veterinarians to work together in an effort to reduce these factors that contribute to neonatal and pediatric losses.

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