

CRITICAL CARE OF THE NEONATE

Justine A. Lee, DVM, DACVECC

University of Minnesota

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Neonatal critical care is markedly different from adult critical care due to physiologic considerations and hemodynamic parameters. One should be aware of the unique differences in neonatal versus adult medicine. In veterinary medicine, the term *pediatric* refers to animals < 6 months of age, while *neonatal* refers to animals aged 0-2 weeks.¹

Neonates requiring critical care are often debilitated from various disease processes. A brief review of infectious, metabolic, or environmental causes for fading puppy/kitten syndrome are listed below, but the reader is referred to a more detailed source for review of these infectious diseases. For the canine, diseases include: herpesvirus, distemper, parvovirus, brucella, rotavirus, toxoplasmosis, hepatozoan canis, bordatella, and mycoplasma/ureaplasma. For the feline, diseases such as rhinotracheitis, feline leukemia, panleukopenia, FIP, mycoplasma/ureaplasma, and bordatella may result in debilitation. Other ruleouts for fading puppy/kitty syndrome include congenital defects, thyroid dysfunction, thymic disorder, environmental conditions, poor mothering or malnutrition, low birth weight, undetected trauma, isoerythrolysis, taurine deficiency, parasitism, or bacterial causes such as E. coli, B hemolytic strep, or Pasturella.^{2,3}

Due to the significant physiologic considerations between adults and neonates, several aspects of neonatal critical care will be discussed including:

- physical examination findings,
- laboratory and radiographic data,
- fluid and drug therapy, and
- critical care and monitoring.

Physical examination findings

The initial approach to medical workup of the neonate should include a thorough ***physical examination***. One must be aware of the specific physical examination signs to look for at particular ages. A strong suckle reflex and rooting behavior (the ability to move the head in search for milk) should be present shortly after birth.⁴ Neonates will also nurse and sleep constantly for the first 2-3 weeks of life.⁴ In order to assess the responsiveness and strength in neonates, one must monitor the suckle response, the ability of the neonate to right themselves when placed on their back, and the rooting response (when the neonate pushes its muzzle into circled fingers and pushes forward strongly).⁴ In addition, evidence of adequate muscling and weight gain should be monitored. Kittens should gain 7-10 g/day, while puppies should gain 1 g/lb of anticipated adult weight/day.⁵ Signs of constant crying, failure to gain weight, and reluctance to nurse are signs of inadequate intake, and alternate feeding methods should be implemented (via the use of tube or bottle feeding).

The physical examination should be done systematically, as in adults. However, unique congenital abnormalities or signs of underlying disease processes should be identified in

neonates, such as umbilical hernias, cleft palates, umbilical infections, open fontanelles, patent urogenital openings, heart murmurs, abnormal auscultation, and nasal or ocular discharge.⁴ It is important to note the normal neonatal parameters, including a resting heart rate of 180-200 beats per minute, a respiratory rate of 25-35 breaths per minute, and a temperature range from 96° to 97°F. Neonatal temperature should increase to 100°F by 4 weeks of age.⁶ Normal physiologic parameters also include the following:

Eyes open	12-14 days
Normal vision	21-28 days
Menace reflex	2-3 months
Withdrawal reflex	7-19 days
Testes descended	4-6 weeks
Pain reflex	at birth
Flexor tone	1-4 days
Extensor tone	5-8 days
Ambulation	16 days

In unstable neonates, initial therapy should include minimal stress, oxygen therapy, and focused/limited physical examination. The cardiopulmonary system should be assessed first. The patient should be in sternal recumbency and have supplemental oxygen during examination. Ideally, a pediatric stethoscope should be used. Observation of the respiratory pattern, rate, effort, and lung sounds should be evaluated. Because respiratory auscultation is more subtle in neonates versus adults, thorough evaluation should be performed in a quiet room. Mucous membrane color and pulse quality will also yield information about the perfusion of the patient. The remaining physical examination should be completed once the patient is more stable.

Laboratory and radiographic data

Neonatal **diagnostic tests** such as complete blood counts, chemistry findings, coagulation tests, and urinalyses also vary from adult parameters. In neonatal puppies, the packed cell volume (PCV) decreases by 1/3; typically, the PCV is 47% at birth but drops to approximately 29% at 28 days.⁷ This is due to a change from the neonatal hypoxic environment to one rich in oxygen and due to lack of iron consumption.⁷ In addition, mean white blood cell count (WBC) is elevated at 12,000 cells/mm³; this may be due to increased lymphocytes and eosinophils (due to increased antibody formation and parasite load, respectively). In neonatal kittens, the PCV is approximately 35% at birth and nadirs to 27% at 28 days.⁸ At birth, the WBC is approximately 9,600 cells/mm³ and increases to 23,000 cells/mm³ at 8 weeks.⁸ The lymphocyte count has been reported at 10,170 cells/mm³ at 8 weeks; this decreases to 8700 cells/mm³ at 16 weeks.⁸ Finally, the eosinophil count has been reported at 2280 cells/mm³ at 8 weeks and drops to 1000 cells/mm³ at 16 weeks.⁸

Chemistry changes seen in neonates include increased alkaline phosphatase and glutamyltransferase (from bone growth), along with increased bilirubin, calcium, and phosphorous.⁹ In addition, neonates have decreased total protein from an immature immune system. Globulin values increase almost linearly with age due to antigenic stimulation.⁹ Glucose, BUN, and cholesterol are also lower than adult animals due to decreased hepatic synthesis.^{4,9} Finally, due to a decrease in glomerular filtration rate (GFR), urine is isosthenuric

until approximately 9-10 weeks of age.^{1,10} Nephrogenesis is incomplete at birth, and tubular maturation occurs later than glomerular maturation.^{11,12}

Clotting tests are also prolonged in neonates. Prothrombin time has been reported to be 1.3X the adult value in puppies on day 1; however, this normalizes to 0.9 by day 7.¹³ Partial thromboplastin time is 1.8X the adult value on day 1; this decreases to 1.6X by day 7.¹³ Finally, antithrombin is decreased at birth, but increases to normal adult levels by day 7.¹³ Current recommendations include treatment with vitamin K with a one time dose of 0.5-2.5 mg/kg (puppies)¹⁴ or 0.01 to 0.1 mg/kg (kittens)¹⁵ subcutaneously once during neonatal days 1-4.

Finally, **radiographic** medicine is unique to neonatal medicine. Due to their small size, the use of fine screen radiographs should be implemented. Neonatal radiographs will also show the thymus sail sign, and their pulmonary interstitium may appear more opaque due to an increased water content of interstitial lung parenchyma.¹⁶ In addition, there will be absence of costochondral mineralization, presence of open growth plates, loss of abdominal detail, and scant abdominal effusion.⁴

Fluid and drug therapy

Fluid requirements in neonates are dramatically increased, with total body water ranging from 60-180 ml/kg/day. This is due to an increased extracellular fluid (ECF) requirement, a higher body surface area, a greater surface area:body weight ratio, lack of body fat, a higher metabolic rate, a decreased ability of immature kidneys to concentrate urine, and finally, an increased respiratory rate leading to greater insensible fluid losses.¹⁷ One of the most common causes of neonatal hypovolemic shock is dehydration, which can occur quickly in these small patients. Due to gastrointestinal losses, higher fluid requirements, or the inability to nurse, these patients can quickly dehydrate.

Fluid therapy can be replaced by oral, subcutaneous (SC), intraperitoneal (IP), intravenous (IV), or intraosseous (IO) routes. In stable patients that are still nursing and minimally dehydrated, the use of a 5 French or 8 French pre-measured infant feeding tube can be used. It is imperative to measure from the tip of the nose to the last rib. While gag reflex is not present until 10 days of age,² passage down the left side of the mouth will allow for easy feeding of milk replacer, oral dextrose, or water. After delivery of fluid, kink the tube prior to withdrawal to prevent aspiration pneumonia. Normal stomach volume is approximately 50-80 ml/kg.² Subcutaneous and intraperitoneal warmed fluids can also be used in neonates that are minimally dehydrated and still nursing. These fluids should not contain dextrose. Oral, SC, or IP fluids should only be given when the neonate is normothermic and should not be used in hypovolemic, shocky patients.

Intravenous access may be difficult to obtain in neonates. Peripheral venous access with a 22 to 24 gauge catheter may be attempted; otherwise, jugular catheter placement may be necessary (providing there are no contraindications, such as head trauma). In the event that central or peripheral venous access is not available, use of an intraosseous catheter may be used for fluid therapy. An 18 to 22 gauge spinal needle or hypodermic needle can be placed in the head of the tibial crest, tibial tuberosity, wing of ilium, trochanteric fossa of the femur, or the greater tubercle of the humerus.

In severely dehydrated or hypovolemic patients, initial shock doses of a balanced crystalloid such as 30-45 ml/kg (canine) or 20-30 ml/kg (feline) should be used. Serial physical examination should be done after the bolus to reassess response and to evaluate the need for further fluid resuscitation. Maintenance fluid rates of 80 ml/kg/day, in addition to adjusting for ongoing losses, should be implemented. Dextrose supplementation (as a 2.5% or 5% constant rate infusion) should be considered in neonates, although blood glucose should still be monitored several times a day.

Drug pharmacokinetics are unique to neonates, and appropriate pharmacologic treatment is necessary due to neonatal absorption, distribution, metabolism, and elimination. This is due to changes in surface area:body weight ratio, decreased body fat, decreased total protein (TP) and albumin (protein binding), reduced renal excretion, decreased GFR and renal blood flow, decreased functioning hepatic enzyme systems (oxidation and glucuronidation), and disruption of the intestinal flora.⁴ Current recommendations are to decrease the total drug dose by 30-50% or to increase the interval by 2-4 hours. Specific antibiotic therapy will be discussed later.

Critical care and monitoring

Unfortunately, monitoring physiologic parameters in neonates is difficult to do due to several factors. Because of increased water content and decreased fat content in the skin, skin turgor is not an accurate measurement of hydration status. Due to immaturity of the autonomic nervous system, heart rate and urine specific gravity cannot be used to reliably assess dehydration. Rather, fluid resuscitation should be monitored and based on serial physical examination, weight gain, improved auscultation of the heart and lungs, chest radiographs, blood glucose, lactate, extremity temperature, mentation, serial PCV/TS, urine output (UOP), and central venous pressure (CVP) measurement. To monitor adequate UOP, or in the event of urethral obstruction, a 3.5 to 5 French red rubber catheter can be used as a urinary collection setup.

There are unique monitoring differences between neonates and adults. Mean arterial pressure is approximately 49 mmHg in neonates. This decrease is hypothesized as being due to immaturity of the muscular component of the arterial wall at birth.¹ In addition, CVP is higher in neonates at 8 cmH₂O.¹⁸ This is 75% higher in comparison to adults, and may be due to low venous compliance and increased plasma volume.¹⁸

Goals

Goals of neonatal medicine include temperature control, fluid therapy, nutrition (with the goal of weight gain), stimulation of urination and defecation, and parasite control. However, in the more critically ill neonate, and due to a neonates' ability to quickly decompensate, our goals should be focused on the following 4H's:²

- Hypothermia
- Hypoglycemia
- Hypovolemia
- Hypoxemia

Hypothermia

Treatment of hypothermia includes careful temperature regulation and awareness of normal homeostatic temperatures in neonates. Human neonatal incubators, heat lamps, circulating hot water blankets, hot water bottles, and warm towels can all be used to increase the ambient environmental temperature (preferable an ambient temperature of 90°F with 55-65% humidity).² It is imperative to prevent any overheating and to be aware of any potentially burning that may occur. One must provide the neonate room to crawl away from the heat source. In addition, as is recommended with hypovolemic, hypothermic adults, hypothermic neonates should be warmed slowly over 1-3 hours to prevent heat stress and dehydration. By rapidly warming a patient, peripheral vasodilation may occur, resulting in core body temperature shock, as a result of decreased circulating volume to the core.

Hypoglycemia

Neonates are prone to hypoglycemia due to inefficient hepatic gluconeogenesis, decreased glycogen stores, and an immature glucose feedback mechanism.¹ Anorexia, vomiting, diarrhea, dehydration, and infection may all result in neonatal hypoglycemia. Because the neonatal brain and heart are dependent on glucose and carbohydrate metabolism (respectively) for energy, permanent brain injury may result from hypoglycemia.^{1,19} This differs from adults, as the myocardium depends on long-chain fatty acids as a substrate.²⁰ Because neonates have inefficient counterregulatory hormonal regulation (epinephrine, glucagon, growth hormone, and cortisol), these hormones will not be released in response to hypoglycemia.¹

Early signs of hypoglycemia may include lethargy, decreased suckle, crying, and a limp body, and should be treated immediately. The use of Karo syrup has not been shown to provide an immediate beneficial response,²¹ and intravenous dextrose boluses should be used (1/4-1/2 g/kg IV of 50% dextrose, diluted 1:1-1:2) instead. Isotonic fluids supplemented with 2.5-5% dextrose can also be used; however, caution should be used to prevent over-supplementation as prolonged hyperglycemic can result in worsening of dehydration via osmotic diuresis (which is contributed from puppies having insulin insensitivity).²²

Hypovolemia

In the adult, compensatory mechanisms in response to hypovolemia include activation of the renin-angiotensin system and the sympathetic nervous system. Tachycardia, increased ADH release, vasoconstriction, and decreased urine output are clinically seen in response to hypovolemia in an attempt to maintain cardiac output. In the neonate, cardiac output (heart rate X stroke volume) cannot be increased by increasing contractility, as only 30% of fetal cardiac muscle is made up of contractile elements.^{1,23} Puppies also appear to have less sympathetic nerve fibers supplying the myocardium than adults.²⁴ As a result, tachycardia in response to hypovolemia may not occur.¹

Because these compensatory mechanisms are not fully developed, our clinical evaluation of the neonate may be more difficult to assess. For example, young puppies have decreased autoregulation of renal blood flow in response to changes in arterial blood pressure or shock.²⁴ Concentration and dilution of urine in response to changes in ECF is limited in neonates, but does increase with age.²⁴ In addition, as previously discussed, neonates have lower levels of BUN and creatinine during the neonatal phase.^{1,4} This, in addition to inefficient countercurrent

mechanisms and short loops of Henle, along with inefficient sodium reabsorption in the thick ascending limb of the loop of Henle, contribute to the inefficiency of urine concentration.²⁵ Hence, prerenal azotemia and concentrated urine specific gravity may not be present in neonates despite profound dehydration.¹

Please see the above notes for fluid therapy and resuscitation.

Hypoxemia

In newborns, lung expansion is essential for release of both surfactant and prostacyclin, which increases pulmonary blood flow and pulmonary vasodilation.¹ In addition, nitric oxide synthesis is probably induced by fetal oxygenation and may also contribute to pulmonary vasodilation.¹ As a result, there is less pulmonary vascular resistance at birth, resulting in closure of the patent ductus arteriosus.

Neonates exhibiting clinical signs of hypoxemia (including cyanosis, orthopnea, tachypnea, dyspnea, and abnormal auscultation) should be immediately treated with oxygen therapy. Respiratory distress may be due to decreased surfactant levels, congenital defects resulting in pulmonary hypertension, meconium aspiration, pneumonia, etc.¹ Respiratory depression may also result due to sedatives or anesthetics involved in Cesarean section; this can often be reversed with drugs (naloxone, flumazenil, or doxapram). Initial first line therapy should include oxygen therapy via face mask, oxygen cage, incubator, face mask, or endotracheal tube. The fraction of inspired oxygen (FiO₂) should not exceed 40-60%, as oxygen toxicity in the form of acute respiratory distress syndrome (ARDS) or retrolental fibroplasias (resulting in blindness) may result.²⁶ If higher levels of oxygen are necessary to relieve signs of respiratory distress, the use of positive pressure ventilation (PPV) with positive end-expiratory pressure (PEEP) can be implemented.

Antibiotic therapy

When using antibiotic therapy in neonates, several antibiotics are contraindicated. Chloramphenicol should never be used in kittens due to hematopoietic effects. Some resources recommend chloramphenicol in severely ill puppies; however, we caution its use in neonatal medicine. In addition, gentocin should be cautiously used in neonates, due to decreased renal blood flow and decreased GFR. It should be used cautiously in hydrated patients who are undergoing fluid therapy. Tetracyclines are not currently recommended due to skeletal retardation and discoloration of deciduous teeth. Finally, quinolones have been shown to result in cartilage lesions in puppies. Currently recommended antibiotic therapy include the following:

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|---------------------------------|------------------------|
| ■ Amoxicillin | 6-20 mg/kg BID PO |
| ■ Amoxicillin + clavulanic acid | 12.5-25 mg/kg BID PO |
| ■ Cephalexin/Cefazolin | 10-30 mg/kg BID-TID PO |
| ■ Ampicillin | 22 mg/kg TID IV |

Necropsy

Finally, if in the event of a death of a neonate, necropsy is often the most useful diagnostic measure. Carcasses should be refrigerated, not frozen, and should be shipped overnight. Virus

isolation and bacterial culture can be performed to rule out infectious disease that would compromise the litter.

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