Pediatric Critical Care

Part 2—Monitoring & Treatment

Justine A. Lee, DVM, DACVECC, DABT
Saint Paul, Minnesota, VETgirl

Leah A. Cohn, DVM, PhD, DACVIM (SAIM)
University of Missouri

Not only does the diagnostic evaluation of neonatal and pediatric patients differ from that in adults, but appropriate treatment and monitoring are also quite specific for critically ill neonates. While their small size and unique physiology present challenges, we have the ability to treat these young animals aggressively. Veterinary professionals must be cognizant of the unique qualities of pediatric patients with regard to monitoring and treatment. Knowledge of normal physiologic parameters for neonates is imperative (**Table 1**, next page).

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Goals of Neonatal Critical Care

Components of neonatal critical care medicine include temperature control, fluid therapy, nutritional support (with the aim of weight gain), stimulation of urination and defecation, and control of infectious disease. However, in the more critically ill neonatal or pediatric patient, goals should be focused on the following four H's, as these patients can quickly decompensate:

- Hypovolemia/hydration
- Hypothermia
- Hypoglycemia
- Hypoxemia

Hypovolemia

In adult animals, compensatory mechanisms in response to hypovolemia include activation of the renin-angiotensin-aldosterone system and the sympathetic nervous system. In a healthy adult, tachycardia, increased antidiuretic hormone release, vasoconstriction, and decreased urine output are observed in response to hypovolemia in an attempt to maintain cardiac output (*cardiac output = heart rate × stroke volume*).

In contrast, in the neonate, cardiac output cannot be increased by increasing cardiac contractility, as only 30% of fetal cardiac muscle is made up of contractile elements.[1,2] Puppies also appear to have fewer sympathetic nerve fibers supplying the myocardium than adults.[3] As a result, tachycardia in response to hypovolemia may not occur.

Because these compensatory mechanisms are not fully developed, clinical evaluation of the neonate may be more difficult. For example, autoregulation of renal blood flow is decreased in young puppies in response to changes in arterial blood pressure or hypovolemia. Concentration and dilution of urine in response to changes in

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extracellular fluid are limited in neonates but do increase with age. Neonates have immature kidneys, a lower glomerular filtration rate, lower blood urea nitrogen concentrations, inefficient countercurrent mechanisms and short loops of Henle, and inefficient sodium reabsorption in the thick ascending limb of the loop of Henle, all of which contribute to the inefficiency of urine concentration.[4]

Table 1. Normal Physiologic Parameters for Neonates[7,11,19]

Parameter	*Value*
Birth weight	Dogs: Varies with breed; most range from 100–650 g Cats: 90–110 g
Rectal temperature	Newborn: 96.8°F–98.6°F (36°C–37°C) 1 month: 100°F (38°C)
Heart rate	>180–200 bpm
Respiratory rate	Neonate: 10–18 bpm 1 week: 15–35 bpm
Urine specific gravity	<1.020
Water requirement	Output: 2.5 mL/100g BW/day
Caloric requirement	Dogs: 20–26 kcal/100 g BW/day Cats: 15–25 kcal/100 g BW/day
Stomach capacity	4–5 mL/100 g BW

BW = body weight

Hydration

Fluid requirements in neonates are dramatically higher than in adults. This is a result of the neonate's increased extracellular fluid requirement, higher body surface area, greater surface area:body weight ratio, lack of body fat, higher metabolic rate, decreased ability of immature kidneys to concentrate urine, and increased respiratory rate leading to greater insensible fluid losses. One of the most common causes of neonatal hypovolemic shock is dehydration, which can occur quickly from GI losses, higher fluid requirements, or the inability to nurse. For neonates, maintenance fluid requirements are 120–180 mL/kg/day, while for pediatric patients they range from 80–120 mL/kg/day.[5,6]

For normothermic, minimally dehydrated neonates that are still nursing, oral–gastric fluid replacement is best. A 5- or 8-French premeasured red rubber feeding tube can be used. Measurement should be made from the tip of the nose to the last rib and the tube marked accordingly. Although the gag reflex is not present until 10 days of age, passage of the tube down the left side of the mouth allows for easy feeding of milk replacer, oral dextrose, or water. After fluid delivery but before tube withdrawal, the tube should be kinked to prevent aspiration.

Normal stomach volume is approximately 50 mL/kg,[5,7] and overfeeding must be avoided. The fluid should be warmed to near body temperature and administered over a few minutes. Owners can be taught how to tube feed if the neonate has a weak suckle reflex or if nursing is discontinued or contraindicated (eg, rejection, eclampsia). For the first weeks of life, feeding every 2–4 hours is ideal. Feeding is contraindicated in hypothermic patients until they have been re-warmed.

Fluid can also be replaced by SC, IP, IV, or IO routes.[6,8,9] In minimally dehydrated patients that are still nursing, SC and IP warmed fluids are adequate. To help prevent infection, abscess formation, or inappropriate osmotic shifts, fluids given by these routes should not contain dextrose. Only warm isotonic crystalloids such as Normosol-R (hospira.com), lactated Ringer's solution (LRS), or 0.9% NaCl should be used SC or IP; note that before 6 weeks of age, the lactate in LRS may not be metabolized effectively to bicarbonate.[8] PO, SC, or IP fluids should only be given when the neonate is normothermic; they should not be used in hypovolemic, shocky patients because of the very slow absorption. When giving IP fluids, aseptic technique is of utmost importance. Repeated doses of IP fluids are not recommended (ie, because of increased risk for septic peritonitis).

IV access may be difficult to obtain in neonates. Peripheral venous access with a 22- to 24-gauge catheter may be attempted. Often, placement of a small cephalic catheter in the jugular vein is necessary, provided there are no contraindications (eg, coagulopathy, thrombocytopenia). Both IV and IO catheters may be flushed to maintain patency when not in constant use. Catheters should be flushed with 0.9% saline; the use of heparinized flushes is not necessary and can result in accidental excessive heparin administration.[10]

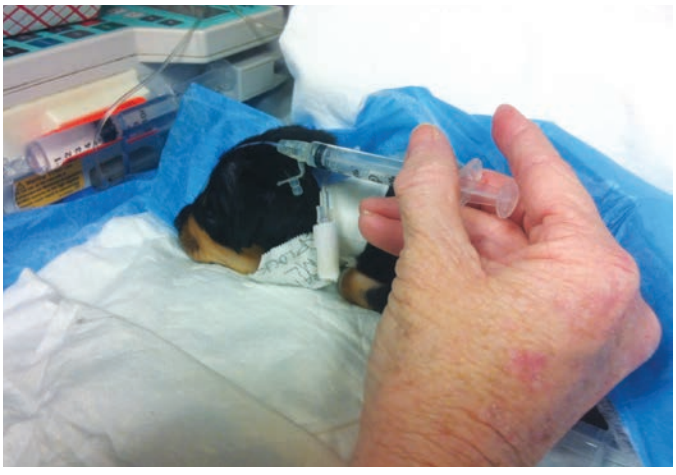
In the event that central or peripheral venous access is not available, use of an IO catheter may be necessary for fluid therapy.

COP = colloid osmotic pressure, LRS = lactated Ringer's solution

An 18- to 22-gauge spinal or hypodermic needle can be placed in the head of the tibial crest, tibial tuberosity, wing of ileum, trochanteric fossa of the femur, or greater tubercle of the humerus.[8,9] Aseptic technique should be used when placing IO catheters. Most drugs, fluids, and even blood products that are typically delivered by the IV route can be delivered through an IO catheter. Although the IO catheter can be lifesaving, it can be difficult to wrap and protect and, rarely, can result in fractures or infection.

In severely dehydrated or hypovolemic patients, initial shock doses of a balanced crystalloid should be used (ie, 30–45 mL/kg for dogs, 20–30 mL/kg for cats). Serial examinations should be done after the bolus to reassess response and evaluate the need for further fluid resuscitation. Maintenance fluid rates of 80 (pediatric) to 180 (neonatal) mL/kg q24h should be implemented depending on the age of the patient, in addition to adjusting for ongoing losses (eg, vomiting, diarrhea).[6] Dextrose supplementation should be implemented quickly in hypoglycemic neonates (eg, 0.5–1.5 mL/kg of 50% dextrose, diluted 1:3, followed by a 2.5%–5% CRI in IV fluids).

Although pediatric pups and kittens are more like adults in terms of vital parameters and renal function, they still have increased maintenance water requirements compared with adults.[6] These slightly older pups and kittens may require fluid therapy as a result of disease associated with ongoing losses (eg, vomiting, diarrhea). Potassium supplementation typically is required, and careful monitoring of blood glucose and electrolytes is warranted. Although colloids can be used, puppies and kittens normally have a lower colloid osmotic pressure (COP) than adults. If necessary, a colloid (eg, hetastarch, 1 mL/kg/h) or plasma can be used to keep COP above 15 mm Hg.[6]



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Hypothermia

In neonates, careful temperature regulation and awareness of normal homeostatic temperatures are imperative. Normal rectal temperature is 96°F ± 1.5°F (35.6°C ± 0.7°C) in the first week of life and 98.6°F–100°F (37°C–37.8°C) in the second and third weeks of life; temperature should approximate that of a normal adult by 7 weeks of age.[11]

While neonates are normally hypothermic compared with adults, they are also likely to decompensate quickly and become severely hypothermic. Hypothermia can lead to bradycardia and intestinal ileus.[6] Human neonatal incubators, heat lamps, circulating hot water blankets, hot water bottles, and warm towels can all be used to increase the environmental temperature, with the ideal ambient temperature for neonates being 90°F with 55%–65% humidity.[9,11]

To prevent overheating and possible thermal injury, neonates should be given room to crawl away from the heat source. In addition, as is recommended for hypovolemic, hypothermic adults, hypothermic neonates should be warmed *slowly* over 1–3 hours to prevent heat stress and dehydration. Rapid warming of a patient may cause peripheral vasodilation, resulting in core body temperature shock as a result of decreased circulating volume to the core (see **Watch Out for Overheating**, next page).

Hypoglycemia

Neonates are prone to hypoglycemia from inefficient hepatic gluconeogenesis, decreased glycogen stores, and an immature glucose feedback mechanism. Anorexia, vomiting, diarrhea, dehydration, and infection may all result in neonatal hypoglycemia. Whereas the adult depends on long-chain fatty acids as a substrate for the myocardium, the neonate depends on glucose

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Watch Out for Overheating

One of the most common errors in the emergency room is to overheat neonatal patients. They are put on heating pads with aggressive heat support (eg, BAIR huggers), only to find that their temperature shoots up to 103°F (39.4°C). As the normal temperature in a neonate (until 2 weeks of age) is 96°F (35.6°C), *this is equivalent to overheating an adult dog to 107°F (41.7°C).* Clinically, neonatal patients can quickly deteriorate when overheating occurs (eg, crying, dehydrated, panting, shock).

and carbohydrate metabolism for energy to the brain and heart, respectively. Persistent or recurrent hypoglycemia in the neonate can potentially result in permanent brain injury.[12] Because neonates have inefficient counterregulatory hormonal regulation (eg, epinephrine, glucagon, growth hormone, and cortisol), these hormones will not be released in response to hypoglycemia.

Early signs of hypoglycemia, which may include lethargy, decreased suckle, crying, and a limp body, should be treated immediately. The use of corn syrup has not been shown to provide an immediate beneficial response in adult humans,[13] but it may have some benefit in neonates. It also provides an emergency treatment option for clients at home. IV dextrose boluses (0.5–1.5 mL/kg IV of 50% dextrose diluted 1:1–1:2, or 2–4 mL/kg of a 10% dextrose solution) are preferred over PO dextrose.[6,9] Isotonic fluids supplemented with 2.5%–5% dextrose as a CRI can also be used; however, caution should be used to prevent over-supplementation, as prolonged hyperglycemia can result in worsening dehydration via osmotic diuresis.

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Hypoxemia

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

Neonates exhibiting clinical signs of hypoxemia (eg, cyanosis, orthopnea, tachypnea, dyspnea, abnormal auscultation) should be treated immediately with oxygen therapy. Because neonates are normally anemic, it may be clinically more difficult to see cyanosis, as detection of cyanosis depends on hemoglobin concentration. Respiratory distress may be a result of decreased surfactant levels, congenital defects resulting in pulmonary hypertension, meconium aspiration, bacterial or viral pneumonia, and other conditions. Respiratory depression may also result from use of sedatives or anesthetics during Cesarean section, but this can be reversed with specific agents (eg, naloxone, flumazenil, doxapram).

Initial therapy should include oxygen supplementation via facemask, oxygen cage, incubator, or endotracheal tube. The fraction of inspired oxygen should not exceed 40%–60%, as oxygen toxicity in the form of acute respiratory distress syndrome or retrolental fibroplasia (resulting in blindness) may result from longer exposures.[14] If higher levels of oxygen are necessary to relieve signs of respiratory distress, the use of positive-pressure ventilation with positive end-expiratory pressure can be implemented; because of the neonate's small size, however, this may be technically challenging.

Immunity

Early immunologic protection is provided by maternal antibody delivered via colostrum suckled during the first hours of life.[15,16] Pups and kittens that fail to nurse colostrum are at significant risk for early infection. The SC administration of serum from the mother or some other healthy, well-vaccinated cat or dog can, in part, make up for a lack of colostrum.[17,18] The general empirical dose for kittens is 15 mL of serum, dosed as 5-mL SC boluses at birth, at 12 hours, and at 24 hours.[17] In puppies, the empirical dose is 22 mL/kg of pooled adult serum; this can be given as split boluses similar to kittens or as one large dose.[18,19]

In kittens, neonatal isoerythrolysis is an important cause of early death but can be avoided with awareness. Queens with type B blood have strong alloantibodies against type A and AB

blood, even if they have never queened before. Type B blood is rare in most domestic cats in the United States but is more common on the West Coast and much more common in certain breeds (eg, British shorthair, Devon rex, Persian, Abyssinian, Turkish angora, Turkish van).[20] If a type B queen is mated with a type A or AB tom, kittens born with those blood types may develop intra- and extravascular hemolysis upon nursing colostrum containing the antibodies. By avoiding such matings, or holding kittens off the queen for the first 24 hours of life (to prevent colostrum ingestion), isoerythrolysis can be prevented.[20] Signs of neonatal isoerythrolysis include weakness, tachypnea, tachycardia, icterus, tail tip necrosis (from thrombus and autoagglutination), anemia, hemoglobinuria, and sudden death.

Even though the immune system is not fully mature until 3–6 months of age, dogs and cats become immune competent (ie, able to respond to vaccinations) by 6–12 weeks of age.[21] Vaccinations are often not effective, however, in the face of maternal antibody to a given antigen. Maternal antibodies usually wane for most vaccinal antigens between 8 and 16 weeks of age; because there is no way to predict the exact age for any particular individual, a repeated series of vaccinations is administered during this age window. During this period, pups and kittens are particularly susceptible to viral infections (eg, distemper, parvovirus, panleukopenia virus) when maternal antibody has waned but vaccine-induced antibody has not yet been stimulated. Fortunately, new vaccine technologies have allowed development of several vaccines that can stimulate immunity even before maternal antibodies have waned.[21]

Drug Pharmacokinetics & Antibiotic Therapy

Drug pharmacokinetics are unique in neonates, and appropriate pharmacologic adjustments are necessary because of neonatal absorption, distribution, metabolism, and elimination.[22,23] Drug clearance does not generally reach adult capacity until about 12 weeks of age, in part because of differences in renal function and hepatic enzyme systems (ie, oxidation and glucuronidation) at various ages.[22] Because hepatic metabolism is decreased, plasma clearance is decreased, plasma half-life of drugs is increased, and high plasma compound concentrations can result.[24]

Drug absorption is altered in neonates, and may be either higher or lower than in mature animals or even older pups or kittens.[22] The most dramatic differences between neonates and older animals are related to drug distribution, which is influenced by body fluid content and compartmentalization as well as binding to serum proteins.[22] While the tendency might be to automatically reduce the dose of drug compared with a more mature animal, often an *increased* dose is required. Water-soluble drugs are distributed into a larger relative volume in neonates, resulting in lower plasma drug concentrations; therefore, higher doses are often required compared with mature animals. That said, neonates also have a more permeable blood–brain barrier; therefore, certain drugs (eg, morphine, pentobarbital) may have up to 6 times CNS permeability.[22,23]

Disposition of a number of antimicrobial agents in neonates has been reviewed (**Table 2**).[25] In general, the β-lactam antimicrobials are often the best choice. Several antibiotics are contraindicated in neonates or juvenile animals.[22,23] Chloramphenicol should never be used in kittens because of potential hematopoietic adverse effects; it should be used with caution in pups.[22,23] Aminoglycosides should be used cautiously in neonates (because of decreased renal blood flow and glomerular filtration rate), and they should be used only in well-hydrated patients. Amikacin is a safer choice than gentamicin if this class of drugs is used.[22]

Tetracyclines are not currently recommended because of the risk for skeletal retardation and discoloration of deciduous teeth (doxycycline does not have the same effects as many other tetracycline formulations).[22] Drugs that undergo enterohepatic recirculation (eg, clindamycin, tetracycline, macrolides) should be avoided to reduce disruption of colonization of the alimentary tract with healthy gut flora.[22] Metronidazole is used for treatment of *Giardia* spp infections and anaerobic infections, but the dose interval should be prolonged and this drug should be

Table 2. Commonly Recommended Drug Dosages in Neonates[9,23,26]

Drug	*Dosage*
Amoxicillin	6–22 mg/kg PO q12h
Amoxicillin + clavulanic acid	12.5–25 mg/kg PO q12h
Cephalexin/cefazolin	10–30 mg/kg PO q8–12h; IV, IM, SC or IO for cefazolin
Ceftiofur	2.5 mg/kg SC q12h
Ampicillin	22 mg/kg IV q8h
Ampicillin/sulbactam	22 mg/kg IV q8h
Trimethoprim/ sulfamethoxazole	30 mg/kg q24h PO only

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avoided altogether before 2 weeks of age because of increased risk for neurotoxicity.[22,26]

Finally, quinolones have been shown to result in cartilage lesions in puppies and should be used only when the benefit outweighs the risk and ideally avoided altogether in growing, large-breed dogs.[27] β-lactam antibiotics are considered the antimicrobial of choice whenever possible, usually at a higher dose but with a bit of a prolonged dose interval as compared with adults.[22]

IM routes should be avoided in neonates because of variable absorption secondary to small muscle size and reduced vascularity.[23] SC administration of drugs gives variable absorption rates because of lack of fat as a percentage of body weight.[23] Other drugs to avoid in neonates include NSAIDs, ivermectin, and long-acting glucocorticoids.[26]

Necropsy

In the event of death, necropsy is often the most useful diagnostic measure to protect other animals in the litter (or even future litters). Carcasses should be refrigerated, not frozen, and should be shipped overnight if sent to a pathologist (ideal). If the veterinarian treating the neonate performs the necropsy, samples should be saved for bacterial culture and viral isolation/polymerase chain reaction in addition to samples fixed for histopathology.

Conclusion

Knowledge of normal physiologic parameters, along with appropriate monitoring and treatment of neonatal and pediatric patients is imperative. Despite their tiny size, critically ill puppies and kittens can be treated successfully, allowing them to go on to have a full life. ■ cb

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