NeoCare
Néonatologie des Carnivores
Reproduction et Elevage

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INVITATION

Hungarian Small Animal Veterinary Association (HSAVA),

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NEONATAL MORTALITY: CAUSES AND DIAGNOSIS

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Stillbirth (birth of an already dead newborn) and neonatal mortality (i.e. death of a puppy or a kitten within the first 21 days of life), affect around 15% of newborn kittens and puppies, with a large majority of deaths (≈75%) occurring within the first week of life. Nevertheless, identification of causes and predisposing factors allow to take corrective actions, saving lives of littermates and of newborns from litters to come.

PREDISPOSING FACTORS

- Dystocia, long labor. Even if born alive, such newborns, having suffered from hypoxia, are at increased risk of mortality within the first 2-3 days of life. Whelpings during more than 5 hours are associated with increased neonatal mortality rate.
- Primiparous bitches, bitches less than 1-year-old (less obvious in queens)
- Litter size: either very small (from 1 to 3 puppies) in dogs; or conversely large litters (> 8 kittens in queens; >10 puppies in bitches, even if it is difficult to set a precise threshold in this species due to large interbreed differences in prolificacy)
- Low birth weight, consequence of intra uterine growth retardation. Puppies and kittens born among the 25% the lightest individuals of their breed are at increased risk of neonatal mortality and those below the lowest decile (10% lightest) are critical.
- Heterogeneity of birth weight within the litter. In addition to the absolute raw value of birth weight, the risk to die during the first three weeks of life is increased when a newborn is lightest than its littermates (relative birth weight). This phenomenon, well known in piglets, has recently been evidenced in dogs and cats.
- No or negative growth rate between birth and 2 days of age. If the newborn did not gain weight at the postnatal Day 2. The common assertion that a 10% weight loss over the first two days of life is normal is totally wrong.
- Low APGAR score within the first 8 hours of life. APGAR score is the addition of scores obtained from five parameters (table 1). Mortality rate within the first 24 hours of life for puppies with APGAR lower than 7 is 7 times higher than that of puppies with higher APGAR scores. Deficit in passive immune transfer. It can be evidenced by a low early weight gain (no weight gain between birth and two days of age) or by assaying gamma glutamyl transferase serum activity (lower than 62 UI/l at Day 2 of life)

Table 1: APGAR score table for puppies.

Parameter	APGAR Score

	0	1	2
Heart rate	<180 bpm	180 – 220 bpm	>220 bpm
Respiration	No crying/ <6 rr	Mild crying/ 6-15 rr	Crying/ >15 rr
Irritability reflex	Absent	Grimace	Vigorous
Motility	Flaccid	Some flexions	Active motion
Mucous colour	Cyanotic	Pale	Pink

CAUSES

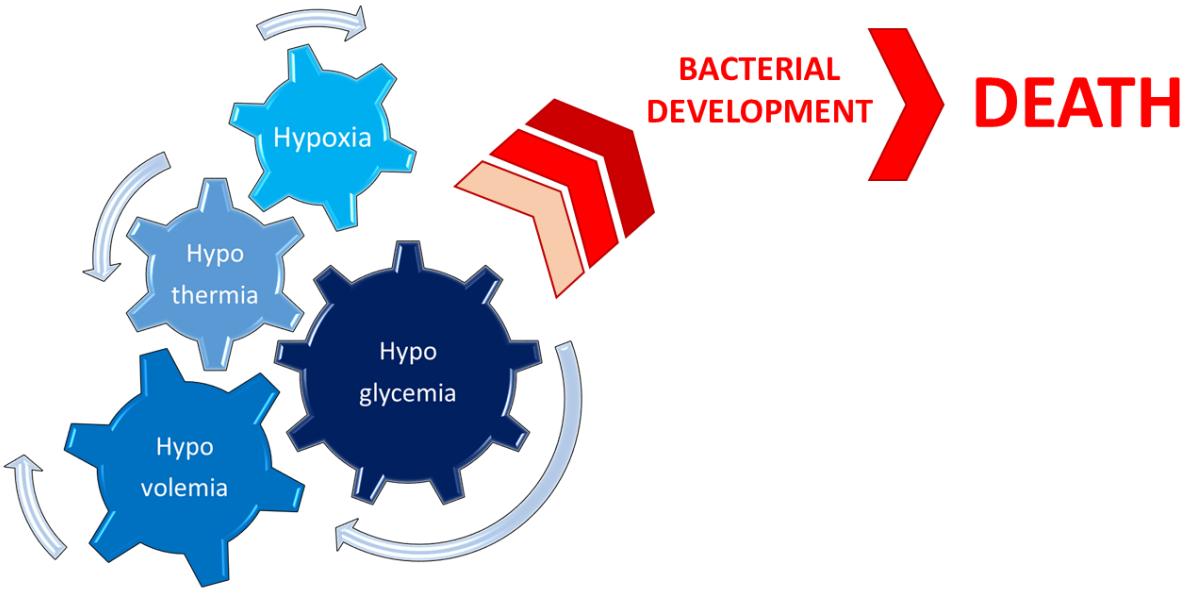
- Congenital abnormalities.
  Some can be identified at clinical examination (hydrocephaly, cleft palate, spina bifida, atresia ani, intestinal externalization) and some others cannot (atresia coli, megaoesophagus, enzymatic deficiencies, hyperinsulinemia/hypoglycemic crisis in case of gestational diabetes mellitus…). Some have a karyotypic or genetic contribution, some are random differentiation accidents, some others are iatrogenic.
- Traumatism
  - "Aggressive" "impatient" bottle feeding, especially in case of weak newborns with inefficient swallowing reflex, responsible for inhalation of milk
  - Injuries applied by the dam. Primiparous and stressed females may bite their newborns, sometimes until cannibalism. When newborns are crushed by their mother, one can make responsible either an inappropriate maternal behavior or weakness of the newborn itself.
- Specific infectious causes

KITTENS	PUPPIES
FHV (Feline Herpesvirus) FeLV (Feline Leukemia Virus) FCV (Feline Calicivirus) FPV (Feline Parvovirus) *Salmonella* *Campylobacter jejuni* *Toxoplasma gondii* *Toxocara cati*	CHV1(Canine Herpesvirus) CPV1 (Canine Parvovirus type 1) CDV (Canine Distemper Virus) CCoV (Canine Coronavirus) CAV2 (Canine Adenovirus type 2) *Brucella* *Salmonella* *Campylobacter jejuni* *Bordetella bronchiseptica* *Neospora* *Toxocara canis*

- Non specific infectious causes: Septicemia
  Newborns are contaminated mainly by the oral route and also by the open umbilical vessels, in direct communication with the liver (via the umbilical vein) and thereby with the systemic circulation. The development of septicemia depends on the exposition to an important bacterial load and/or intrinsic weaknesses of the neonate (hypothermia-hypoglycemia-hypoxia-hypovolemia syndrome).
  - *Exposition to a high bacterial load:*
    - Environmental hygiene defect (in the maternity box)
    - Infectious site borne by the dam: dental calculus, otitis, mastitis, metritis, poor hygiene in the perivulval and mammary areas
  - *Hypothermia-Hypoglycemia-Hypoxia-Hypovolemia syndrom:*
    Opportunistic bacteria are the effective inducers of the death and are evidenced by bacteriological analysis, but their development has been made possible by these four non infectious factors. Bacterial infection is secondary to one or several elements of the syndrome Hypothermia-Hypoglycemia-Hypoxia-Hypovolemia, these four symptoms forming a vicious circle (figure 1). There are several circumstances leading to this syndrome: perinatal (prolonged delivery - dystocia), nutritional (limited access to colostrum and milk due to poor milk production, inappropriate maternal behaviour), environmental (low or high ambient temperature for example).

- Intense parasitism. Especially by round worms (*Toxocara*), hookworms (*Ankylostoma*), coccidia (*Cytoisospora*).
- Immune disease (neonatal isoerythrolysis, in kittens) in Group A or AB kittens born from (or fed colostrum from) a Group B female.

Figure 1: Factors predisposing to septicemia in newborns



DIAGNOSIS: Necropsy and complementary tests

Owners and breeders are often reluctant to enter into a diagnostic procedure in case a newborn (0-21 days) is dead. Although 60% of deaths (puppies born alive) occurring before the age of 2 months are neonatal, breeders are more sensitive to pediatric deaths (during the second months of life). The more precocious are the deaths, the less diagnostic procedures are attempted.

To optimize the quality of the conclusions that can be drawn, the conditions of preservation after death are crucial: no freezing (histopathology is no more possible, and even gross examination after thawing becomes confusing), storage at +4°C as soon as possible after death, and necropsy is to be performed then in the shortest delay. It can be performed either at the veterinary clinics, or at a specialized lab. Due to the difficulties of sending corpse safely (without any risk of leaking, with low temperature being maintained) and in short delays (ideally same day or next day delivery), one can suggest that the necropsy is performed on fresh cadaver by the vet practitioner; pictures are taken from most organs in order to allow a posteriori (re)interpretation of gross lesions; organs are then sampled, ideally following a systematic protocol or chosen depending on symptoms. Samples are transferred to the appropriate lab for analysis, together with identification of the dead animal and description of macroscopic lesions.

1. Identification

- Breed (to be aware of the known genetic defects)
- Age at death
- Symptoms observed before death
- Symptoms observed in the littermates, the dam, within the kennel/cattery

2. Gross examination

First, weight the corpse and compare to the expected weight for the age (from breed-specific references curves). Growth rate from birth also provides information about the quantity of colostrum/milk ingested (starvation is a frequent cause of neonatal death, without any specific lesion at necropsy except the demonstration of an abnormally low growth).

Second, a complete external examination is to be conducted.

Third, after conventional opening of large cavities (abdomen, thorax), organs are observed in place, then isolated for detailed observation. Intestines have to be open on their whole length to identify even localized mucosal lesions or intraluminal parasites.

3. Samples management

- *Bacteriology*: only if death occurred less than 6 hours before necropsy. A sterile swab is introduced deep into the splenic parenchyma and transferred into a sterile vial. Attention has to be paid to avoid contamination during the first sections for abdominal opening. The spleen can also be collected in a sterile way as a whole. Samples are refrigerated before being brought/sent to the lab. They have to be received by the lab for analysis within the following 24 hours.

- *Histology*: samples transferred into plastic jars filled hallway with 10% formalin (3.4% formaldehyde) should not be thicker than 5 mm and should be processed by the lab (paraffin inclusion) within 7 days after collection (for the quality of tissue at microscopic examination).

- *Parasitology*: on intestinal/rectal content and on histological samples (for *Neospora* and *Toxoplasma* for example)

- *PCR*: samples submitted to molecular biology can be frozen (if the cadaver was frozen before necropsy and/or with signs of autolysis, PCR remains the only reliable examination possible). For most agents, quantitative (real time) PCR provides useful information by evaluating the viral load.

CONCLUSION: PREVENTION IS CRUCIAL.

In most of the cases, symptoms before death are of short duration (several hours) and very similar whatever the underlying cause making unsuccessful any attempt of treatment. Deficit in colostrum/milk ingestion is a frequent primary cause of mortality, allowing the secondary development of viral and bacterial pathogens. Preventive actions must be implemented to control neonatal mortality. To advise appropriate actions, the practitioner has to visit the facility to evaluate the peripartum management focusing on pregnancy/whelping management, reanimation/nutrition of the newborns, hygiene procedures and environmental ambiance.