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Εάν ης φιλομαθής, έσει και πολυμαθής

(If you are fond of learning, you will soon
be full of knowledge)

“*Omnium Rerum Principia Parva Sunt*” – Cicero (106-43 BC)
(The beginnings of all things are small)

Our modern world owes much to the languages of ancient nations, in that a huge number of Latin and Greek words (and roots of words) have become widespread in many of today's languages, and especially within science, theology and law. Certainly, it is impossible to go far in veterinary medicine without encountering a reminder of what these age-old civilizations have passed down to us, whether in an anatomical term that relates to the argot of the Roman Empire, or a pathological description that can be traced back to a time in Greece when Hippocrates was still young. Take, for example, *leuc* (or *leuk*), the original Greek word for white, which is to be found in leucocytes and leukemia, whilst their word for red – *erythro* – crops up in erythrocytes and erythropoietin. The Latin root *parvi* (meaning small or rare) – as seen in the heading above – makes its way into parvovirus, and the prefixes *hypo* and *sub* (from Greek and Latin, respectively), meaning underneath, are found almost wherever one cares to look in the medical world, whether that is in hypophysis, hypotensive or hypoplasia, subchondral, subluxation or subcutaneous.

In the animal world, *precocial* species produce offspring that can soon fend for themselves – a term that again is of Latin derivation, stemming from *praecox* (*prae*, meaning ahead of, and *coquere*, to cook or ripen). By contrast, dogs and cats are *altricial*, in that their young are born underdeveloped and require nurturing to develop and mature; the word is derived from the

Latin root *alere*, meaning “to nurse or rear”. Which brings us to this issue of *Veterinary Focus*, as it looks at how we as clinicians can optimize conditions for young puppies and kittens, and the following articles should be of benefit to all who seek education; as an ancient Greek scholar put it, if you are fond of learning, you will soon be full of knowledge.



Ewan McNeill
Editor-in-chief

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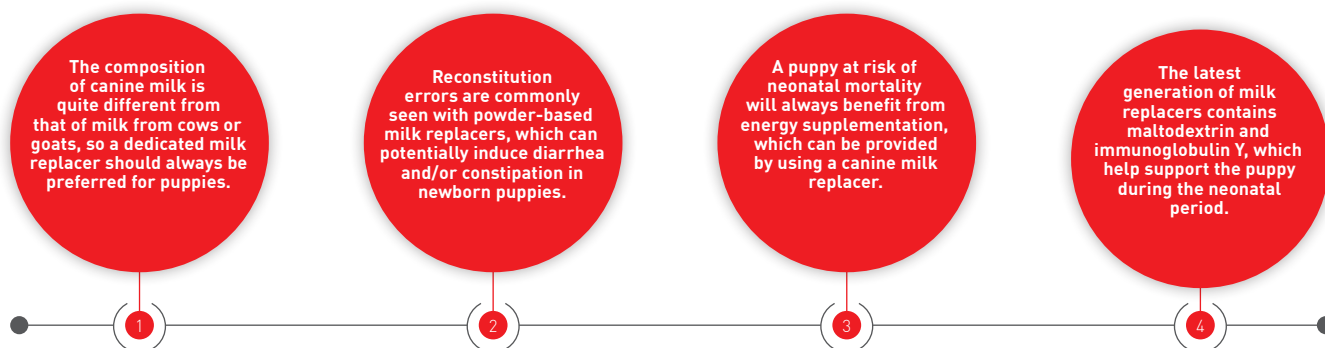
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CANINE MILK REPLACERS

It may sound simple enough to offer milk to newborn puppies, but various pitfalls await the unwary, as Emmanuel Fontaine describes.

KEY POINTS



Introduction

You finish performing the ultrasound scan, smile at the client and say “Congratulations! She’s pregnant.” This scene could occur in any veterinary clinic, but as you hang up your ultrasound probe, remember: the consultation is far from over. In fact, a new – and very important – conversation with the owner is about to begin. Part of it will focus on canine neonatology, and how to properly care for newborn puppies, and a useful mantra is “An ounce of prevention is worth a pound of cure”. During the discussion, milk replacers are an important factor to include in the topics covered – and in fact milk replacers should be part of any maternity “toolkit” – but various questions arise at this point. Which one to pick? What are the important factors to check? What are the best ways to use them and when should they be used? This article will aim to answer all these questions and allow the veterinarian to feel comfortable advising owners in the clinic.

What’s the best milk replacement for puppies?

Look for nutritional adequacy

Many owners assume that any milk will be suitable for newborn puppies. The milk in their fridge, a human baby milk replacer bought at the local grocery store, a home-made formula using a recipe found on the Internet... those are options that will often be considered if the owner has not been properly briefed. It is therefore important to let them know that their bitch’s milk is very specific. This is because canine milk, when compared to other species, is more energy dense, has higher levels of

minerals (e.g., calcium and phosphorus) and contains more protein (**Table 1**). It is obvious that cow’s milk or goat’s milk (the latter being an Internet favorite) are quite different in composition, and they do not offer the proper nutritional balance to sustain healthy growth in newborn puppies.

Human milk replacers are not recommended either. These products contain starch, which acts as a thickener and helps babies feel full, as well as providing carbohydrate. However, newborn puppies do not possess the necessary enzymes (amylase and maltase) to properly digest starch (1), so such products should be avoided. In theory it is possible to create a home-made formula that resembles canine milk using recipes from the Internet, but this is both time-consuming and difficult, as it is essential to ensure that various parameters – such as nutritional balance, sterility and correct osmolality – are optimal, and the risks clearly outweigh the benefits. For owners who insist on going down this route, it is advisable to consult with a veterinary clinical nutritionist to ensure that the chosen recipe is appropriate.

Table 1. Average composition of dog, cow and goat milk.

	Dog (from 2)	Cow (adapted from 3)	Goat (adapted from 3)
Energy (kcal/L)	1560	630	710
Protein (g/Mcal)	56.7	21.8	46
Calcium (g/Mcal)	2.13	0.55	1.7
Phosphorus g/Mcal	1.37	0.48	1.46
Lactose (g/Mcal)	20	28.8	57.7



Emmanuel Fontaine

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Dr. Fontaine graduated from Toulouse Veterinary School in 2004 and continued his studies at the Alfort Veterinary School, Paris in the domestic carnivore unit of the Reproduction Department. From 2005 to 2011 he worked at the Centre d'Étude en Reproduction des Carnivores [Research Center for Reproduction in Carnivores], a unit specializing in pet breeding. Dr Fontaine completed his PhD in 2012 on the use of GnRH agonists in canines, and also holds a diploma from the European College for Animal Reproduction (ECAR). He joined Royal Canin in 2011 as Technical Services Veterinarian for the PRO team, and is currently in charge of Regional Scientific Communication for the Americas.

Osmolality is vital

Osmolality refers to the osmotic pressure produced by dissolved particles in the milk. A large quantity of highly osmolar particles in the digestive tract of the newborn can induce osmotic diarrhea, and since a puppy's body is 84% water (4) it is important that this is avoided, and especially during the neonatal period. Lactose will affect milk's osmolality, and given its high levels in cow or goat milk when compared to the bitch, this is another reason why it is better to avoid such options for newborn puppies.

The preferred option

Nowadays dedicated canine milk replacers are widely available, and they should always be the preferred option. Obviously, it is important that their composition is as close as possible to the typical composition of the bitch's milk, although some reports indicate that this is not always the case with certain products (2,5), so veterinarians would be prudent to check this if there is any doubt. Some milk replacers may also contain several "optional" constituents, as shown in **Table 2**, but most dedicated canine milk replacers are satisfactory and offer both convenience and peace of mind, and their use should always be recommended in newborn puppies. Many markets now offer two options for canine milk replacers, either liquid or powder-based products, and both have their pros and cons.

Liquid milk replacers are clearly easier to use: because they come ready-mixed, no preparation is necessary, and simply require warming up before being administered. They also avoid the most common mistake seen when using a powder-based product, which is that owners tend to either add too much water (so that the product is too dilute) or insufficient water (so that the product is too concentrated) (6). However, once opened, liquid replacements should not be stored in a refrigerator for long, and the usual recommendation should be to discard them at a maximum of 72 hours.

Powdered milk replacers, on the other hand, can be stored for much longer – typically a month once opened. As mentioned above, reconstitution mistakes can and do occur, which will impact on the osmolality of the milk, resulting in either diarrhea or constipation in the newborn. However, powder-base products offer the option of varying the osmolality of the solution in order to address some nutrition-induced conditions, as discussed below.

●●● When do newborn puppies need a milk replacer?

Conditions related to the mother

Availability & behavior

There will be times when an owner will have to rely on a milk replacer to ensure neonatal puppies are properly fed. In some cases, newborn puppies may have no mother – for example, following an accident, or an anesthetic problem during a caesarean section. Whilst not frequent, such scenarios are unpredictable, and when they occur, they obviously prevent the usual maternal nursing. The other situation is where orphaned newborn puppies are abandoned at an animal shelter. While these places typically deal more with orphaned kittens, they will

Table 2. Other possible components in canine milk replacers.

Component	Why consider?
DHA (doco-sahexaenoic acid)	Several milk replacers are enriched with the omega-3 fatty acid DHA. The bitch has a limited capacity to produce this nutrient during lactation (7), and supplementation in newborn puppies has been shown to support development of cognitive and ocular functions (8).
Prebiotics	Prebiotics such as fructo-oligosaccharide (FOS) are found in some milk formulas. They help support the newborn's digestive function as well as participate in the development of immune health by helping to establish and maintain an optimal microbiota balance (9).
Malto-dextrin	Maltodextrin is an oligosaccharide that is used in milk formulas for pre-term infants. In a recent study a puppy milk replacer was supplemented with this ingredient to provide extra energy to newborn pups (10). Administering the supplement immediately after birth helped support the early growth rate and aided maintenance of body temperature, and also reduced the number of puppies at risk for neonatal mortality.
Immuno-globulin Y (IgY)	IgY supplementation in newborns has been demonstrated to support neonatal growth. In large breed puppies it has also been shown to aid positive development of the microbiota (11).

sometimes see orphaned puppies too, and staff and foster parents at these establishments need to be equipped with an appropriate milk replacer. It is also important not to overlook the risks from poor maternal behavior; some mothers neglect their puppies, whilst others can be aggressive towards them. Primiparous bitches are more prone to this (12) and the problem may be seen more frequently in certain breeds (e.g., English Bull Terriers) (13). Owners should be aware of this risk to help them better anticipate the situation.

Lactation-related disorders

Whilst the use of milk replacers is mandatory if the dam suffers from agalactia, the situation is less clear cut when it comes to the most common lactation disorder encountered in canines, namely acute mastitis. This typically occurs either immediately after parturition, or at around three weeks postpartum, when lactation is at its peak (14). Clinical signs involve inflammation of one or more mammary glands, often accompanied by a change in milk color, usually to a yellowish-brown appearance. More general signs – lethargy, pyrexia, discomfort when puppies are suckling – may also be observed but are not always present. It is therefore important to recommend that an owner checks the dam's mammary glands daily. Mastitis can have a major impact on newborn puppies, leading to failure to thrive, neonatal diarrhea and/or colitis. Treatment of acute mastitis involves antibiotics, with cephalosporins often used as first-line treatment (15). However, opinions differ on what to do with the puppies. Some authors recommend that pups can continue to suckle the mother during treatment (as long as there is no discomfort for the dam) and will prevent galactostasis – which has a negative impact on treatment efficacy. Antibiotics are also excreted in the milk, which may offer the puppies some protection from the side effects of the mastitis (although there is always the risk of dysbiosis and neonatal diarrhea, so the clinician should judge each situation on its merits). However, other authors recommend that the whole litter should be immediately switched to a milk replacer while the mastitis is treated, the reasoning being that newborn puppies are fragile and can crash quickly, and that consumption of contaminated milk may increase the risk. To prevent galactostasis in the mother, lactation can be stopped by using dopaminergic drugs such as cabergoline (16).

Both options have their pros and cons, and it is the author's opinion that the decision must always be taken with the health of the newborns as a priority. Above all, if the puppies develop signs of ill-health, they should not be allowed to nurse on the mother and should be switched onto a milk replacer immediately.

It is also important to be aware of "toxic milk syndrome" which is described in several canine neonatology textbooks. This is where some puppies from a litter develop neonatal diarrhea or colitis, although the dam shows no clinical signs of mastitis. Affected pups fail to thrive and suffer from

abdominal pain after feeding, although sometimes only one puppy in the litter will exhibit clinical signs whilst the others remain well. Recent studies suggest that this could be related to subclinical mastitis (17), which (although not routinely done in veterinary clinics) can be diagnosed via microscopic examination of the milk, looking for increased numbers of neutrophils per high power field. Subclinical mastitis should always be a differential diagnosis when a neonate is unwell, even if only one puppy in a litter is exhibiting clinical signs. If seen, the puppy should immediately be moved onto a milk replacer, and if other puppies start to develop the same signs it would be advisable to switch the entire litter onto the milk product.

Conditions related to the newborn

Cleft palate

As soon as a puppy is born and properly resuscitated, it should be checked for a cleft palate – one of the most common congenital abnormalities encountered in newborn puppies (18). In some cases, there is the option to repair the defect via a palatoplasty, but this surgery can only be performed at a later date, usually between 2.5-14 months of age (depending on various factors and the surgeon's preference). However, during the neonatal period, affected puppies cannot suckle and will aspirate the milk. This may cause them to choke, or can lead to bronchopneumonia, which is often fatal. These risks decrease when the puppy starts eating solid food, so (assuming the owners wish to consider surgery at a later date) early weaning at 3 weeks of age can be considered. However, for the first three weeks of life tube-feeding with an adapted canine milk replacer will be mandatory to avoid complications.

Risk of neonatal mortality

Recent studies (19) have helped define guidelines for early detection of newborn puppies at risk of neonatal mortality (**Figure 1**) and owners must be alerted to this. These studies have shown that at-risk puppies will benefit from energy supplementation, and so such individuals should be offered an appropriate milk replacer when identified. Growth curves are also starting to become available for dog breeders and veterinarians (20,21) which will assist in monitoring the growth of puppies during the neonatal period. These can help in early identification of potential problems, as a lack of weight gain is often one of the first indicators of poor health. Nutritional supplementation via a milk replacer is certainly an option in these cases.

Heterogenous litters

"Litter heterogeneity" refers to the weight difference seen between the biggest and smallest puppies in a litter. This has recently been identified as a risk factor for early neonatal mortality (21). When high litter heterogeneity is detected (e.g., a weight difference between 9.9-16.8%, depending on the breed), the litter should be flagged as being potentially at risk. This is also a reminder that, in

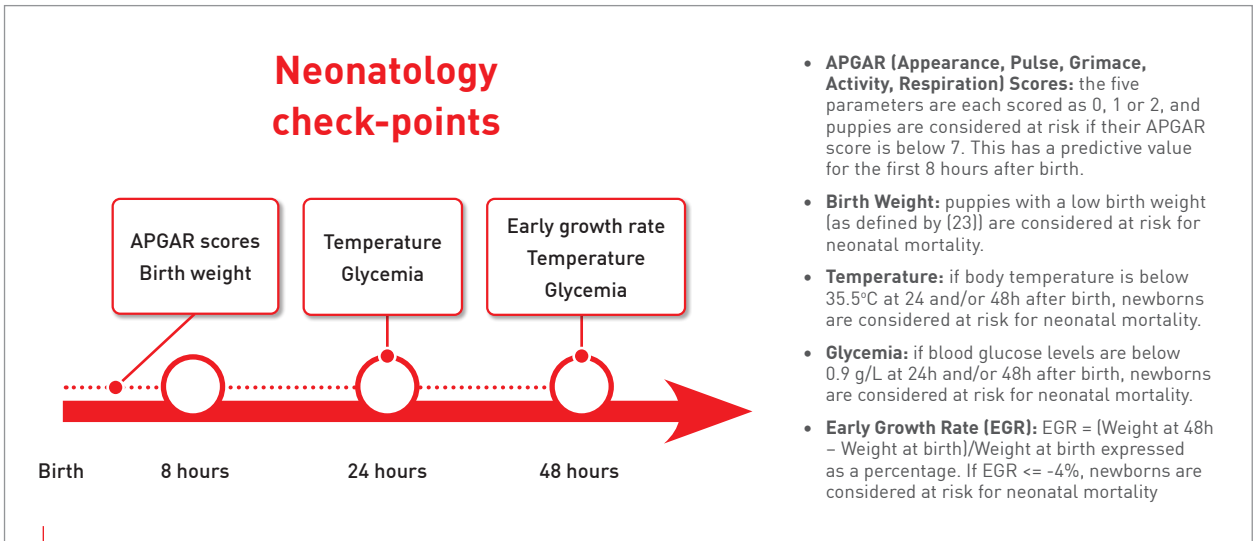


Figure 1. Factors that aid identification of puppies at risk of neonatal mortality during the first 48h after birth (from [19]).

neonatology, the litter should always be considered in its entirety. The difference in weight will accentuate competition for accessing the mammary glands, and supplementation with a milk replacer should help minimize the deleterious effects of the heterogeneity.

Other reasons

Weaning

At weaning, which typically starts around 4-4.5 weeks of age, it is recommended that the transition from milk to solid food is as smooth as possible. If using kibble, it should be rehydrated during the first few weeks of weaning to make it easier for the puppies to ingest and digest the food [22] (Figure 2), and, in the author's opinion, a milk replacer can be used instead of water during the first week to ease this transition.



Figure 2. The weaning process for puppies should be as smooth as possible; the image shows the ratio of water to kibble to be used (by volume, not weight) to rehydrate dry food. During the first week of weaning, milk replacer can be used instead of water.

Immunoglobulin supplementation

Over 18% of newborn puppies do not receive enough immunoglobulins from their dam's colostrum [19], and these individuals have been identified as being at risk for neonatal mortality, so milk replacers that contain Immunoglobulin Y (IgY) are a potentially useful option here. IgY will be taken up from a puppy's digestive tract during the period when colostrum is absorbed [24] so even though the IgY in those milk replacers currently only target a limited number of pathogens, their use immediately after birth makes sense to ensure that puppies receive at least a degree of protection against some of the most common digestive canine pathogens.

••• How should milk replacers be used?

Check the puppy's temperature first

Before a milk replacer is fed to newborn puppies, whether they are debilitated or not, it is essential to check their body temperature. During the first week of life, the newborn's body temperature is between 35.5-36.5°C. It will only reach adult body temperature three weeks after birth [25], but if a puppy's temperature drops below 34°C the digestive tract goes into stasis, preventing digestion of food, so that administration of milk will lead to bloating and abdominal discomfort. This is a common mistake, especially encountered with orphaned pups; owners often think that the priority is to bottle-feed them, but neglect to first check their body temperature to ensure it is safe to do so. Puppies cannot thermoregulate during the first three weeks of life, so if hypothermia develops they must be warmed up before being bottle-fed. Infrared lamps, heating pads, water bottles or incubators are all options to be considered, but the warming process should be gradual, taking at least an hour before starting the bottle feed.

Owners should also be advised that it is important to optimize the temperature inside the nest in order to prevent hypothermia and its consequences. The author recommends 30°C inside the nest during the first week after birth, 28°C for the second week and 25°C for the third week. After this period puppies will be able to thermoregulate, and hypothermia is less of a concern.

Follow the instructions

As mentioned above, reconstitution errors are the most common mistake encountered when preparing powder-based milk replacers. It is therefore important to discuss this with the owner and to emphasize what often seems a trivial detail – it is essential to use the ratio of water to milk powder that is recommended by the manufacturer. It is also important to remind owners that “more is not better”, as they may think that mixing the powder with another type of milk (goat’s milk for instance) will lead to a more nutrient-dense solution which is beneficial to the newborn. Unfortunately, this again can dramatically impact the osmolality of the solution and lead to neonatal digestive disorders.

Bottle-feeding or tube feeding?

When feeding newborns with a milk replacer, bottle-feeding and tube-feeding are the only two options. The author believes that, whenever possible, bottle-feeding is to be preferred. Specific puppy bottles should be used, as they come with adapted nipples which ensure optimal milk flow during feeding. This is an important detail: if the milk flow is too fast (e.g., if using human bottles on small breed newborn puppies), aspiration can occur. The author also prefers to use a bottle with pre-prepared nipples; some are supplied with nipples which requires the tip to be cut before use, but if not



“In theory it is possible to recreate a home-made formula that resembles canine milk using recipes from the Internet, but this is both time-consuming and difficult, as it is essential to ensure that various parameters – such as nutritional balance, sterility and correct osmolality – are correct, and the risks clearly outweigh the benefits.”

Emmanuel Fontaine



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Figure 3. When feeding a newborn puppy, the nipple should be aligned straight into the mouth. This is important, since the nursing neonate rolls its tongue around the nipple and creates a seal when suckling. If the nipple is placed at an angle, a seal cannot be formed, and the neonate will swallow air and develop colic. Gently holding the puppy’s head will also help while bottle-feeding, as some very active puppies will move their heads in all directions, losing the nipple.

done properly, this can again lead to an over-fast delivery of milk with the same unwanted consequences. It is also very important to discuss how to hold the puppy and bottle for feeding, as an owner will often think that puppies should be bottle-fed the same way as a human baby; this is wrong and can again lead to aspiration. **Figure 3** shows the correct position for bottle feeding a puppy.

Tube-feeding, on the other hand, should be reserved for puppies too weak to be bottle-fed or for those born with a cleft palate; it should not be employed simply in order to feed an entire healthy litter faster. It is important to note that tube-feeding should only be a temporary solution (other than with a cleft palate case); as soon as the puppy is strong enough, it should be moved to bottle-feeding or feeding from the mother, depending on the options available.

Clients must also be reminded that newborn puppies cannot defecate or urinate by themselves. This is a reflex action stimulated by the mother licking the puppy’s perineal region, so after each feeding session the owner should simulate this by rubbing the perineal area with gauze moistened with lukewarm water.

How many meals per day?

When feeding newborn puppies with a milk replacer, the author recommends 8 meals per day during the first week after birth, 6 meals per day in the second week, and 4 meals per day in the third week. It is also important to note that individuals in a litter of orphaned puppies may start suckling on each other, to the point where severe inflammation and even abscesses develop. This behavior is usually seen when the puppies are hungry. However, increasing the amount fed could increase the risk of neonatal diarrhea because of the neonate’s limited



digestive capacity, so one practical option is simply to increase the number of meals given. For instance, during first week of life, instead of 8 meals per day, moving to 10 can be recommended. The author has successfully implemented this approach in animal shelters, and while obviously more time-consuming, it is perhaps the simplest answer to the problem.

How much milk per meal?

By default, when a newborn's nutrition solely depends on the milk replacer, clients should be advised to follow the manufacturer's recommendations, although the development of neonatal growth curves will help tailor this advice. Recent research has also shown that for puppies which are nursing on the mother but are identified as at risk for neonatal mortality, supplemental milk replacers can be given *ad lib* [19]. The authors of this study did not experience any complications with this protocol, and found that the puppies would almost self-regulate their milk intake. That said, it would always be wise to recommend caution here – some voracious puppies might over-consume, which could lead to diarrhea – and the author has observed this on occasion, especially with Labrador Retrievers. It would therefore be prudent to recommend that an owner does not allow puppies to exceed the maximum volume recommended by the manufacturer.

Clinical tip: play with the dilutions

Veterinarians should be aware that – as in the human situation – the water:milk powder ratio for powder-based milk replacers can be altered on occasions to their advantage. Varying the product's osmolality can come in handy when dealing with cases of uncomplicated neonatal diarrhea or constipation (*i.e.*, when nutrition-related [26]). From personal experience, the author prefers to use 80% of the recommended volume of water to prepare the product for a puppy with constipation, whereas for diarrhea it is recommended to use 120% of the recommended water volume. In either case reverting to normal ration can be done as soon as the clinical signs resolve.



CONCLUSION

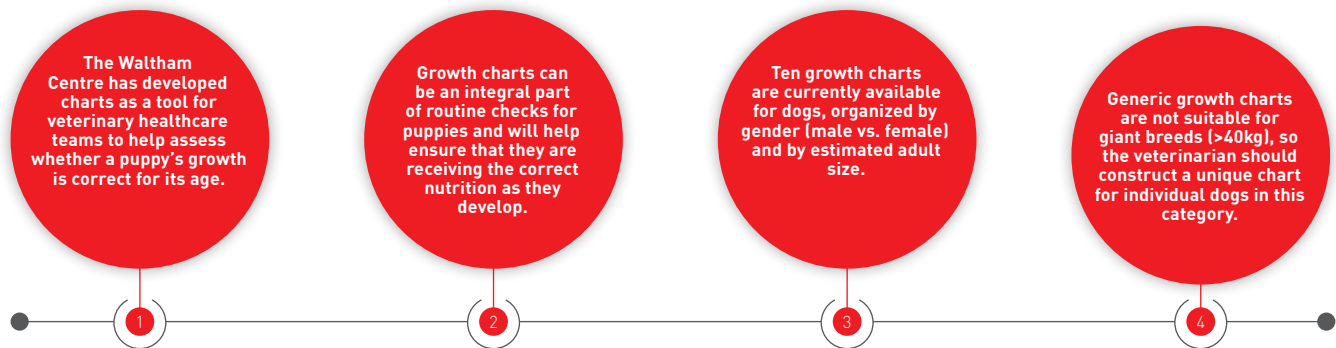
Milk replacers must be part of every neonatology toolkit. Every client who has a pregnant bitch should be equipped with the correct milk replacer, and it is important to educate them on how to avoid some of the most common mistakes encountered. There are plenty of situations where milk replacers will come in handy, and when used properly, they are a great asset in optimizing the health of newborn puppies.

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PUPPY GROWTH CHARTS

Growth charts for children are nothing new, but recent work has resulted in the concept being developed for dogs, and they are now an essential part of the veterinarian's toolkit.

KEY POINTS



●○○○ Introduction

Puppy and kitten consultations are a daily occurrence for the veterinary team, and they tend to be enjoyable for all concerned, but they are also hugely important when it comes to getting a new pet off to the best possible start. At least part of the consultation should involve a discussion on how to ensure the most appropriate diet for the new arrival – so before talking about growth charts, it is important to first review why conversations about nutrition are so important to incorporate into these initial visits.

●●○○ Why talk about nutrition?

○○○○ Socialization and habituation

Visits to the clinic every few weeks for weight checks can be a great way to not only monitor the growth of the patient, but also to socialize a new puppy. Pets may learn to have positive associations with the clinic if they get praise and treats for things like going on the scale or allowing a brief physical exam for assessment of body condition score (BCS).

Frequent visits

New puppies and kittens will visit the clinic a lot in their first year – for vaccine appointments, testing for heartworm and other parasites, and spay and neuter surgery. These are all great opportunities to check in with the pet owner and to assess how well their new family member is growing, and to see whether they have questions about what they are feeding (**Figure 1**).

Prevention

The Association for Pet Obesity Prevention reported in 2018 that nearly 60% of pet dogs and cats in the US were overweight or obese (1). Weight loss plans can be tough! Owners may take some convincing before they are even ready to broach the topic of weight loss, and helping a pet achieve an ideal body condition score when they have maybe 15 or 20% (or even more) excess body fat can take time. Veterinary

Figure 1. A new puppy's first visits to the veterinary clinic are a great opportunity to discuss feeding and weight management with the owners.



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healthcare teams need to be comfortable having these difficult conversations and initiating a weight loss plan, but another approach to the obesity epidemic is to focus on prevention. What better time to prevent obesity than when the pet is still young and healthy? If the team can talk about the risks of obesity at this stage, and provide eager owners with tools to prevent their new pets from getting too heavy, it may be possible to reduce the number of animals that become overweight or obese. If pet parents are trained on matters such as ideal weight gain, body condition scoring, portion control and “smart” treats, they will be more receptive to early recommendations if their pet starts to put on too much weight.

Expert advice

Owners want to talk about nutrition with their pet’s veterinary healthcare team, and having these conversations early on in a pet’s life demonstrates a proactive approach and conveys the message that the veterinary clinic is the best source of good information when it comes to nutrition. In this way, when pet parents get dietary recommendations from their breeder, friend, pet store employee, or other well-meaning person, they will hopefully bring that recommendation back to the clinic to double check before following it.

Owner interest and readiness to learn

There is a reason why everyone loves puppy or kitten appointments – aside from the chance to cuddle a healthy and adorable patient. New pet parents are just as excited as the veterinary healthcare team and often look forward to showing off their cute new family member. These owners are also likely to be more determined to do everything they can to keep their pet healthy and are often motivated to listen to advice on how to provide the best nutrition. Suggestions like weighing food with a gram scale or avoiding high calorie treats may seem daunting to owners of sick pets, as they may be overwhelmed with many other treatment recommendations, and nutrition gets bumped to the bottom. New pet parents can be more eager and receptive to these types of suggestions, and if they learn that behavior early on, it can be much easier to keep it up for the duration of the pet’s life. Furthermore, research investigating communication with clients in a

veterinary setting has found that pet owners want to be in a partnership with the veterinarian [2]. By having nutrition conversations earlier on, we can establish this partnership with our clients and have a stronger veterinary-client relationship.

With all of that in mind, it is time to look at an exciting tool that every veterinary healthcare team should have in their nutrition toolkit – Growth Charts.

●●● What are growth charts?



Growth charts may be more familiar to any pet owners that also have children, as they are a tool used by pediatricians and nurses to track the growth of infants and youngsters. They consist of percentile curves using a series of measurements [height, weight, body mass index (BMI) and age] [3], and have been used in human medicine since 1977 as a tool to assess whether a child’s growth is adequate. In a similar way, growth charts for dogs have now been developed by the Waltham Centre, an institute for science and research owned by Mars Petcare [4]. These charts were developed based on data from tens of thousands of healthy dogs and they now provide a tool for veterinary healthcare teams to help assess whether a puppy’s growth is on track for its age.

However, one additional factor that had to be considered during the development of the Puppy Growth Charts is that there is a huge variety in dog breeds – so one size does not fit all for a growth curve. There are therefore currently ten growth charts available for dogs – organized by sex (male vs. female) and by estimated adult size (<6.5 kg, 6.5-9 kg, 9-15 kg, 15-30 kg, and 30-40 kg) [5].

●●● What information is needed?



In order to use a growth chart for a puppy, the following information is required:

- Sex of the puppy – there are separate charts available for males and females
- Estimated adult weight of the puppy; this can be determined either by using the weight of the parents (note that this assumes the parents are in ideal body condition) or via the breed standard
- Age of the puppy in weeks
- Weight of the puppy in kilograms

Once these details are to hand, the correct growth chart can be printed off, and the puppy's weight and age plotted. For downloadable PDFs of all 10 growth curves available, visit: <https://www.waltham.com/resources/puppy-growth-charts>

●●● How often should you measure?

In order to interpret the data most accurately, frequent measurements are needed, especially early in the puppy's life. This allows determination of what percentile curve the puppy is starting out on within the first couple of months of life, which gives a better idea of what the target weight should be at any given age. At a minimum, puppies should be weighed every two weeks, but the best option is to weigh them weekly. Make sure that these weights are recorded at the same time of day, as time of last meal, bowel movements and hydration status can all cause the weight to fluctuate during the day.

Bringing a puppy in for weekly weight checks may not be possible for some owners with busy schedules or who live further away, so the following home-based options can be considered:

- **Bathroom scales:** if the owner can safely lift the puppy, they can weigh themselves with the puppy and then subtract their own weight.
- **Luggage scales:** small puppies can be put into a pet carrier and weighed on luggage scales – again subtract the weight of the empty carrier from the gross weight.
- **Pet scales:** these can be purchased online and will range in cost depending on the size of the scales.

If the owner is able to do some weekly weights at home, ideally the puppy should still attend the clinic for an assessment every four weeks



“Growth charts were developed based on data from tens of thousands of healthy dogs and they now provide a tool for veterinary healthcare teams to help assess whether a puppy's growth is on track for its age.”

Caitlin Grant

(which will often line up with booster vaccine appointments), allowing the veterinary healthcare team to both ensure the puppy is growing well and to perform a BCS assessment.

●●● Putting the growth curve to work

Once a growth chart for a patient has been started, it is important to use it properly! The chart will give a fairly accurate prediction of the expected growth rate of a puppy once the percentile curve they are growing on is established. A recent study compared healthy dogs and dogs with abnormal body condition to their growth chart data (6) and found that departure from the original percentile line was very rare in healthy dogs, but dogs who were obese by the age of three years showed more rapid growth, and the majority had crossed two or more percentile lines during their growth period. The chart should therefore be used to check that a puppy is growing according to the percentile curve that they started with, and they should avoid crossing a percentile line. If a puppy approaches a line above their curve, they are growing too quickly, and energy intake should be reduced, whereas if they approach a line below their curve, they are growing too slowly, and energy intake should be increased.

●●● What else should be done at weight checks?

The weight checks do not simply include a visit to the scales and a recording of weight on the growth chart. The veterinary healthcare team can use this opportunity to check in on a few other important topics:

- **Diet history:** ask what food the puppy is eating and how much. The owners may have switched foods since the last visit, or adjusted the portion size on their own.
- **BCS:** the body condition score system is not yet validated in puppies, but it can still be useful in conjunction with weight and the growth chart to determine if the puppy is over- or under-weight. It can also help get the puppy accustomed to having this assessment performed, and the owner may be encouraged to do a regular BCS at home.
- **Activity:** ask about the puppy's activity levels – are they starting obedience classes or going for more walks? An increase in activity may warrant an increase in energy intake.

●●● Limitations of growth charts

- **Giant breed dogs (i.e., those exceeding an adult body weight of 40 kg):** the growth charts currently available stop at 40 kg, as researchers found that giant breed dogs have variable breed-dependent growth, which prevents the creation of standard



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Figure 2. Remus at 12 weeks of age.

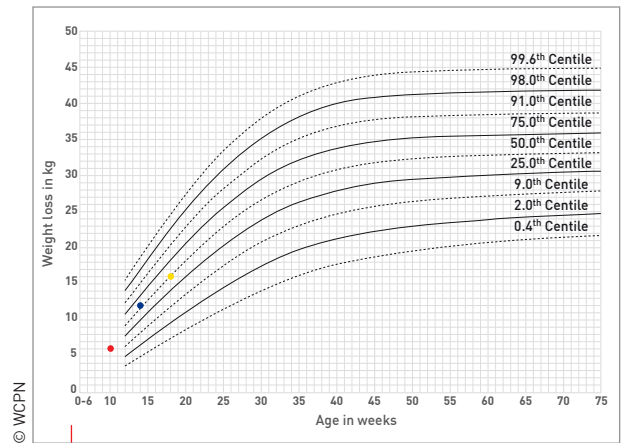
curves (5). For a giant breed patient, the veterinarian can still follow all of the suggestions above, but should create a unique chart to track weight and age. This allows monitoring of the growth patterns and the energy intake can be adjusted if a large increase in weight is noted, or if the pet gains less weight than expected.

- **Mixed breed dogs:** the growth charts can be used for mixed breeds, but the challenge here is that identifying the target adult weight of a puppy may be difficult if the breed makeup is uncertain. The author's recommendation is to make a "best guess" and use the first few recorded weights to help decide whereabouts the puppy might fall on a growth curve. Another option is to suggest genetic testing if the owner is interested to know what their pet's make-up involves.
- **Cats:** there are currently no growth charts published for cats, but as with the comments above for giant breeds, it is possible to make a chart for each patient using its individual data and following the same guidelines.

Case example – Remus

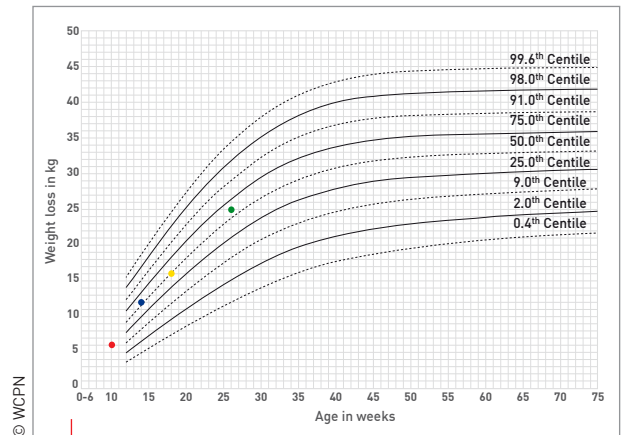
Remus is a male Shepherd X Collie mix puppy (Figure 2) adopted from a shelter by his new owner, and who started to feed him a commercial puppy food designed for German Shepherds. Remus had his weight recorded at his first clinic visit when he was 10 weeks old, and his owner had his 8-week weight from the adoption shelter. Given that he is a mixed breed dog, it was more challenging to determine what his adult weight would be, but the 30-40 kg chart was chosen as the best match for him.

His weight at 10 weeks was 6 kg, and this was plotted on the growth curve. His owner decided to feed him a commercial food formulated for puppies, specifically Royal Canin Puppy Large dry food. This food provides 366.7 kcal per 100 grams, or 352 kcal per cup.



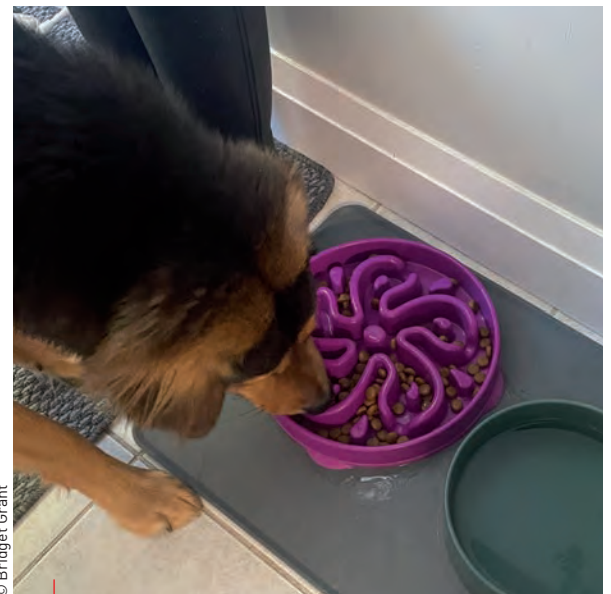
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Figure 3. Remus had his initial weights marked on the growth chart at 10 (red dot), 14 (blue dot) and 18 (yellow dot) weeks. This established him to be on the 50th centile.



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Figure 4. At 26 weeks of age Remus weighed in at 25 kg, which, when plotted on the chart, showed him to be slightly above the 50th centile (green dot).



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Figure 5. A puzzle feeder was introduced to ensure that Remus ate his reduced food portion slowly.

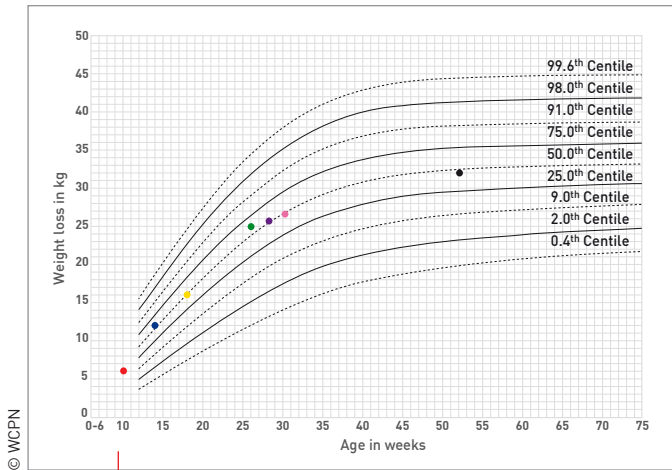


Figure 6. Remus had nearly reverted to the 50th centile at 28 weeks of age (when he weighed 26 kg – purple dot) and was 27 kg two weeks later (pink dot), At one year old he weighed 32 kg (black dot), his ideal weight as predicted by the growth chart.



Figure 7. Remus being weighed at home.

Remus' energy requirement was estimated to be 805 calories per day (RER multiplied by a DER factor of 3 since he was under 4 months of age¹) (7) (2 X RER is typically used for a puppy over 4 months of age, whilst neutered adult dogs usually require between 1.4-1.6 X RER, although this can be higher or lower depending on activity levels). Remus was prescribed a daily ration of 2 ¼ cups (792 calories).

His follow-up weights at 14 and 18 weeks were 12 kg and 16 kg respectively (Figure 3) which corresponded to the 50th percentile trend. His food amount was increased to 3 ¼ cups (1,144 calories) at this latter point. Remus was next seen at 6 months of age for a heartworm test and to weigh for oral preventative medicines. His weight at this visit was 25 kg which, according to the growth chart, was slightly higher than predicted by his growth curve (Figure 4). At this time, he was being fed a

¹ RER = resting energy requirement; DER = daily energy requirement

total of 4 ½ cups (1,584 calories) per day, so a 10% reduction in calorie intake was recommended (i.e., 389 grams [1,426 calories]). His owner was also instructed to weigh his food on a gram scale for better precision (8), and since she was concerned that he would beg more if his food amount was reduced, she began to feed him with a food puzzle (Figure 5).

Remus then came in for follow up assessments at 28 and 30 weeks; his weight at 28 weeks was 26 kg and since it seemed to be trending closer to the curve (Figure 6), no change in food amount was recommended. At 30 weeks, his weight was back on the 50th percentile curve, with him weighing in at 27 kg. Remus' owner decided to purchase a scale to use at home so she could weigh him more frequently and adjust his food intake up or down if needed (Figure 7). His weight on his first birthday was reported to be 32 kg, which according to the growth chart was exactly where he was predicted to end up!



CONCLUSION

Ultimately, our goal as veterinarians is to set pet owners up for success, and the best time to start this is at the early stages of puppy and kittenhood. Having conversations around nutrition, selecting an appropriate food, and advising on proper portion control are all part of the veterinary team's responsibility, along with monitoring weight and body condition, and advising on the use of low calorie treats and a gram scale to weigh food. Introduction of all these measures at an early stage can help to educate owners on how to ensure their pet is healthy and allow them to live a long and happy life.



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KITTEN VACCINATIONS AND IMMUNITY



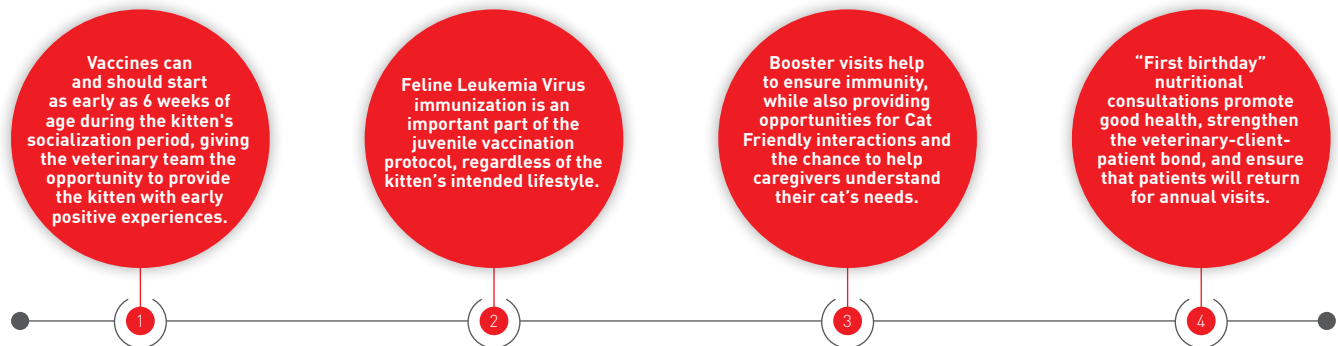
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Dr. St. Denis studied for her Bachelor of Science in Molecular Biology and Genetics at the University of Guelph and qualified in 1992 before obtaining a Master of Science in Immunology from the University of Toronto in 1994. She graduated from the Ontario Veterinary College (University of Guelph) in 1999 and earned Diplomate status with the American Board of Veterinary Practitioners (Feline Practice) in 2013. Dr St. Denis is a consultant on the Veterinary Information Network in feline internal medicine matters, and is immediate past president of the American Association of Feline Practitioners.

Ensuring kittens have an optimal vaccination schedule whilst creating positive patient experiences at the veterinary clinic can be a win-win situation, as Kelly St. Denis describes.

KEY POINTS



Introduction

Feline vaccinology has experienced dramatic shifts over the last few decades. While the infectious agents against which we vaccinate kittens have not changed greatly, in other contexts there has been immense change. There has been progress in our knowledge and understanding of some of these infectious agents and the role of vaccination in their prevention; there have been many changes in recommendations for timing, age and frequency of vaccinations and booster vaccinations; we have additional knowledge about maternally derived immunity and its impact on immunity; the scientific design of available feline vaccinations has changed dramatically; and the approved and recommended sites of injection have been modified. Furthermore, the way we interact with our feline patients has been revolutionized by the adaptation of Cat Friendly principles. These changes make

vaccinology in the feline species more challenging to implement but more rewarding than ever before. They also impact all life stages of the domestic cat, with the foundations for immunity and Cat Friendly visits being laid in the first year of life. This article will review vaccination protocols and their implementation for the juvenile pet cat primarily from a North American viewpoint, and the reader is encouraged to seek further detail for all life stages in the recently updated AAHA/AAFP guidelines¹ (1).



Maternal-derived immunity

Maternal immunity, in the form of maternally derived antibodies (MDA), is passively transferred from the immune queen to kitten during lactation.

¹ AAHA: American Animal Hospital Association; AAFP: American Association of Feline Practitioners

Transplacental transfer of antibodies is not significant in the feline species (2). The availability of immunoglobulins IgA and IgG to the neonate is impacted by the concentration of the proteins in colostrum, the volume ingested, and the capacity of the neonatal intestine to absorb the protein, all of which are largely time-dependent. The immunoglobulin concentration is highest in the colostrum, with levels rapidly decreasing 3 days post-partum (3). The neonate absorbs the immunoglobulins primarily in the first 24 hours of life, although evidence suggests that absorption decreases dramatically after only 16 hours (3). Kittens that do not ingest sufficient colostrum during the first 24 hours post-partum will be at risk of failure of passive transfer, increasing the potential for infectious disease during a period when the immune system is undeveloped.

MDA persist in the kitten for variable time periods, dependent on the antibody titer of the queen and the amount of immunoglobulin absorbed by the neonate. A nadir may be reached as early as 3 to 4 weeks of age (2), although some kittens maintain high levels beyond 16 weeks (4). While MDA provides protection in the immune incompetent neonate, it is described as one of the most common reasons for vaccine failure (1). Through a negative feedback mechanism, serum MDA can interfere with neonatal production of immunoglobulins, and its presence can also lead to neutralization of vaccine-delivered antigens, thus limiting the vaccine response. There is therefore a “window of susceptibility” between loss of MDA and development of individual immunity, when the MDA levels may be high enough to interfere with the development of vaccine-dependent immunity but insufficient to protect against natural infection (1). This window of susceptibility must be considered when developing vaccination protocols for kittens. For this reason, vaccinations against feline viral rhinotracheitis/calicivirus/panleukopenia (FVRCP) have increased likelihood of success if given every 2-4 weeks until a kitten is at least 16-20 weeks of age (1). The exact interval between booster vaccinations should follow manufacturer guidelines, but a final booster is ideally administered 3 to 4 weeks after MDA has decreased below interference levels, which can vary between litters, between kittens within litters, and with the infectious disease being vaccinated against. Recent guidelines (1,5) recommend replacing the 1-year FVRCP booster with a 6-month booster against FVRCP.



Vaccine concepts revisited – vaccine design

There are numerous commercial vaccines available worldwide that target several infectious feline agents. The 2020 AAHA/AAFP Feline Vaccination Task Force has categorized vaccines against these agents as being either “Core” or “Non-core” based on relative risk and vaccine efficacy and safety (Table 1). Vaccines are designed using a variety of approaches, including inactivated (killed), modified live (attenuated), and genetically engineered recombinant subunit vaccines. Each design is based on different strategies to induce immunity, with the selection depending on many factors including the infectious agent itself, applicable vaccine technology, host immune response, and potential side effects. A basic understanding of these differences, as well as an awareness of which vaccine design is being administered, is critical to understanding the impacts on the patient; these include the type of immunity, efficacy, and potential vaccine adverse events.

Killed vaccines contain inactivated viral particles incapable of setting up an active infection in the patient. Appropriate stimulation of the immune response often requires additional vaccine ingredients, which may include the use of adjuvants. These enhance inflammation at the site of injection, stimulate the innate arm of the immune system, and trigger the necessary immune responses. Compounds utilized in vaccine products include Complete Freund’s Adjuvant, aluminum salts, lipids in water-based emulsions, saponin-based adjuvants, and ligands (oligonucleotides). Response to vaccination with a killed vaccine is primarily antibody/humoral in nature, generally producing a weaker immune response compared with other technologies, with immunity lasting for shorter time periods. More frequent booster vaccinations are likely necessary.

Modified live (attenuated) virus (MLV) vaccines contain viral particles that have partial viability, with a reduced ability to infect host cells. This attenuated viral activity generates an immune response that mimics protection from natural infection, and involves both humoral (antibody-mediated) and cell-mediated immunity without inducing actual disease. The response to MLV is generally more rapid in comparison to killed vaccines. In the absence of MDA, only one dose of vaccine may be sufficient to provide protection.

Table 1. Vaccination recommendations for pet kittens. Vaccination protocols start as early as 4-6 weeks with boosters administered at 3-to-4-week intervals until 16 or 20 weeks of age for FVRCP, and at 3 to 4 weeks after the initial vaccination for FeLV and FIV.

Vaccine	First vaccine & boosters (weeks of age)
FHV*-1 +FCV (IN)	4 weeks + q 3-4 weeks >16-20 weeks
FHV-1 + FPV** + FCV*** (SC)	6 weeks + booster q 3-4 weeks >16-20 weeks
FeLV (SC)	8 weeks + 1 booster at q 3-4 weeks
Rabies (SC)	12-16 weeks + booster in 1 year
FIV (SC)	8 weeks + 1 booster at q 3-4 weeks

Legend: Grey boxes: core vaccines; pink box: non-core vaccines; IN: intranasal; SC: subcutaneous
*FHV = Feline Herpes Virus, **FPV = Feline Panleukopenia Virus, ***FCV = Feline Calicivirus

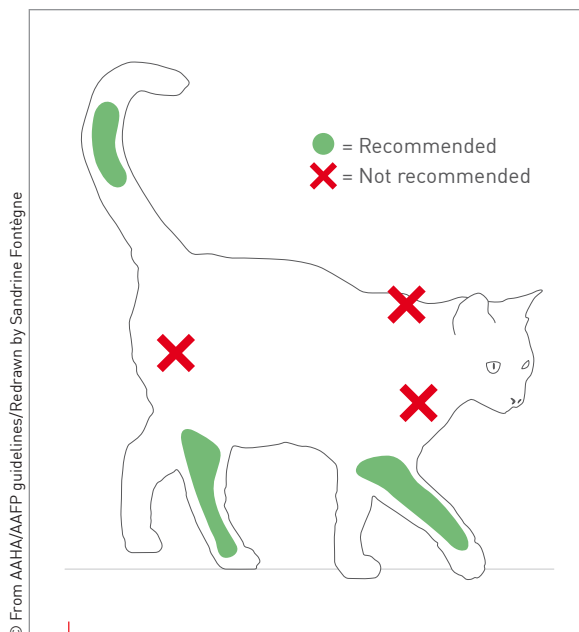
The most common recombinant vaccines in veterinary medicine contain a gene or genes encoding protein(s) from the infectious agent spliced into the genetic material of a virus from an unrelated species. For example, the gene for the rabies surface antigen was spliced into the Canary Pox Virus to create a recombinant rabies vaccination. The vaccine vector cannot cause disease in the feline species but allows presentation of a targeted viral antigen to the immune system.

●●● Vaccine concepts revisited – adverse events

Administration of vaccinations is a daily practice in veterinary medicine and is generally uneventful and low risk. As the immune system recognizes and responds to the vaccine, minor side effects may occur. This normal immune response includes the release of cytokines which, in mimicking the response to infection, will cause systemic effects such as fever, joint ache, and general malaise. An affected kitten may benefit from symptomatic-based treatment to reduce any ill effects, but the term “vaccine reaction” as applied to these types of natural side effects is ill-advised and can lead to mistrust of the vaccines by the caregiver. Explanation of anticipated natural responses to vaccinations and potential related side effects will assist in alerting the caregiver to these should they occur, will facilitate early treatment, and will avoid causing distrust of the inoculation.

Less commonly, feline patients may experience vaccine adverse events, which may include protracted fever, vomiting, diarrhea, and inappetence or anorexia. The latter may stem from untreated side effects, as described above. In the feline species it is rare to observe severe, acute reactions such as sudden onset vomiting, diarrhea, tachycardia, tachypnea, disorientation and/or collapse. If such acute reactions do occur, it is often prior to departure from the veterinary clinic, but caregivers should be aware of the potential so that the patient can be returned immediately for possible urgent care.

Vaccine injection site sarcomas (VISS) are the most reported cause of feline injection site sarcoma (FISS) (1). The rate of occurrence is low and varies geographically, and the development of FISS is complex and poorly understood. An inflammatory component at the injection site may play a role, although direct evidence for cause and effect is elusive. There may be a role involving genetic mutations, including those in tumor suppressor genes and oncogenes. The presence of inflammatory adjuvants in certain vaccine types has been hypothesized to be a contributing factor. Causal data remain inconclusive, although anecdotal reports suggest reduced incidence of VISS with the use of non-adjuvanted vaccines. Since FISS are highly invasive neoplasms which can be very difficult to remove surgically, any suspicious swelling or mass at a known or suspected



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Figure 1. Recommended vaccination sites are shown in green; sites which are often used, but which should be avoided, are shown in red. The vaccine injection site must be recorded in the patient’s records.

vaccination injection site should be monitored closely. The **3-2-1 protocol** provides guidance on how to handle these; a wedge biopsy should be obtained from any reaction at an injection site that persists beyond 3 months, is larger than 2 cm and/or increases in size within one month following injection (6). Excisional biopsies are not appropriate, as these will most likely miss margins, allowing the locally invasive FISS the opportunity to continue to spread, and making further removal challenging. Surgical excision requires a specific diagnosis and a planned approach that includes two fascial planes. With a lack of complete understanding of VISS etiology, and given the aggressive requirements for surgery, all feline vaccines should be administered below the elbow or stifle, or in the distal tail (**Figure 1**).

●●● Vaccine concepts revisited – kitten vaccine protocols

Preparing a vaccination plan for a kitten starts with considering the needs of the individual animal. Factors to consider include environmental risk factors, epidemiologic factors, vaccine availability and lifestyle factors. A caregiver may have very specific goals for their kitten’s future lifestyle; this might include status as a single, exclusively indoor cat, it may be living in a multi-cat household with constant outdoor access, or it may fall somewhere in between these two extremes. Whatever the plan, a cat’s lifestyle may well change in the future, so vaccination protocols should be developed with the assumption that exposure to other cats is a likelihood. Even where a caregiver is firm about

their goals for their kitten's indoor lifestyle, it should be recognized that indoor cats are in no way risk-free when it comes to infectious disease.

Developing a vaccination plan must also consider whether a specific vaccine is classified as core or non-core. Core vaccines are those which are recommended for all kittens regardless of lifestyle, including those with unknown vaccination history, and include those which protect against zoonotic disease such as rabies. Such vaccines should offer good protection against prevalent diseases of known significant morbidity and mortality. The AAHA/AAFP Task Force has designated Feline herpes virus-1 (FHV-1), Feline Calicivirus (FCV), Feline Panleukopenia Virus (FPV), rabies and Feline Leukemia Virus (FeLV) as core infectious agents against which vaccines should be given to all kittens (**Table 1**). Non-core vaccines against certain infectious agents are those which are considered optional, based on exposure risk, geographic distribution, and the patient's current and possible future lifestyle. Non-core vaccines include Feline Leukemia Virus (for cats older than 1 year), *Chlamydia felis* and *Bordetella bronchiseptica*. Vaccines for diseases which are of low clinical significance or which show a good response to treatment, and vaccines that show minimal to no field evidence for efficacy, or that have a relative increased risk of adverse events, are designated as "not recommended". Vaccinations currently not recommended by the task force include Feline Infectious Peritonitis Virus (FIPV).

Except for the intranasal FHV-1/FCV (which can be started as early as 4 weeks of age) vaccination should commence at 6 to 8 weeks in all pet kittens. This early start facilitates increased interaction with the veterinary team during the kitten socialization period. The initial FVRCP vaccination should be administered during this first visit. The AAHA/AAFP Task Force recommends administering boosters against FVRCP every 3 to 4 weeks until 16 to 20 weeks of age, with a further FVRCP booster at 6 months when MDA has waned, which is in lieu of the first annual booster. Intranasal FHV-1/FCV can start at 4 to 6 weeks of age, followed with booster vaccinations every 3 to 4 weeks until 16 to 20 weeks of age. FeLV vaccination is considered a core vaccination for pet kittens, and should commence at 8 weeks of age, with a second dose administered 3 to 4 weeks later, followed by a booster at 1 year of age (**Table 1**).

Rabies is a zoonotic disease with high mortality rates and is a significant public health concern worldwide. Mandatory vaccination of pets against rabies is common in many communities, and the veterinary team will need to consult local legislation to make accurate vaccination recommendations. Timing for rabies vaccinations in the kitten should be based on the manufacturer's instructions, often starting no earlier than 12 weeks and most commonly at 16 weeks of age. A booster should be administered

at one year of age. Beyond this point, vaccines which have been legally approved for an extended 3-year usage can be administered at this interval. Annual vaccination for all other products is recommended.



Retrovirus testing and vaccination

Retrovirus testing is recommended for all newly acquired kittens (7), with additional FeLV and FIV testing recommended at 30 and 60 days respectively following the first test. For ease of use, the second set of testing can be conducted at 60 or more days. The retrovirus status of kittens should be known, with at least one negative test confirmed prior to vaccination against FeLV or FIV. Vaccination against FeLV does not interfere with current standard testing methods, which measure for viral antigen or viral RNA. Standard testing for FIV includes measurement of FIV-directed antibodies, and therefore vaccination will result in false positive testing. This is an important consideration in certain geographical areas such as Australia, where FIV vaccinations are commonly administered, and antibodies generated from FIV vaccines may persist for more than 7 years (8). The 2020 Feline Retrovirus Testing and Management Task Force recommends follow-up testing for all FIV and FeLV positive cases, using a different manufacturer's ELISA test or a different test type (7).

Kittens have an increased risk of infection with FeLV upon exposure, with risks declining with increasing age (7) and therefore, as noted above, vaccination against FeLV is recommended for all kittens regardless of lifestyle. Based on current studies, there is insufficient evidence to show that vaccination prevents all outcomes of FeLV infection, however there is sufficient protection to warrant use of the vaccine (7). Despite assumptions to the contrary, a 2019 Australian study showed that the threat of FeLV in the general cat population in that country was still high, and warranted ongoing testing, vaccination, and appropriate management of potentially infected or known infected populations (9).

The FIV vaccination has limited availability worldwide; however, in areas such as Australia, where FIV has a higher prevalence, the vaccine is still available. In these areas, kittens living at increased risk for FIV exposure (lifestyle, geographical) are recommended to receive the FIV vaccination series wherever possible; this should start at 8 weeks of age, with a second dose 3-4 weeks later and boosters given annually thereafter. Retrovirus status should be confirmed negative prior to vaccination, as false positives can occur as early as a few weeks after first vaccination. The 2020 Guidelines provide additional information on testing and vaccination recommendations based on lifestyle and geographical location (7).



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Figure 2. Warm blankets sprayed with pheromone will calm feline patients during their clinic visit.

staff and with high quality control standards for incoming ingredients and outgoing final products, demonstrating a commitment to safe, high caliber diets. As kittens transition to adulthood, a “first birthday visit” with a veterinary team member to assess body weight and body condition score will help keep kittens on track. This visit is a perfect opportunity to assist the caregiver in transitioning the pet to adult food, promoting a better understanding of weight management, and enhancing the veterinary-client patient bond. It can also provide an opportunity to ensure all booster vaccinations are up to date, or to pre-book appointments to meet upcoming vaccine needs.

●●●● The kitten friendly visit: forging lifelong bonds

In 2012 the International Society of Feline Medicine (ISFM) and American Association of Feline Practitioners (AAFP) developed the Cat Friendly Clinic and Cat Friendly Practice Programs, respectively. Since then, “Cat Friendly” care has become a well-established principle in feline medicine around the world, and the concept applies to kitten visits as much as any other age group. The domestic cat’s socialization period starts around 2 to 3 weeks of age and ends around to 9 to 10 weeks of age (10), and this is a crucial period in which to develop good experiences around the veterinary visit. With such a short window of opportunity, it is essential that a kitten has a positive experience during a clinic visit. With vaccination protocols starting at 4-6 weeks of age the veterinary team has perhaps only one to three opportunities to create a positive Cat Friendly experience. Veterinary visits should include Cat Friendly interactions, with plenty of positive reinforcement, conducted with minimal restrictive handling or

●●●● Nutrition for life

Nutrition provides the building blocks for normal, healthy growth and sets the stage for a healthy adulthood. The guidance of the veterinary professional is invaluable in this matter, enhancing the veterinary-client relationship, and building trust for future visits, including vaccination visits. Even before the first clinic appointment, the veterinary team can provide direction on feeding as kittens transition from nursing to solid food. To develop food texture experiences, it is ideal to expose kittens to both canned and dry food, in a variety of textures and flavors, particularly during the socialization period. This will facilitate acceptance of any necessary dietary changes during adulthood. When choosing a food, high quality, balanced kitten formulations are ideal, preferably sourced from a manufacturer who has veterinary nutritionists on

Table 2. Suggestions for Cat Friendly care principles as applied to each step of the veterinary visit, starting at the caregiver’s home. These are essential to providing positive, rewarding veterinary experiences early in the cat’s life.

Location	Suggestions
At home	<ul style="list-style-type: none"> • Choosing the right cat carrier, including an easily removeable lid • Training the cat to use the carrier • Preparing the cat and carrier for travel • Following safe automobile travel practices
Reception room	<ul style="list-style-type: none"> • Cat-only waiting zone or cat-only appointment hours • Consider putting cat and caregiver into examination room on arrival • Elevated tables for carriers to sit on • Blankets sprayed with pheromone to cover carriers • Minimize waiting times
Examination room	<ul style="list-style-type: none"> • Longer appointment times: >30 minutes • Place carrier on floor with door open • Allow the cat to come out of the carrier on their own • If patient will not voluntarily come out of carrier, remove, or open carrier lid and gently lift patient out. Avoid pulling, shaking and other aggressive maneuvers that will frighten the cat. • Utilize warm, pheromone-sprayed blankets to lay under and over cat during examination (Figure 2) • Patients too frightened for the examination should receive anxiolytic and sedative medications
Injections & blood sampling	<ul style="list-style-type: none"> • Utilize toy and food distractions whenever possible • Consider anxiolytics, analgesics and/or sedatives • Eliminate restraint methods including scruffing, pinning, limb restraint and muzzles



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Figure 3. It is important to put kittens at ease in the clinic, using distraction methods such as food, toys, head-rubs and other accepted forms of positive reinforcement.



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Figure 4. Kittens can be distracted with food before being vaccinated at or below the elbow.

restraint, setting the stage for the patient and owner's comfort with future veterinary visits and forging a stronger veterinary-client-patient relationship. Development of Cat Friendly care can start with small changes in the clinic (11), and both the ISFM and AAFP offer programs to assist with this. Individuals within a practice may also elect to become "Cat Friendly Certified" through the AAFP.

Even minor changes will make a difference in the veterinary experience for kitten, caregiver, and the veterinary team (**Table 2**). Kittens are busy and playful, so to complete a physical examination and administer the necessary vaccinations and other medications the veterinarian must be creative in interacting with kittens. Forceful restraint and aggressive handling just to "get the job done" or because the "kitten won't cooperate" will set everyone up for failure during future visits. Human impatience can contribute to so-called "fractious" behavior. The way ahead is to take a patient-focused approach that seeks methods to put the kitten at ease, distracting with food, toys, head-rubs and other accepted forms of positive

reinforcement (**Figure 3**). With appropriate diversions, administration of vaccines at the recommended injection sites (**Figure 4**) is possible.



CONCLUSION

Kitten vaccinations are essential to ensuring appropriate immunity to prevalent and potentially harmful infectious disease. They are a key component of overall preventive healthcare for kittens, but equally as important, they provide interaction opportunities during which the veterinary team can set the stage for affirmative experiences and positive future interactions. Employing Cat Friendly principles while preventing disease through appropriate vaccinology based on patient needs sets the foundation for future feline wellness.



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ANTIMICROBIAL USE IN PUPPIES AND KITTENS



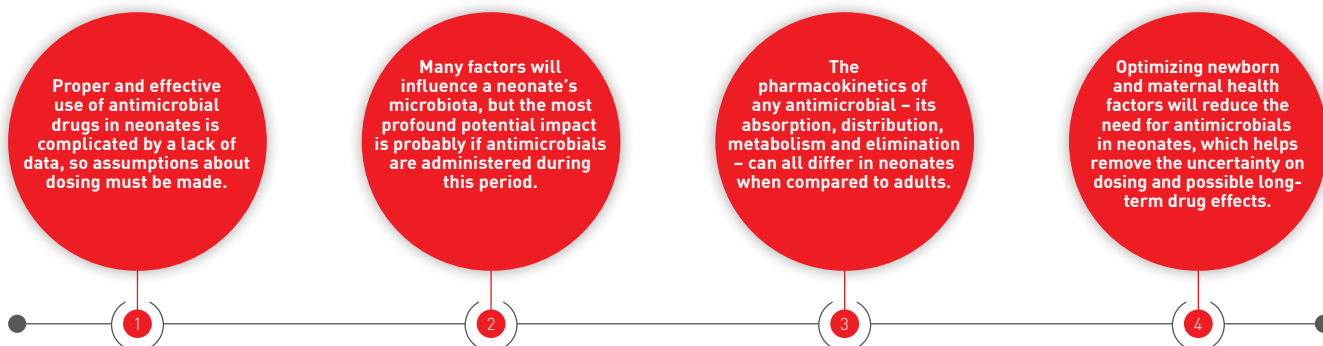
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How should we approach the problematic choice of antibiotic in young puppies and kittens? J. Scott Weese offers a practical guide to this all-too-common scenario in small animal practice.

KEY POINTS



Introduction

It is well understood that puppies and kittens are not just smaller versions of dogs and cats, respectively, but beyond this, puppy- and kittenhood encompasses a highly dynamic period of life, where there are substantial changes in various factors that influence the pharmacokinetics of drugs and the risks of adverse events. The variable and rapidly changing physiology in early life can impact both efficacy and safety of antimicrobial therapy, and there is limited species- and drug-specific information available for this critical neonatal period. Clinical trials regarding optimal antimicrobial regimens, and even data on whether antimicrobials are beneficial, are largely non-existent for young puppies and kittens. These factors complicate development of evidence-based

treatment plans that maximize the potential therapeutic benefits while minimizing the risks. Furthermore, the scope of potential risks is also poorly understood, and even where the risks are known, our comprehension is often limited, with restricted information about incidence and long-term impact in clinically relevant situations.

The neonatal period is also highly variable and changeable microbiologically, as the individual develops its critical and complex commensal microbiota. Consideration of "adverse effects" has typically focused on drug-patient interactions, with limited thought as to drug-microbiota interactions. The impact of antimicrobials on the commensal microbiota is an area that is of increasing interest and attention, but one where objective data are very sparse. Proper cost-benefit assessment and use



Figure 1. An animal's age can affect the absorption of an antimicrobial; drugs given orally are particularly prone to being affected.

of evidence-based treatment regimens is therefore a challenge in the management of neonatal infectious disease.

●●○○ Antimicrobial pharmacokinetics in neonates

Pharmacokinetics involves what the body does to a drug after administration, something that is a function of absorption, distribution, metabolism and elimination. All of these factors can be different in neonates when compared to adults, and are also changeable throughout the neonatal period. The impact on pharmacokinetic properties (e.g., half-life, bioavailability, volume of distribution) can impact the potential for efficacy, as well as adverse event risks.

After administration, antimicrobials must be absorbed into the circulation, and this may be unpredictable or different in neonates. Oral absorption in particular can be impacted by age (**Figure 1**). In the first 24 hours of life, absorption may be very high, resulting in unexpected and possibly unwanted bioavailability. Potentially toxic drugs that are not meant to be highly absorbed (e.g., neomycin) should therefore be avoided in very young individuals. Nursing can also impact the absorption of some drugs, either because a drug binds to milk components, or because it makes it impossible to administer a drug on an empty stomach (**Figure 2**). Slower gastric emptying can be a factor, as this can delay absorption but also potentially ultimately increase bioavailability from longer mucosal contact (1). A higher gastric pH than adults – a common situation in nursing individuals – can decrease absorption of drugs that are weak acids (e.g., fluoroquinolones); one study reports failure of oral administration of enrofloxacin to produce therapeutic drug levels in nursing 6–8-week-old kittens, which highlights potential issues (2). So while there is little information about commonly used drugs in puppies and kittens, there are competing factors that may increase or decrease oral bioavailability in this age of animal.

Other routes of administration may also be used. Administration by gastric tube may be required in puppies and kittens that cannot be effectively treated *per os* but are deemed adequately stable and to have good gastrointestinal motility. Subcutaneous administration likely results in similar drug levels to intravenous and oral administration, but may be affected by inadequate hydration and perfusion, something that can be of greater likelihood in compromised neonates. Intra-osseous administration is also an option for some drugs.

After absorption, antimicrobials distribute through serum to tissues. Neonates have a larger fraction of extracellular fluid, up to twice as large as adults, along with less adipose tissue and muscle, resulting in increased distribution of water-soluble drugs (e.g., penicillins, cephalosporins, aminoglycosides) and correspondingly lower tissue levels. Lower serum protein concentrations and lower affinity of protein binding in neonates may increase free (active) drug levels of highly protein-bound compounds such as cefovecin, and this also increases the rate of elimination. The free antimicrobial at the affected site is the factor that will influence potential antibacterial efficacy, so the clinician should be aware that a dosage may need to be increased or decreased depending on the drug and individual patient.

Metabolism may also be impacted by lower levels of enzymes involved in hepatic drug metabolism, particularly in the first four weeks of life. The kidneys are the site of elimination of many drugs, and renal excretion is impacted by glomerular filtration rate and renal tubular transport mechanisms, both of which change over time. This is mainly relevant very early in life, as renal and hepatic function are likely at near-adult levels by 4–6 weeks of age. Before that timepoint there may be increased risk of toxicity, particularly from drugs such as chloramphenicol that have narrower margins of safety and rely on hepatic metabolism. The half-life of enrofloxacin in



Figure 2. Nursing can affect antibiotic uptake by neonates, as some antibiotics can bind to milk products, and also because nursing prevents drugs being given on an empty stomach.

2-, 6- and 8-week-old puppies has been shown to be significantly shorter than in adults because of a greater rate of elimination, resulting in lower peak drug concentrations [2].

●●● Dosing adjustments for neonates

A lack of data creates challenges in tailoring treatments for neonates. It is apparent from the above that there may be factors which can lead a need for higher doses (e.g., larger volume of distribution) or, conversely, lower doses or prolonged dosing intervals (e.g., delayed clearance). Given that metabolism and excretion can be unpredictable in young individuals and will vary greatly by age in the first month of life, and between individuals, predicting the pharmacokinetics at the patient level is difficult, and there are no evidence-based recommendations for puppies and kittens. For highly water-soluble drugs with wide margins of safety (e.g., beta-lactams) dosing at the high end of the adult dose with the adult dosing interval is reasonable, particularly in individuals

that are four weeks of age or older. Historic literature recommendations that may advise reduced adult doses (sometimes substantially) are unsubstantiated and should be avoided. **Table 1** identifies common antimicrobials and suggests likely dosages for use in young animals. Once puppies and kittens have reached 6 weeks of age, normal adult doses can probably be comfortably used for most antimicrobials.

●●● Drug-specific issues

Aminoglycosides

Aminoglycosides have excellent activity against Gram negative bacteria (including most multidrug resistant bacteria and *Pseudomonas* spp.) and good staphylococcal activity, with limited efficacy against other Gram positives and no activity against anaerobes. They must be administered parenterally and can be associated with nephrotoxicity and ototoxicity; the risks are lower with amikacin compared to gentamicin. Nephrotoxicity risks are greatest with dehydration or poor perfusion, but the incidence of toxicity is unknown. While it is common

Table 1. Potential dosing approaches for young puppies and kittens.

Drug and adult dose	Neonate considerations
Amikacin 10-15 (cats) or 15-30 (dogs) mg/kg IV/SC/IM q 24h	Greater distribution than in adults. Reduced renal elimination. Risk of oto- and nephro-toxicity. Variable dosing recommendations in human infants. Consider extending dosing interval for young puppies/kittens. Therapeutic drug monitoring is ideal. Reserve for serious infections.
Amoxicillin 11-20 mg/kg PO q 8-12h	Greater distribution and wide margin of safety. Wide dosing range in human infants, so 20-50 mg/kg q 12h, but q 8h dosing and lower doses should be considered in older (>1 month) individuals.
Amoxicillin + clavulanic acid 13.75-20 mg/kg PO q 12h	Little is known about clavulanic acid pharmacokinetics. 15 mg/kg PO q 12h has been recommended in humans, but higher doses of amoxicillin are typically used. Given potential adverse effects from clavulanic acid, lower doses than for amoxicillin alone are reasonable (e.g., 15-20 mg/kg PO q 12h)
Ampicillin 20-40 mg/kg IV q 4-8h	Greater distribution and wide margin of safety. 50 mg/kg IV q 4-6h. Higher doses may be appropriate in some situations.
Ceftiofur sodium 2.2 mg/kg IV/SC/IM q 12-24h	2.5 mg/kg SC q 12h Different ceftiofur preparations are available. Ceftiofur crystalline-free acid is best avoided because the pharmacokinetics of this sustained release formulation are unknown and may be unpredictable in young puppies/kittens.
Cephalexin 22-30 mg/kg PO q 12h	Adult doses are likely appropriate; high end of the dosing range is probably ideal.
Cefotaxime 40-50 mg/kg IV/SC/IM q 8h	Good choice for broad spectrum systemic coverage in critically ill patients. High end of adult dosing range is probably appropriate. Consider prolonged dosing interval (q 12h) in animals <1 week of age
Clindamycin 10-15 mg/kg PO/IV q 12h	Adult doses are likely appropriate, but lower end of dosing range should be considered in very young (<1 week) animals
Doxycycline 5-10 mg/kg PO/IV q 12-24h	Tooth staining is not a concern. Regular adult doses are likely appropriate.
Fluoroquinolones Enrofloxacin Dogs: 5-20 mg/kg PO/IV q 24h Marbofloxacin 2.75-5.5 mg/kg PO q 24h Orbifloxacin 2.5-7.5 mg/kg PO q 24h Pradofloxacin Dogs: 3-4.5 mg/kg PO q 24h; Cats: 7.5 mg/kg PO q 24h	Greater distribution. Reduced renal elimination. Avoid in growing animals unless essential. Short-term use at regular doses probably poses limited risk but risk of arthropathy or tendinopathy remains. Avoid enrofloxacin in kittens because of retinopathy. Low end of typical q 24h doses may be best in very young (<1 week) individuals

to see statements that aminoglycosides should be avoided in puppies and kittens, there are no actual data supporting such a recommendation, and this class of drug is used, when needed, in neonates of various other species, including humans. In fact, gentamicin has been reported as being the second most commonly used antimicrobial in human neonatal intensive care units (NICUs) after ampicillin (1). While not recommended for routine use, aminoglycosides may be useful for culture-directed treatment of many multidrug resistant bacteria, and as an empirical choice for Gram negative coverage in particularly high-risk patients (e.g., sepsis), where the risk of toxicity is outweighed by the risk of imminent death from infection. Ensuring good perfusion and hydration will reduce risks. An important point to note is that early signs of toxicity seen in adults (the development of granular casts) are not as consistently noted in neonates, complicating the monitoring for such cases.

Little is known about dosing of this drug class in young puppies and kittens. Neonates will have wider distribution of the drug but reduced renal elimination. In foals, higher doses are used compared to adult horses (e.g., amikacin 20-25 mg/kg q 24h vs. 10-15 mg/kg q 24h), but in neonatal babies the drug dosage tends to be similar to adults, although with an extended dosing interval – for babies of normal birthweight less than one week of age, q 30-36h administration has been recommended (1), but drug monitoring typically guides both dose and frequency. In theory at least, assessment of peak and trough drug levels can allow for better tailoring of doses for the individual, which could require a higher dose (because of greater distribution) but longer dosing interval (because of decreased renal elimination).

Doxycycline

Doxycycline is a broad-spectrum antimicrobial with activity against a range of Gram positive, Gram negative, vector borne and atypical bacterial pathogens. While tetracycline use can result in tooth staining if used in growing individuals (3), those risks are not present with doxycycline, as it does not have the same affinity for binding to calcium as tetracycline. It is therefore not contraindicated in young children¹, and there is no need to avoid its use in puppies and kittens because of concerns about tooth staining or development. Earlier concerns about tooth staining in children likely contributed to minimal investigation of using doxycycline in neonates, as little information is available. No significant differences in pharmacokinetics have been identified in 2 to 8 years of age vs. older children (4), but data for younger children are lacking. Since it is generally regarded as safe – dosing is not altered in human patients with renal compromise – adult doses are reasonable for kittens and puppies.

Cephalosporins

Cephalosporins are generally safe and effective options in young animals. Cephalexin is commonly used and provides excellent Gram-positive coverage

(e.g., against *Staphylococcus* and *Streptococcus* spp.) with rather limited Gram-negative effects. Given orally and with a wide safety margin, it is a good option for situations where the focus is on Gram positive pathogens.

Third generation cephalosporins such as cefotaxime and ceftiofur are good, extra-label options for situations where broad-spectrum coverage is needed. This drug class provides excellent activity against Gram negatives while retaining good activity against Gram positives, but has no activity against enterococci, and most are ineffective against *Pseudomonas* spp. (except anti-pseudomonal cephalosporins such as ceftazidime). These antibiotics are good options for culture-directed treatment and for empirical treatment of seriously ill patients where reliable broad-spectrum coverage is needed. Cefotaxime is also commonly used when central nervous system (CNS) infection is suspected, because of reasonable blood-brain barrier penetration and the ability to administer high doses safely. Oral cefpodoxime can also be used.

As with other beta-lactams, renal elimination is reduced in early life, although the wide safety margin means that this may be of limited concern. However, human neonates are given higher doses and longer dosing intervals (50 mg/kg q 12h for 0-7 days of age and q 8h for 7-28 days of age) compared to the recommendations for babies older than 28 days of age (37.5 mg/kg q 6h) (1).

Cefovecin is not recommended for routine use; as a highly protein-bound drug, its pharmacokinetic properties may be quite different in neonates. It is also a poor choice for *E. coli*, apart from lower urinary tract infections. Since this drug is best positioned for treatment of superficial folliculitis and bacterial cystitis in patients where administration is problematic, there is limited indication in puppies and kittens.

Clindamycin

Clindamycin is another oral option with excellent activity against Gram positive and anaerobic bacteria. In humans, daily doses of 15-20 mg/kg are recommended for babies less than 28 days of age, compared to 20-40 mg/kg in older babies (in both cases, divided over 3-4 doses), although 9 mg/kg q 8h has been suggested for all infants of normal birth weight (5). No data are available for dogs and cats, and similar dosing regimens to those used in adults are probably reasonable. The lower end of the dosing range could be considered for very young individuals, as a result of presumed slower clearance.

Fluoroquinolones

Fluoroquinolones are excellent Gram-negative drugs, with less Gram-positive activity and no (apart from pradofloxacin) activity against anaerobes. The most recognized concern with administration of fluoroquinolones to growing animals is development of cartilage defects. Toxic effects of enrofloxacin on canine chondrocytes and tendon cells have been

¹ www.cdc.gov/rmsf/doxycycline/index.html

identified *in vitro* [6,7] and the US product insert for enrofloxacin indicates that microscopic changes in articular cartilage developed in older puppies with 30 days dosage at 5-25 mg/kg. However, clinical abnormalities were not reported in 2-week- or 29-34-week-old puppies given 25 mg/kg/daily for 30 days. Two recent studies in foals have not identified cartilage lesions after treatment of mares during late pregnancy [8,9], but severe cartilage erosions were identified in 2/2 foals treated postnatally using standard doses [9]. This is consistent with an earlier report (only published as an abstract), which noted articular cartilage damage in 4/4 treated neonatal foals [10]. The limited number and size of studies complicates safety assessment, as does the complete absence of field studies using clinically applicable doses over a range of ages. There may also be concerns about tendon rupture (based on canine cell culture study [7]), but the incidence of this in human adolescents is very low [11] and nothing is known about the risks in dogs and cats.

Retinopathy is also recognized with this class of drug, reported as a dose-dependent problem in cats treated with enrofloxacin [12]. Lower doses (5 mg/kg q 24h) have been recommended to reduce the risk; however, this may not be adequate for young animals with potentially decreased renal clearance. Lower doses are also undesirable for a concentration-dependent drug where high peak drug levels and AUC:MIC ratios² are important for bactericidal activity.

Overall, the risks posed by short duration use of clinically relevant doses in puppies and kittens are unclear, although they are probably higher in very young individuals. However, there are few indications for fluoroquinolone use in puppies and kittens, as other safer drugs that provide a similar antimicrobial spectrum (*e.g.*, 3rd generation cephalosporins) are available. Their use could be considered, ideally for a short duration, in limited situations where other routine antimicrobials are not indicated for bacterial or patient factors, as the benefits may outweigh the risks. Lower doses might reduce the risk but also may be undesirable from a bactericidal efficacy standpoint, so the focus is probably best on minimizing duration of treatment rather than reducing the dose.

Penicillins

Antibiotics in this category, including potentiated penicillins, are widely used in neonates, particularly oral amoxicillin and clavulanic acid, and parenteral ampicillin. They are also widely used in neonates of other species, with ampicillin being the most commonly used drug in human NICUs [1]. There may be greater distribution and slower elimination in neonates, something that has been shown in puppies with ampicillin, with a corresponding dosing recommendation of 50 mg/kg IV q 4-6h for 6-week-old puppies [13]. Higher doses could be considered for younger puppies. In humans,

² AUC- area under curve; MIC = minimum inhibitory concentration



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Figure 3. The microbiota of a puppy or kitten is influenced from the moment of delivery (if not before) and events such as delivery by caesarean section may have a long-term impact on an animal's microbiome.

a neonatal dose of up to 200 mg/kg q 6h is used, compared to 20-40 mg/kg q 4-6h for adults. Ampicillin can also be administered intra-osseously to puppies and kittens at the same dose as for IV use, when venous access is not available [13,14].

A similar approach can be taken with amoxicillin, a drug that is largely analogous to ampicillin but with excellent oral bioavailability. Given the larger volume of distribution and safety, higher doses have been recommended in human neonates (50 mg/kg PO q 12h) [15]. Since the half life is short, more frequent (q 8h) dosing should be considered in older puppies and kittens (*e.g.*, >1 month). Amoxicillin-clavulanic acid is a very commonly used drug in neonates and can be obtained in an easy-to-use oral suspension. Amoxicillin pharmacokinetic issues are as described above, but little is known about clavulanic acid, so as a result, use of the high end of normal dosing ranges would be reasonable.



Antimicrobials and the commensal microbiota

The body contains a vast microbial population (the microbiota) and its complement of genes (the microbiome). While there have been tremendous advances in our ability to study these complex microbial populations that are present in the gut, respiratory tract, skin and other sites, understanding how these populations interact with the host, and the impact to and from the microbiota, remain unclear. Yet it is undeniable that the microbiota (particularly the intestinal fraction) has profound and complex interactions with the body, both locally within the gut and beyond.

At the time of birth, a puppy or kitten is inundated with microbial exposures, from the moment of delivery (if not before) and continuing throughout life. Neonates are exposed to the dam's microbiota from her vagina, skin, milk, respiratory tract and intestinal tract, as well as the microbes from the environment, human handlers and any other contacts (**Figure 3**). These early exposures shape

the development of the microbiota, and some can have long-lasting impacts. For example, human babies born by caesarean section develop a microbiota that is different from those born vaginally, and these changes can persist for months [16]. However, probably the most profound influencer of the microbiota is antimicrobial exposure, as gut microbiota can be significantly impacted by antimicrobial therapy [17-19]. These impacts can persist well beyond the time of treatment, and such therapy could disrupt the important development of the commensal microbiota and influence its complex interactions with the body.

A key aspect of immunological development is tolerance, where the body learns how to regulate the immune response and not respond (or over-respond) to the massive commensal antigenic burden. For example, antibiotic usage in infants has been associated with increased risk of asthma, linked to changes in the gut microbiota [20]. Other studies have also reported associations between antimicrobial use in children and subsequent risk of allergic disorders, including asthma, atopy and food allergy [21-23]. While this has not been studied in dogs and cats, it is reasonable to suspect that changes in the gut microbiota from early antimicrobial use could similarly impact the risk of immunologically-mediated diseases such as atopy and food allergy. Antimicrobial use in the mother during pregnancy can also impact the microbiota in humans (and presumably other species), and prenatal antimicrobial exposure is associated with increased risk of allergic disease in humans [23]. While antimicrobials are necessary for treatment of bacterial diseases, these concerns highlight the need for good antimicrobial stewardship. Measures to reduce the risk of disease [e.g., good management, proper post-natal care] with antimicrobial use limited to where it is clearly indicated, can presumably have long-lasting benefits on puppy and kitten health.

●●● Examples of antimicrobial use in neonates

Respiratory tract disease

Infectious respiratory tract disease is common, especially in kennel and shelter settings that involve abundant animal movement and mixing. A range of pathogens can be involved, only a subset of which are bacterial. Even when bacterial pathogens are involved, antimicrobial treatment is not always required, with the decision being influenced by disease severity and chronicity, if there is lower respiratory tract involvement, and the animal's age.

Doxycycline is a good option for upper respiratory tract infection where it appears to have a bacterial component, or if there is concern about progression to bacterial pneumonia. This drug is also indicated if *Mycoplasma* spp. is suspected to be involved, although determining the relevance



“Penicillins have a wide safety margin in neonates.”

J. Scott Weese

of this organism can be challenging. Amoxicillin/clavulanic acid may be considered for mild to moderate disease, but is suboptimal compared to doxycycline because of resistance in some important pathogens [e.g., *Bordetella* spp.], no activity against *Mycoplasma*, relatively poor activity against beta-lactamase producing Gram negative bacteria, and relatively poor penetration of epithelial lining fluid.

With more severe or rapidly progressive disease, broad spectrum coverage is indicated. Parenteral treatment is usually indicated with this severity of disease [e.g., cefotaxime, ceftiofur, ampicillin + amikacin, clindamycin + amikacin]; however, of those, only clindamycin has some activity against *Mycoplasma*, and that is only marginal. Since this organism probably plays, at best, a co-infection role in patients with serious disease, these drugs remain good options for individuals with evidence of severe bacterial pneumonia, with or without sepsis. Oral treatment can be used in patients that have good gastrointestinal motility; options include cefpodoxime, but this should be avoided in severely ill patients. When ocular involvement is the main clinical issue, topical antimicrobials may be all that are required.

Septicemia

Septicemia is an acutely life-threatening condition that requires prompt and effective antimicrobial therapy. While culture-directed treatment is ideal, based on blood samples or culture of specimens from other affected sites, results are not available until days into treatment. Prompt and effective empirical treatment is therefore required, and unless a cause is strongly suspected [e.g., development of sepsis from a known septic focus from which culture results have been obtained], empirical broad-spectrum coverage is needed, with particular efficacy against enterobacteriales, staphylococci and streptococci species. Parenteral administration is indicated because of the potential for poor oral absorption, with the IV route used whenever possible. Various options for broad spectrum coverage include a 3rd generation cephalosporin [e.g., cefotaxime, ceftiofur], or combinations of clindamycin and

amikacin or ampicillin and amikacin. Cefotaxime or ceftiofur are likely safer options initially in highly compromised patients, because of the increased risk of nephrotoxicity and ototoxicity in dehydrated or otherwise poorly perfused patients, and is a common recommendation for human neonatal sepsis, with or without ampicillin. Cefovecin is not indicated because of its inactivity against *E. coli* in tissue and unclear pharmacokinetics in neonates. If enterococcal involvement is suspected – most often a concern in hospital-associated infections – ampicillin should be part of the chosen regimen (e.g., ampicillin + cefotaxime, ampicillin + amikacin).

Neonatal diarrhea

Neonatal diarrhea is common in most species and can have myriad infectious and non-infectious (e.g., dietary) causes. Diarrhea itself is not an indication for antimicrobial treatment, and indeed might be contraindicated, as the impact on the microbiota could be detrimental. Antimicrobial therapy decisions should be based on the systemic status of the individual and whether there is reasonable concern that the patient is, or is at high risk of becoming, septic. Altered mental status, abnormal body temperature and bloody diarrhea would raise concerns about bacterial translocation and sepsis, and are all reasonable

indicators for initiating antimicrobial therapy. Since antimicrobials are directed at treating or preventing sepsis, the approach is the same as for sepsis (e.g., cefotaxime, ceftiofur).



CONCLUSION

Antimicrobials are potentially life-saving drugs, but they can also be life-altering through adverse effects and long-term developmental impacts. Proper and effective use of antimicrobial drugs in neonatal puppies and kittens is complicated by a lack of data, so assumptions about dosing must be made. Differences between young animals and their adult counterparts must be considered when choosing drugs and dosing regimens, to maximize the likelihood of efficacy and minimize the risk of adverse effects. Above all, efforts should be taken to optimize maternal and newborn health in order to reduce the need for antimicrobials, removing issues about uncertain dosing and long-term effects.



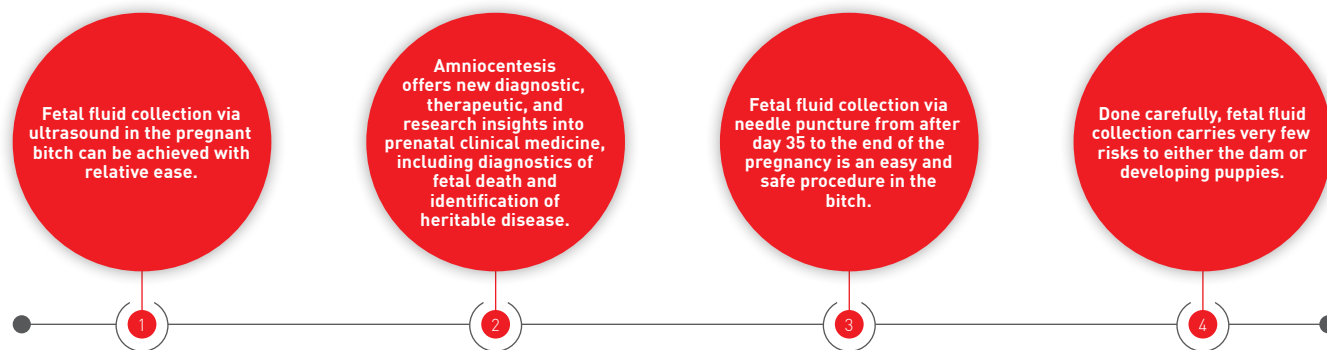
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FETAL FLUID CENTESIS IN THE BITCH

To date, amniocentesis has rarely been used in veterinary medicine, despite having tremendous potential for both clinical and research applications; this paper discusses an established method for fetal fluid sampling in bitches.

KEY POINTS



Introduction

Breeders invest much time and effort in designing the best breeding protocols to ensure healthy litters, but there is currently very little information relating to the immediate environment of the canine fetal “unit”. The fetal membranes contain the developing puppy throughout pregnancy and, along with the placenta, play an integral role in fetal growth and progression (1), as they are essential for the metabolic, gaseous, and hormonal exchanges between dam and fetus (2). The fetal membranes of the canine species are the allantois, amnion, chorion and yolk sac (3), but the ones pertinent to fetal fluid sampling in this species are the amnion and the allantois (**Figure 1**).

What are fetal fluids?

The amniotic cavity provides physical protection for the developing fetus within a liquid medium (4), the amniotic fluid. This is a complex biofluid which allows both mechanical and antimicrobial protection for the fetus as well as lubrication, nutrition, and growth factors, all of which are important for normal development (5). Amniotic fluid is formed with contributions from oral, nasopharyngeal, tracheal and pulmonary secretions, and urine excretion from the conceptus (6).

The allantoic fluid in carnivores accumulates within the allantoic membrane surrounding the amnion (7). The allantoic sac grows to line the chorionic sac

almost entirely and persists until parturition. It communicates with the urinary apparatus of the fetus and acts as a waste reservoir for fetal metabolic products (4). The main mechanisms for the initial accumulation of allantoic fluid are probably the transmembrane transport and the secretory activity of the extra-embryonic membranes, and – later in pregnancy – from the mesonephros, metanephros and kidney secretions (8).

As a result, fetal fluid can be collected from both amniotic and allantoic cavities in the dog (**Figure 2**). Any change in the volume and composition of either fluid may indicate the metabolic, pathologic or developmental status of the fetus at a particular gestational stage (8). Fetal fluid collection in the bitch is feasible from the second half of pregnancy onwards, as there is sufficient fluid and the amniotic and allantoic membranes are discernible on ultrasound scan (9). Centesis is performed using a needle via a transabdominal approach and under continuous ultrasound guidance (10).

Why perform fetal fluid centesis?

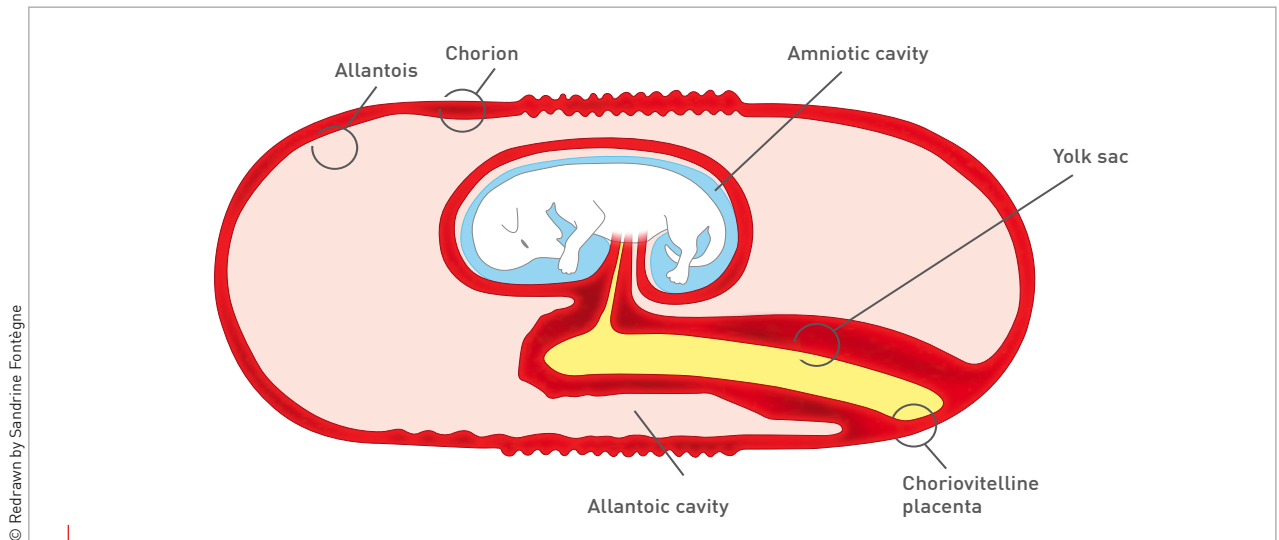
The main reason for collecting fluid is to allow antepartum assessment of fetal viability and detection of disease (11-13). Analysis of amniotic biofluid is used



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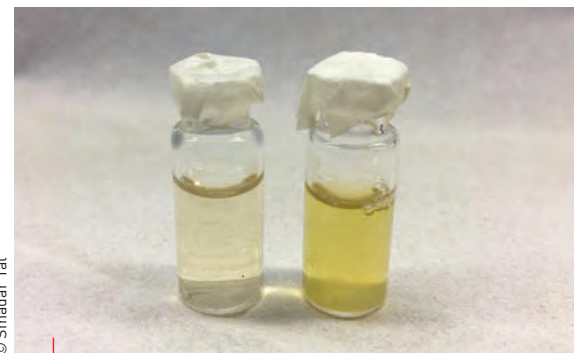


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Figure 1. A schematic diagram of the canine placental structure in late pregnancy.

extensively in human clinical medicine for diagnosis of chromosomal abnormalities or single gene disorders, as well as for the evaluation of fetal lung maturity, microbial invasion of the amniotic cavity, intra-amniotic inflammation, fetal infections, and gender determination (14-16). In veterinary medicine, early detection of abnormalities is important for the welfare of the animals, and is also advantageous for the breeder, both in terms of producing healthy puppies (and keeping the dam healthy), and from a financial perspective. So far, only a few studies have analyzed fetal fluids from at-term bitches (17,18); one case study has shown the feasibility of performing gender analysis from amniotic cells of a singleton canine pregnancy (19). In addition, puncture of the amniotic or allantoic cavities have been used in the canine species for research purposes (20,21), gene therapy and induction of abortion (22), and there is interest in how the technique may contribute towards "One Health" – given that dogs and their owners share the same habitat and are exposed to the same environmental conditions, dogs may make a good model for studying certain environmental effects, such as toxins (**Figure 3**).

Going forward, fetal fluid collection is essential in order to establish a database to characterize the amniotic and allantoic fluids in healthy pregnant bitches; this will enable the determination of biomarkers that can be used as predictors of perinatal outcome.

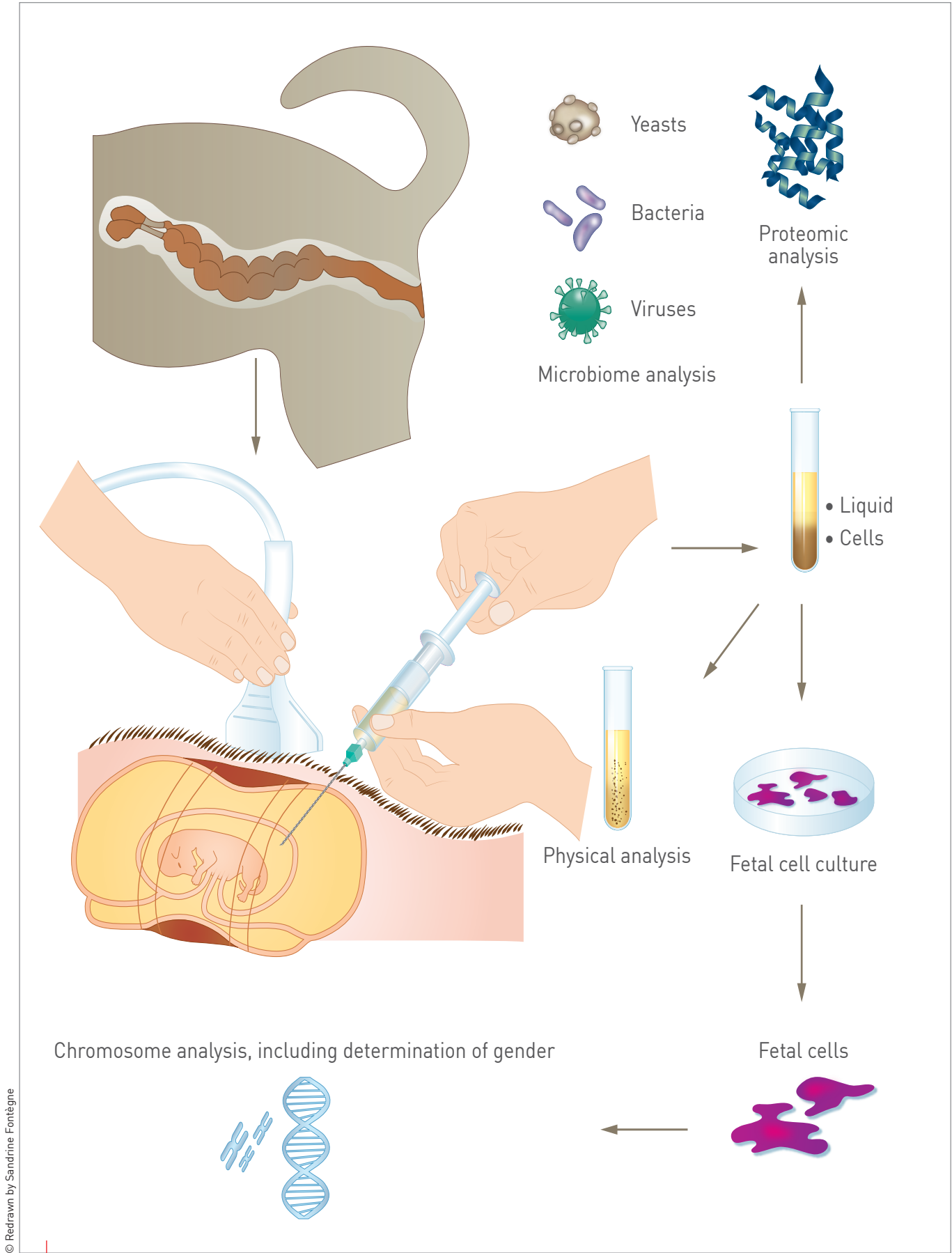


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Figure 2. Normal amniotic (transparent) and allantoic (yellow) fluids obtained by centesis.

When should centesis be done?

An efficient and viable technique for fetal fluid centesis in pregnant bitches during the second half of pregnancy has been established by the author. The procedure is conducted in a similar fashion to the one used in humans, using guided ultrasound (9). Prior to day 35 post-conception, the volume of fetal fluids in the bitch is low, and it can be assumed that the potential risk for injuring the conceptus is



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Figure 3. Fetal fluid centesis lends itself to various diagnostic and research applications, including analysis for microbial organisms, genetic characterization, culture of fetal cells and physical analysis of the fluid.

higher. Fetal fluid collection via needle puncture from after day 35 to the end of the pregnancy is expected to be a safe procedure [17,19].

Methodology

A bitch scheduled for fetal fluid sampling should undergo a full general and gynecological examination, including at least urinalysis, blood tests (complete blood count and biochemistry panel) and abdominal ultrasound, in order to ascertain a baseline for her health and the pregnancy status.

Prior to sampling, the abdomen should be clipped and disinfected using povidone iodine surgical scrub solution and 70% ethanol solution. 30-60 minutes prior to the procedure, topical local anesthetic cream (lidocaine/prilocaine) is applied to the skin at a maximum 0.4 mL/kg over the area into which the needles are to be inserted. The treated skin is then covered by an adhesive bandage until collection commences [23].

There are two options for sampling, both of which employ a disposable spinal needle (18-21G x 3½ inch/9 cm).

Freehand technique

This method is performed without a needle guide. The uterine and gestational cavity, as well as the fetus, are first examined via ultrasonography, and a site that appears to be optimal for fluid collection without injuring the fetus or the fetal membranes is selected. At the same time the location of the fetus (in the left or right uterine horn) and the collection site (allantois or amnion) are estimated. The spinal needle is then inserted at an angle of almost 90° through the abdominal wall and advanced firstly into the uterine cavity and then into the gestational sac (amnion or allantois). Both amniotic and allantoic membranes are often visible on the scan, but it is not always possible to identify the exact position of



“Any change in the volume and composition of the amniotic or allantoic fluid may indicate the metabolic, pathologic or developmental status of the fetus at a particular gestational stage.”

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Figure 4. Performing centesis using the “freehand” technique.



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Figure 5. Centesis using a guide with ultrasound.

the needle tip (**Figure 4**). Once the needle is in position, fluid is aspirated using a 3 or 5 mL syringe and immediately transferred to a sterile tube and frozen at -20°C or -80°C for future analysis.

Needle-guided technique

This method involves a needle-guiding device which can be attached to the curved array ultrasound transducer. Prior to collection, the guide must be sterilized in an autoclave, and (when undertaking multiple samplings from one bitch) should be disinfected with 70% ethanol between sampling each gestational sac. The guide is attached to the probe according to the manufacturer’s instructions, and the spinal needle inserted through a small hole in a preset position on the guide (**Figure 5**). Penetration of the fetal membranes, fluid collection and processing then follow the same procedure as described for the “free hand” technique.

Using a guide may be a safer and easier option for less experienced operators, although the main drawback is the need to sterilize the apparatus

between multiple fetal fluid samplings from different conceptuses in one bitch during the procedure. With experience, the “free hand” technique is preferable for experienced operators.

The amount of fluid retrieved from each conceptus varies between 0.5-5.0 mL, depending on the size of the bitch, the day of pregnancy, and the position of the fetus. Following sampling, the volume of fluid removed should be replaced by an equal volume of sterile 0.9% sodium chloride solution prior to removal of the spinal needle. After collection, the bitch should be kept in a quiet environment for at least 24 hours in order to prevent any possible short-term complications.

What are the risks?

Potential complications of amniocentesis in human medicine include infection of the amniotic sac, induction of preterm labor, respiratory distress in the mother, fetal deformities, alloimmunization, and failure of the puncture wound to heal properly (24). Although very uncommon in human medicine, fetal injury can occur secondary to trauma from the needle. To date, the author has not detected any macroscopic fetal injury after performing centesis

in bitches, although it is possible that microscopic injuries may occur – it is not impossible that some microscopic puncture sites in the uterus, fetal membranes or in the fetus itself have gone undetected, although it can be assumed that if they had occurred they were not of clinical relevance (9).



CONCLUSION

Although still in its infancy, fetal fluid collection in the bitch is a technique that can offer various benefits to small animal veterinarians, breeders and owners alike in the years ahead. A skilled clinician should be able to collect either allantoic or amniotic fluid without too much difficulty and with minimal risk to the conceptus. Analysis of the fluid should assist in early detection of abnormalities and gene disorders, placental defects, microbial infection of the dam or fetus, and gender determination.



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DEALING WITH THE SICK NEWBORN PUPPY



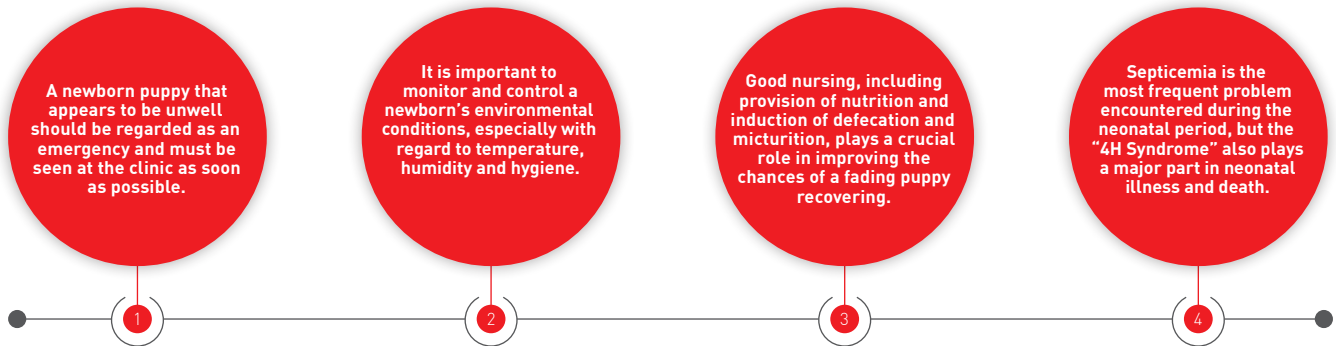
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Dr. Chastant obtained her veterinary diploma in 1990 from the National Veterinary School of Alfort (France), and was awarded her doctorate for research into pre-implantation of mammalian embryos in 1995. A diplomate of ECAR (the European College for Animal Reproduction), she is currently a professor at the National Veterinary School of Toulouse, where she teaches small animal reproduction and heads up Neocare, a center dedicated to all aspects of puppy and kitten neonatology and pediatrics.

The “Fading Puppy Syndrome” is well recognized in veterinary practice; this paper offers a practical approach to the problem.

KEY POINTS



Introduction

Veterinary patients younger than three weeks of age are fragile and — for various reasons — can deteriorate very rapidly when ill. For 85% of puppies that die within the first month of life, clinical signs appear less than five days before death, so newborn puppies that appear to be unwell must be seen as an emergency as soon as an owner has contacted the clinic — and treatment is usually implemented before (and most of the time without) any precise etiological diagnosis. Clinical signs in neonatal puppies are usually nonspecific, and can include respiratory distress, crying, abdominal distension and pain, anorexia, poor weight gain, weakness and hypothermia, but none are pathognomonic for a particular underlying cause.



Initial factors to consider

The owner should be asked to bring not only the sick puppy to the clinic, but also its littermates and the dam; apart from anything else, checking all individuals in a litter can allow early identification of other sick puppies. Examination of the dam may identify a condition that can impact on a puppy's health — such as metritis, mastitis, agalactia/hypogalactia, invaginated teats [which prevent suckling], or (rarely) vulvar vesicles indicative of a maternal herpesvirus infection. If the owner has been monitoring the weights of the neonates, it is useful for them to bring the figures or growth curves as well. Advice on the correct way to transport neonatal puppies is also vital; since newborn pups have poor thermogenesis, it is important that the ambient temperature during transportation is maintained at around 28°C. However, excess heat is also to be avoided, since newborns are unable to



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Figure 1. The clinician should not neglect to check the dam; this includes verifying that she is producing sufficient milk to feed her puppies properly, that teats are available to the newborn, and that the teats are not invaginated.

move away from anything that is too hot. Microwavable heated pads or hot water bottles should be used with caution to avoid induced hyperthermia and to prevent skin burns (and cylindrical bottles may also roll and crush newborns). Hyperthermia will not only interfere with the clinical evaluation, as overheated newborns cry and are often hyperactive, it also increases a puppy's metabolism and thus its energetic expenditure.

Once at the clinic, certain hygiene precautions are advisable. Newborns have an immature immune system and must be protected against nosocomial infections, so time spent in the waiting room should be as short as possible, with no contact with any surface or other animals. Examination should be on a clean, dry surface, preferably heated (e.g., a heat pad set at 28-35°C), using disinfected gloved hands. Ideally, the clinician should also wear fresh clothing.

●●● Clinical examination of the dam

A general clinical examination should include an assessment for signs of bacteremia; for example, is there evidence of infection on the skin, ears or mouth (including dental tartar) of the dam that could represent a source of bacteria? Is there any foul-smelling vaginal discharge indicative of metritis? Check the mammary glands for signs of mastitis, inadequate development of the mammary tissue, and the teat anatomy to verify if the neonates can suckle easily (**Figure 1**). The dam's body condition score should also be evaluated to check on her ability to secrete sufficient milk, and her maternal behavior should also be assessed; is the dam interested in her crying pups? However, the

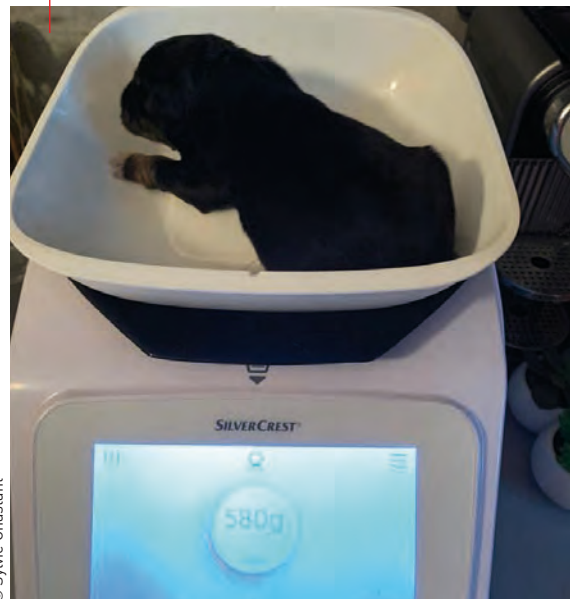
clinician should be cautious of the mother when handling the litter, since over-maternal dams may bite in such situations.

●●● The neonatal clinical examination

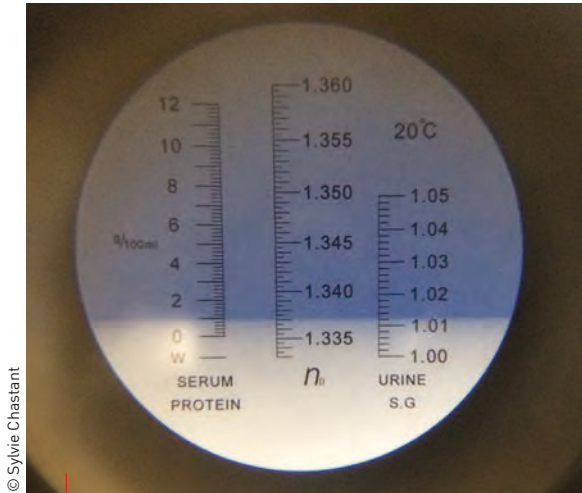
The clinician should first verify some key facts regarding a puppy's nutrition over the previous days: how was feeding during the first 8 hours of life managed (i.e., the period where the intestinal barrier is open to allow passive transfer of colostral antibodies) (1), and is the owner bottle-feeding the puppies (as aspiration with potential respiratory complications is possible)? If the puppies were weighed, calculating their growth rate between birth and two days of age is also informative: 96% of puppies that lose weight over this period have had inadequate passive immune transfer (2). Ideally, there should be no weight loss over the two first days of life. Later on, the weights should be compared to the reference growth curve for the breed (**Figure 2**) (3). The aim is a daily gain of around 2-4 g per kilogram of the expected adult weight, with a minimum target of 1.5 times the birth weight at day 7 and 3 times the birth weight at day 21.

The puppy's temperature should be measured using a pediatric electronic thermometer with a smooth tip; infrared contactless thermometers are, as yet, unverified for neonates. The normal temperature of the newborn is below that of an adult. As a guide, most puppies will have a mean temperature of 36.5±1°C at day 1, 37.0±1.3°C at day 7 and 37.2±0.5°C at days 14-21 (4). There are two critical points to note here. Firstly, a hypothermic puppy should be warmed gradually (increasing at a maximum of 1°C per hour); abrupt warming can lead to death due to peripheral vasodilation and over-activation of cellular metabolism. Warming is ideally done via an incubator, progressively increasing the

Figure 2. Weight is a pivotal element of the clinical examination and follow-up of the newborn.



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Figure 3. A refractometer is the only accurate way to check a puppy's hydration status by measuring its urine specific gravity; any value over 1.030 is suggestive of dehydration.

temperature by one degree more than that of the neonate until 37°C is reached. The incubator should be set at around 55-65% humidity. Secondly, feeding must be delayed until newborns have reached 35°C: a temperature below this point induces intestinal stasis and inhibits digestive enzymatic activity. As a consequence, milk will either stagnate in the stomach and/or remain undigested, providing conditions for bacterial proliferation and leading to bacteremia and death.

A newborn puppy's hydration status can be difficult to determine, as tenting of the skin is not informative at this age. Dehydration can be determined either subjectively, by assessing the dryness of the oral mucosae, or objectively, by measuring urine specific gravity (SG) using a refractometer (**Figure 3**). Urine can be collected into a small plastic tube by massaging the perineal region with a cotton bud moistened with lukewarm water, with any SG value higher than 1.030 considered significant. In the absence of a refractometer, the urine color can be helpful; since neonate urine is usually almost colorless, a dark yellow color is indicative of dehydration.

Particular attention should be paid to the umbilicus; this is a major route for bacterial penetration, since the umbilical vein is in direct

connection with the liver, and the umbilical arteries with the iliac artery. If the cord remnant has not dried and dropped off within a week of birth, this can be indicative of omphalitis/omphalophlebitis and possibly bacteriemia.

Even if the puppy is already several days old, it is important to assess for congenital abnormalities; these include hydrocephalus, cleft palate and *atresia ani*. Verify if the owner has noted the passage of meconium or feces, although this can be difficult to ascertain due to maternal cleaning of the puppies. Cardiac assessment may reveal a bradycardia (100-150 bpm); this is often a protective reflex associated with hypothermia, and is not an indication to administer any cardiac drug.



Further diagnostic tests

Blood sampling

Blood can be collected at any age by jugular puncture (using a 23-25G needle), although in neonates it is important to avoid using alcohol on the skin (to limit post-sample bleeding and cooling of the newborn), and the site should be compressed thoroughly for at least a minute afterwards. Nevertheless, jugular puncture is usually much easier for the practitioner than anticipated, and is quite safe for the newborn. Reference values for neonates differ from those in adults (**Table 1**). Glycemia is the easiest (and most useful) parameter to measure, using a glucometer designed for diabetic patients, and requires only a single drop of blood from an ear prick or paw; collection can be aided by the application of petroleum jelly to the skin.

Diagnostic imaging

Radiographic and ultrasonographic examinations can be confusing, because various findings which would be abnormal in adults may be of no significance in newborns (**Figure 4**). For example, peritoneal effusion is observed in 60% of puppies during the two first weeks of life (and in 30% at one month of age) and is of no clinical consequence; the fluid will spontaneously resolve. Similarly, dilatation of the renal pelvis is observed in 40% of puppies scanned at day 2, 25% at day 7 and 5% at two months of age, without any clinical signs. The neonate renal cortex can exhibit two distinct layers (the external layer being hypoechogenic, the internal more echogenic) on a scan until day 14. Up to day 21, the splenic

Table 1. Reference values for blood parameters in neonatal puppies (adapted from 5-8).

Age in weeks	1	2	3
Urea (g/L)	0.35-1.01	0.12-0.6	0.19-0.49
Creatinine (mg/L)	<1-7	2-10	2-7
Alkaline phosphatase (IU/L)	3000-7000	600-1300	110-260
Total proteins (g/L)	32-45	25-42	33-43
Glucose (g/L)	0.7-1.5	0.7-1.4	0.5-1.6
Hematocrit (%)	21-46	18-33	21-37
Red blood cell count (x10 ⁶ /μL)	3.6-5.9	3.4-4.4	2.8-4.3
White blood cell count (x10 ⁹ /μL)	4-23	1.7-19	2.1-21



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Figure 4. A DV radiograph showing the thorax of a 7-day-old crossbred puppy. The caudal lobe of the right lung appears abnormally radio-opaque, indicating hepatization. The puppy was severely dyspneic, but resolved after systemic antibiotic therapy and corticosteroid nebulization.

parenchyma can exhibit a very characteristic “leopard” echotexture, suspected to be associated with activation of the newborn’s immune system [author’s unpublished data].

Further details on clinical examination of the neonatal puppy are available on-line (in French, English and German) as open access at <https://neocare.pro/le-developpement-du-chiot/>.

●●● Hospitalization – why, who and where

Why hospitalize?

Hospitalization will not only allow specific treatment procedures to be performed (orogastric intubation, fluid administration and drug therapy), it will help ensure intensive monitoring and nursing: the poorly newborn can deteriorate rapidly and often without prior warning. The vast majority of disorders in the young puppy have a bacterial component, but three factors will combine to make the animal a lot worse; hypothermia, hypoglycemia, and dehydration. Hospitalization will help control these elements, and without proper nursing, medical treatments are ineffective. Hospitalization may also help reduce an owner’s concerns and – if death does occur – will enable an autopsy to be performed quickly *post-mortem* (see page 37).

Who to hospitalize?

Hospitalizing the dam has the benefit of reducing the nursing burden on the ill puppy, but this means keeping the whole litter, including individuals who are doing well: they are then unnecessarily exposed to the risk of nosocomial disease. In addition, it is difficult to perform intensive care (such as fluid infusion) in young puppies placed next to their mother, as she will lick them and may damage a drip line or other equipment. In general, only the sick newborn should be hospitalized, but if several puppies from the same litter are admitted they must be identified using colored collars. If some or all of litter remain at the clinic, it is important to guard against the development of mastitis in the dam due to lack of suckling activity.

Where to hospitalize?

Ideally, a newborn puppy should be in a room away from other in-patients — with an oxygen supply to hand — in a thermostatically controlled pen. This can be a dedicated puppy incubator, a second-hand human neonatal incubator (**Figure 5**), an avian incubator, or even a home-made device using a large plastic container or aquarium fitted with a cover (but one that allows circulation of air). Small incubators have the advantage of being portable: if the clinic does not have dedicated overnight staff, the veterinarian can take the litter home for treatment, although this is not ideal. Incubators will usually also allow a high humidity (60%) to be maintained: newborns can become significantly dehydrated, losing moisture both via the skin and by the respiratory route, particularly when they breathe open-mouthed. The incubator temperature should typically be around 28-30°C for the first week of life and 26-28°C for the following week, but it should be adapted as necessary according to the temperature of the newborns to keep them between 36 and 38°C. Remember that incubators only provide warmth: they cannot reduce the temperature below the ambient room temperature. In the absence of a thermostatically controlled incubator, heating mats or microwave-safe pads can be used (after checking the temperature at the contact point with the newborns); infra-red lamps are not recommended.



“A hospitalized puppy should ideally be kept in an incubator which will maintain the optimal temperature and humidity required for a neonate.”

Sylvie Chastant



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Figure 5. Hospitalized puppies should be kept in a dedicated incubator, which allows accurate control of both temperature and humidity.

Both the incubator and all surfaces in the holding room should be cleaned and disinfected regularly to ensure a neonate is not contaminated with bacteria from hospitalized adult animals. However, the choice of disinfectant is important, as some can damage delicate neonatal skin. The requirement for disinfection also applies to all equipment needed for feeding the puppies, such as bottles, teats and syringes, and if milk replacer is used, it should be stored as per the manufacturer's instructions (including between successive hospitalizations).



Medical treatment and intensive care

Rehydration of neonates can be performed by the subcutaneous, intravenous (IV) or intraosseous (IO) routes (the latter using the femur). For the last two options it is important to eliminate air from the administration set before connection to the puppy. Note that the risk for fluid overload (and consequently pulmonary edema) is high in newborn puppies, so when treating moderate to severe dehydration, a bolus of isotonic lactated Ringer's solution (30-45 mL/kg) should be given, followed by continuous rate infusion (CRI) maintenance at 3-4 mL/kg/h (with dextrose added if necessary) (9). The IV route is to be preferred (10), but an IO catheter should not be left in place for more than 3 days because of the risk of osteomyelitis. Warming the infusion is unnecessary because of the low flow rate involved; heated fluids will simply cool as they pass through the administration set.

To treat hypoglycemia, the puppy should be given an IV bolus of 12.5% dextrose (50% dextrose diluted 1:4) at a dose of 1 mL/kg, followed by CRI using an isotonic (Ringers) solution with added dextrose (1.25-5%). A less-critical newborn with normal body temperature can be given a 5-10% glucose solution at 0.25 mL/30 g (9,10). Sugar solutions (30% glucose or honey) can be administered orally in order to avoid hypoglycemia, with a few drops applied on the tongue or the inside of the mouth.

Drug therapy in newborns is potentially problematic; before any medication is administered, its safety for neonates must be assessed, and this is best sourced from textbooks (e.g., 11) rather than using a manufacturer's recommendations, since most drugs have not been evaluated for neonates before approval. Since the majority of neonatal illnesses have a bacterial component, antibiotic therapy is nearly always given routinely. Wherever possible this should be via the subcutaneous or intravenous route; oral administration in smaller animals requires liquid preparations, with a risk of uncontrolled dosage and misdosing. Moreover, some antibiotics given orally (especially ampicillin, metronidazole and amoxicillin) may modify (at least temporarily) the digestive flora, increasing the risk of diarrhea. The author's first-choice antibiotics are ampicillin/amoxicillin, and amoxicillin-clavulanic acid, followed by some of the macrolides (erythromycin, tylosin) and cefalexin or ceftiofur. Other antibiotics with known side effects (e.g., aminoglycosides – which can cause nephrotoxicity – and tetracyclines – which can discolor tooth enamel) may be considered, but only for a short period of time, and where no other antibiotic is effective (e.g., if there is no clinical improvement after three days of treatment), or if indicated by the antibiogram results.



Puppy nursing

The success of both medical and surgical treatment relies on the quality of nursing. In addition to administration of injections, fluid infusions and the like, puppies require much more intensive care than older animals, including daily weighing, frequent feeding, and induction of defecation/micturition, not to mention routine preventatives such as scheduled worm treatments. The nursing team will benefit from specific training for neonate evaluation and care. Appropriate nutrition is especially important; feeding can be achieved by either bottle or tube methods (**Table 2**), but the rectal temperature must first be checked (feed only if temperature >35°C) and the stomach assessed (feed only if the stomach is empty). If the stomach has not emptied 4 hours after the last meal, check for hypothermia and verify if the puppy has defecated; if the rectum is full, defecation can be stimulated with the tip of a thermometer.

Table 2. Feeding options for neonatal puppies.

	Advantages	Disadvantages
Bottle feeding	<ul style="list-style-type: none"> The neonate can feed <i>ad libitum</i> Relaxing activity for the neonate Stimulates digestion 	<ul style="list-style-type: none"> Time consuming Risk of inhalation Impossible if suckling reflex is absent Contra-indicated if there is a cleft palate
Tube feeding	<ul style="list-style-type: none"> Rapid Possible if suckling reflex is absent Safe feeding if puppy has cleft palate 	<ul style="list-style-type: none"> Risk of administration into the respiratory tract (limited) Requires training (but easy) Risk of stomach overload and vomiting/regurgitation

Box 1. Safe tube feeding.

- Select a tube that is 1.5 mm in diameter for animals less than 300 g, 2.6-3.3 mm above this weight.
- Determine the correct length to introduce by measuring the distance between the puppy's chin and the point of the elbow; mark the distance with a felt-tip pen.
- Fill the syringe with milk warmed to 37°C, allowing 4-5 mL/100 g body weight.
- Attach the tube to the syringe and fill with milk, ensuring all the air is removed.
- Place the newborn in ventral recumbency, with the head and body aligned. Slightly open the mouth by pressing against the sides of the mouth. Keep the head straight and introduce the tube into the mouth (**Figure 6**).
- Advance the tube towards the pharynx and allow the newborn to swallow it (this should happen even with weak puppies). Note that there is no cough reflex, even if the tube enters the trachea, until 6-10 days of age.
- To avoid regurgitation, the volume of milk is limited (4-5 mL per 100 g body weight) and given over 1-2 minutes to allow the stomach to fill gradually.
- Once feeding is finished, fold the tube in half (to stop further milk flow) before removing it.
- The tube should be cleaned immediately with hot water and detergent, then rinsed and dried before storing in a clean place until the next meal.
- The artificial milk replacer should be freshly prepared for each feeding session.



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Figure 6. The correct position for holding a neonatal puppy when placing the feeding tube.

Clinical improvement of a poorly puppy is usually demonstrated initially by cessation of constant crying, an improved vitality and normalization of rectal temperature; further reassurance is gained if the hospitalized puppy begins to gain weight within a day or so. It is also essential not to neglect the owners, who will be very worried, and it is important to ensure they are kept informed of the patient's status, at least once, if not twice, daily. Sending weight charts, photographs or short videos of the puppy feeding keeps owners up to date without wasting a lot of time, and the nursing team can play a central role in this communication.

Continuing treatment – home hospitalization?

Even if the newborn puppy is a potentially valuable pedigree animal, it is often difficult to charge properly for the time spent on hospital care (and perhaps even more so if dealing with a crossbred or unregistered animal). Home hospitalization may be an option after the initial in-clinic treatment, and can be facilitated by owner education sessions; these are especially effective for breeders, as they

have more time, a strong motivation, and will often have their own incubator. The ongoing costs are then reduced, and the risks of nosocomial infection reduced. Training the owner in basic techniques (subcutaneous injections, urine SG measurement, and tube feeding (**Box 1**)) is worthwhile, and once the puppy is back home progress can be monitored via a daily telephone update using the nursing team.

Main causes of neonatal mortality

If a puppy dies, necropsy, followed by bacteriological, histological and/or PCR examination, can help to identify the underlying cause, which can often be multi-factorial (**Box 2**). Various specific pathogens have been implicated (**Table 3**) but non-specific opportunistic bacterial infections leading to septicemia are considered to be responsible for 40-65% of all neonatal deaths (12,13). Newborns are infected mainly by the oral route and/or the open umbilical vessels, with the development of septicemia being dependent on exposure to a significant bacterial load (from the environment or the mother) and/or an intrinsic weakness of the neonate arising from the so-called "4H syndrome" (hypothermia-hypoglycemia-hypoxia-hypovolemia). Other factors may also be involved. Significant parasite burdens (especially roundworms, hookworms, and coccidia) can be a major factor, either by direct competition for nutrients and/or indirectly through causing diarrhea. Parasitism can also be indirectly responsible for bacteremia, with migrating *Toxocara* larva crossing from the digestive tract to the lungs through the liver, spreading bacteria from the gastrointestinal tract. Finally, some form of trauma

Box 2. Factors predisposing to death in newborn puppies.

Opportunistic bacteria → septicemia
"4H" syndrome: Hypothermia-hypovolemia-hypoglycemia-hypoxia
Specific pathogens
Trauma
Congenital abnormalities
Parasite burden

Table 3. Specific infectious causes of neonatal death (0-21 days of life).

Viruses	Bacteria	Parasites
<ul style="list-style-type: none"> • CHV1 (Canine Herpesvirus) • CPV1 (Canine Parvovirus type 1) • CDV (Canine Distemper Virus) • CCoV (Canine Coronavirus) • CAV2 (Canine Adenovirus type 2) 	<ul style="list-style-type: none"> • <i>Brucella</i> spp. • <i>Salmonella</i> spp. • <i>Campylobacter jejuni</i> • <i>Bordetella bronchiseptica</i> 	<ul style="list-style-type: none"> • <i>Neospora caninum</i> • <i>Toxocara canis</i> • <i>Ancylostoma</i> spp.

may be involved. This may be accidental in origin, with the owner being “aggressive” or impatient when bottle feeding; this is especially possible with weak newborns who have an inefficient swallowing reflex, causing inhalation of milk. Injuries caused by the dam are also possible; if newborns are crushed or bitten by their mother, this may be attributed to inappropriate maternal behavior, but weakness of the newborn itself (from hypoglycemia and hypothermia) is often the initial trigger.

Necropsy and complementary tests

If a puppy dies it is important to perform a necropsy examination, but certain factors are crucial to optimize the quality of the results: if the examination cannot be performed immediately after death, the puppy should be stored at +4°C. Freezing is inappropriate, as this interferes with histopathology and can confuse even the gross examination after thawing. Practitioners often have to be encouraged to perform a necropsy, possibly because they are concerned that the differences between newborns and adults will be confusing. Nevertheless, gross observation often provides evidence as to the cause of death. For example, it may reveal a failure to ingest milk (empty stomach and intestines, full gallbladder, meconium retention), a major congenital abnormality (e.g., *atresia jejunii*) or a large parasite burden (parasites visible within the intestines or hepatic scars of *Toxocara* larval migrans). Photographs of organs at post-mortem can also allow retrospective analysis. Frequently, there will be no obvious lesions at necropsy, but samples should be taken for additional examination (bacteriology, histology, PCR and parasitology) that can help determine the cause of death.

Bacteriological culture is only informative if death occurred less than 6 hours before necropsy, otherwise bacteria escape from the digestive tract and contaminate other organs. A sterile swab is introduced deep into the splenic parenchyma and transferred into a sterile vial, having taken care to avoid contamination when opening into the

abdominal cavity. The entire spleen can also be collected in a sterile manner. If necessary, samples should be refrigerated before being sent to the laboratory, which should receive them for analysis within 24 hours.

Tissues for histology should be taken into 10% formalin (3.4% formaldehyde). Samples should be no more than 5 mm in thickness, and must be processed (using a paraffin-embedded technique) within 7 days of collection to allow optimal interpretation by the pathology laboratory.

Parasitology assessment can be via gross examination of intestinal and rectal contents, but can also be aided by histological samples (e.g., for *Neospora* and *Toxoplasma*).

Finally, if the cadaver was frozen before necropsy and/or there are signs of autolysis, PCR is the only reliable examination option; quantitative (real time) PCR can provide useful information for most infectious agents.



CONCLUSION

Caring for a sick neonatal puppy relies much more on appropriate nursing, supportive fluids and antibiotics therapy than on any specific medication. Rapid instigation of treatment is a key element for success, together with appropriate preventative measures for all littermates. In most cases, clinical signs before death are of short duration and very similar whatever the underlying cause, and treatment is not infrequently unsuccessful. A proactive approach should be implemented to control neonatal mortality, and a visit to the breeding facility is the best way to evaluate the peripartum organization, with a focus on pregnancy and whelping management, revival and nutrition of the newborns, hygiene procedures and environmental conditions.



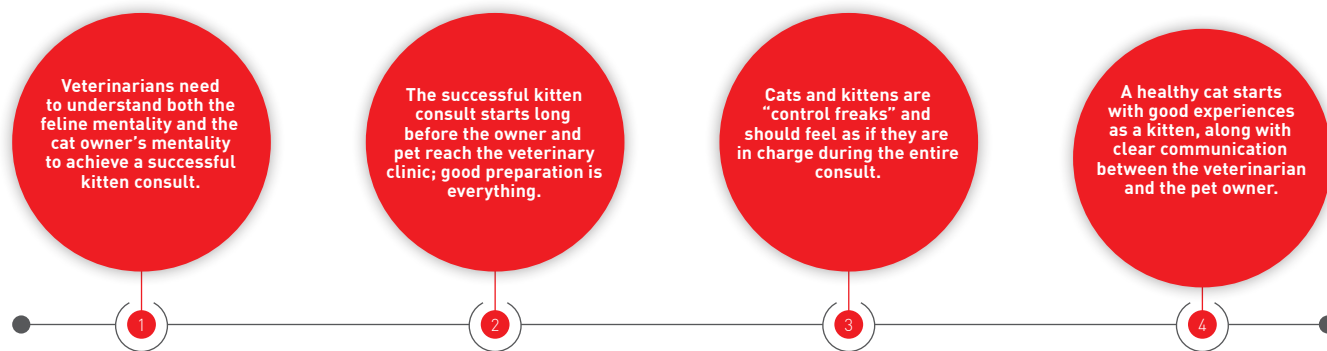
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SUCCESSFUL KITTEN CONSULTS

Successful kitten visits to the clinic will set the feline patient up for a lifetime of veterinary care, as Elizabeth O'Brien explains.

KEY POINTS



Introduction

According to Leonardo Da Vinci "The smallest feline is a masterpiece", so it should perhaps not be surprising that kittens are incredibly popular with animal lovers, and therefore make up a significant proportion of the veterinary patient population in both first opinion small animal and feline specialty practices. Providing a positive experience for every owner and kitten at both their initial and consecutive clinic visits is critical, with the start of life stage being the veterinary team's opportunity to educate the client and develop a long-term and trusted relationship, which will lay the foundation for a lifetime of preventive healthcare for their pet.

Understanding the feline patient

It is vital to understand the feline patient, not just in their needs, but also how they – and their owners – perceive the veterinary visit. More than any other species, cats need good preventive healthcare and early disease detection, which is only possible with regular veterinary visits. Cats are masters at hiding illness, and their signs of sickness are subtle. Yet despite the requirement for regular preventive healthcare, cat owners visit veterinary practices far less than dog owners, although a 2006 US survey indicates that 78% of cat families considered their pets to actually be family members [1]. Part of the reason that cats are less likely to be taken to the veterinary clinic is the "stress" of the veterinary visit, for both cat and the client. A recent study revealed that 58.2% of clients hate bringing their

cat to the veterinarian and 38% feel stressed just thinking about it [2], and in reality, such visits are often extremely challenging for cats, clients and the veterinary team as well. A further factor to consider is owner perception; in North America, the majority of cats are kept as exclusively indoor pets, and their owners often falsely believe that they are free from disease risk. This "Myth of the Indoor Cat" can make it difficult for veterinary teams to convince clients to bring their cats in for an annual or biannual appointment. However, the multiple visits required to complete the necessary preventive healthcare steps for a kitten offer the opportunity to create a wonderful "cat centric" experience, one that is both enjoyed by the client and does not result in undue stress for the patient. In addition, the appointments and communications provide an ideal time to educate the client and plant the seeds for a future of regular veterinary care.

It is essential to recognize that for the cat and the client, a feline veterinary visit lasts much longer than the time of the scheduled appointment. It begins well before arrival at the clinic, and ends much later – sometimes days – after the appointment, with a post-visit feline household that is unhappy and unsettled. From the carrier to the traveling, to the exposure to foreign sights, smells and sounds at the clinic, the cat has many valid reasons to be distrustful. Their solitary nature, and the fact that they evolved at risk of being preyed upon, leads them to be naturally self-defensive, with the need to protect themselves at all times. In addition, cats have good long-term memory, and previous negative experiences can affect their response in a similar situation later on, so a bad clinic visit can negatively impact a cat's welfare



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both short- and long-term (3,4). It is therefore imperative for the clinic personnel to prioritize a Cat Centric experience for all feline patients and clients alike. Fortunately, with resources such as the AAFP¹/ISFM² Cat Friendly Practice[®] Program, and the AAFP Cat Friendly Certificate Program for individuals, veterinary teams are developing a much better understanding of this amazing species and are now able to take measures to prevent environmental and handling stressors, resulting in improved patient and client experiences.

Getting a kitten for the first time – or adding another kitten to an existing feline family – is an exciting time for the owner, and the initial communication between the clinic and the new cat parent is critical. It needs to be engaging, educational and compassionate. Even if there is already a long-standing relationship with a client, this is the opportunity to share in their excitement and create or enhance your bond with them. Clients need to feel from the very start that the whole veterinary team has a true awareness and concern for their cat. For example, the receptionist needs to show an interest and connect with the client by asking questions about where they got the kitten, how they chose the name, and finding out little things that are unique to the new family member. It is beneficial to include this information in the cat's records, as it allows all team members to relate with the client on a more personal basis.

●●● Making for easier travel

As mentioned earlier, the veterinary visit for the cat and its family begins long before the appointment. For many cats, the carrier is the initial roadblock to a successful visit. Getting a kitten into a carrier for the first time might not be too much of a challenge, but it is very likely to become more of an issue with repeated visits. In the author's opinion, the best carriers are inexpensive hard-sided ones that open from both the top and front, and can also be taken apart in the middle (**Figure 1**). The alternative is the soft "pod-like" carriers that have a bed that the cat sleeps in, with a zippered closure. Either option allows for an easily removable top which avoids the traumatic "dumping or dragging" of a cat from its carrier. It also permits an animal which is fearful, anxious, or in pain to stay in the bottom half of the carrier for the entire examination. Although the top of the carrier should be easily removable, it needs to



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Figure 1. An ideal cat carrier must be secure but should also have a top that can be easily removed in order to allow examine a shy or fearful kitten to be examined whilst remaining in the bottom half.

be solid enough to ensure it does not come apart when being carried, and all carriers should be double-checked for stability prior to use. In addition, educating the client to make sure they support the carrier from the bottom and carry it level with the ground will decrease the kitten's stress and the potential for motion sickness. A thick blanket or towel should be placed in the carrier for comfort and to help stop the kitten from sliding around. Synthetic pheromone analogues can be sprayed onto the bedding 30 minutes before travel to ease apprehension. The first kitten consult is also the opportunity to advise the client not to store the carrier in a dusty cupboard, shed or garage, where it remains out of site until it is required for a veterinary visit.

Ideally, kittens and cats can be trained to like their carrier and to become accustomed to travel. Their self-defensive nature means they are very suspicious of anything new in the environment, and the appearance of the carrier is usually a signal to quickly hide as far under the bed as possible. Luckily, kittens are naturally curious and more adventuresome than their adult counterparts and are not initially concerned with the presence of a carrier, and owners should be encouraged to take advantage of this. Advise the client to leave the carrier (with the door open or removed) in a room that the kitten frequents, set up as a comfortable bed complete with thick blanket, toys and treats. It is good idea to get kittens accustomed to automobile travel by advising clients to take them for short rides in their carrier, but stress the

¹ American Association of Feline Practitioners
² International Society for Feline Medicine

importance of never leaving a pet in the vehicle unattended. The safest place for a carrier is in the footwell behind the front seats; otherwise, the carrier should be held in place with a seat belt. Partially covering the carrier with a towel sprayed with synthetic pheromones again provides additional comfort to the kitten.

The rule of thumb for adult cats is one cat for carrier, but the author is comfortable for a pair of kittens (or even the whole litter) to travel to the clinic in one carrier for the first couple of visits. Once they start getting a little bigger and more independent, it is critical that each kitten has their own carrier. Adult cats should preferably be fasted prior to a clinic visit so that treats, which are wonderful distractions, are more interesting to the patient and more readily received. However, kittens are so curious that toys work as great diversions and treats can be as interesting to check out as they are to eat. This makes fasting a kitten unbeneficial, and it is not recommended anyway as they have such a high metabolic rate.

Appropriate preparation by the reception team will set the first and subsequent kitten visits up for success, and posting or emailing a welcome letter and information sheet that covers the important topics outlined above, including pictures of the preferred carrier designs, ahead of the appointment will be of enormous benefit.

●●● Cat friendly and cat centric clinic experiences

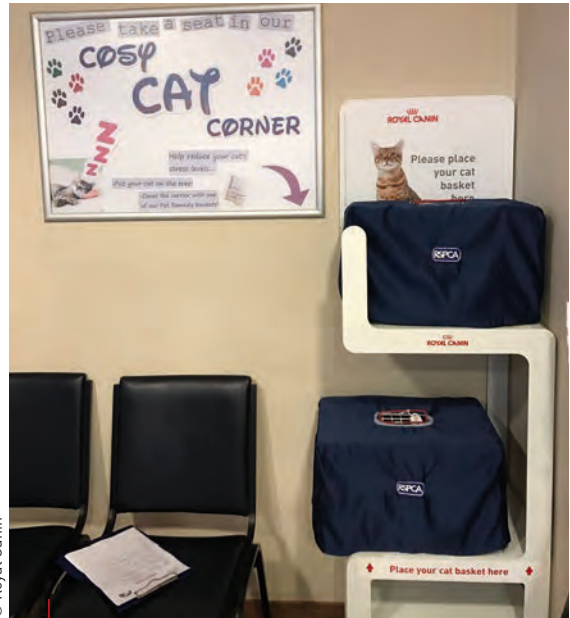
The waiting room/reception

The new patient has arrived in a carrier they love, unstressed by the trip to the clinic, so aim to continue this success. Cats feel insecure if they are placed on the floor, so all clinics should have a clearly identified area in the reception away from dogs and other cats where the carrier can be rested off the ground – ideally 48 inches/120 cm or more from the floor. Cats like to be high up, so they can look down on the world, and kittens are no exception (**Figure 2**). Towels that have been pre-treated with synthetic pheromones should be readily available to partially cover the carrier if not



“More than any other species, cats need good preventive healthcare and early disease detection, which is only possible with regular veterinary visits.”

Elizabeth O'Brien



© Royal Canin

Figure 2. All clinics should have a clearly identified area in the reception area away from dogs where the carrier can be rested off the ground.

already done by the client; providing the towels in a basket – very similar to a spa – with an educative but inviting sign is a cute idea and is extremely well received by owners. Such touches demonstrate the team's deep commitment to the feline patient.

Surprisingly, many clinics appear to be focused on dogs. It is advisable for the veterinary team to enter the practice by the client's route and look at the reception area and examination rooms; does the clinic and the staff give the appearance to a new cat parent that everyone loves cats? The clinic's front office and examination rooms should convey this message by ensuring that cats are at least as well represented as dogs in terms of educational materials and merchandise (e.g., cat toys, carriers and collars) (**Figure 3**). Obviously, this is for the benefit of the client and not the cat, but the clinic and the team have to win over the owner in order to care for the feline patient. Being "Cat



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Figure 3. Toys, collars and an overall "cat focus" at the front desk, along with a resident cat ambassador, shows that the clinic team is "cat-centric".



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Figure 4. A well-designed cat examination room, with a blanket sprayed with pheromone and treats to create a positive visit for the kitten and the client, along with feline-based pictures on the walls.

Centric”, where it’s all about the kitten and client is critical. Even the artwork on the walls should be tipped towards the feline species – although it is recommended to avoid pictures of real cats that can be seen from the examination table or carrier rest, as this has been known to trigger a negative reaction in some cats; art deco and abstract type pictures are to be preferred.

Starting the consult

Ideally, it is a good idea to get the kitten into an examination room as quickly as possible, partly as reception areas tend to be busy and noisy. “Feline Only” examination rooms are ideal and should include a pheromone diffuser. The carrier should be placed on the floor or a low bench and opened, with the kitten encouraged to come out on its own. Treats, food and toys just outside the carrier are helpful. The author also likes to have an industrial-grade mat in the examination room; because cats are control freaks, a mat gives the kitten traction and security, and allows the pet to play while the clinician acquires the history before starting the examination (**Figure 4**).

If the kitten is shy and has decided to remain in the carrier, the lid can be removed or unzipped, allowing the kitten to remain sitting securely in the bottom half. Most kittens at this point will decide to explore, but care should be taken if this is done on the examination table. Ensure the kitten does not jump down, which could lead to injury; rather be sure to assist him or her gently onto the floor. The kitten should be allowed to roam the room freely and chase and play with toys prior to the examination, and if there is more than one kitten, they should all be able to make themselves at home in the examination room together. Cats and kittens need to feel that they “own the examination room” and are “in charge” of the appointment. Giving them the opportunity to play and to mark the room with their own facial pheromones by rubbing up against the table, the corners, the cabinets – and even the

veterinarian – is ideal. There should also be a place to hide, as some kittens are shy; the lid of the carrier or pet tents are ideal for this purpose. Referring to the kitten by their name and correct gender are critical and necessary for the continued success of the client/patient relationship.

The examination

The examination room should be equipped with everything the clinician needs for the appointment readily available, but should also be fun and educational. Cat scales or pediatric scales should be on the table or floor for easy and accurate measurement of weight (**Figure 5**). The consult table should be covered with a thick blanket or towel, which will give the kitten security and traction, with a yoga mat or rubber bathmat laid underneath to keep it in place. Remember, even kittens are control freaks; slipping on a stainless steel or laminate table is a frightening experience for the feline species. Ideally pheromone diffusers will be in the room, but if not available the table covering can be sprayed prior to the appointment to help keep the kitten at ease. The towel or blanket can of course also be useful to gently wrap the kitten if it is fidgety or nervous; after the visit, the mat and table can be disinfected, and the towel or blanket put for laundry.

Normally, the author works through an assessment checklist in her head, but the kitten is allowed to roam freely, and the examination itself often occurs in multiple locations throughout the room – on the mat or countertop, the examination table, windowsill, climbers or wherever the kitten is most comfortable.

All the necessary vaccinations, deworming and retrovirus testing can be done in this way – the kitten controls where and how the examination proceeds. The Cat Healthy Preventive Healthcare Protocols, and in particular the Cat Healthy Simplified Protocols, are an excellent reference for the healthcare requirements of kittens in their first year of life³.

³ <https://www.cathealthy.ca/>



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Figure 5. A pediatric scale, along with everything else required for the examination, should be readily available and within reach of the clinician.

Gentle handling of the kitten is very important, with all procedures done on a previously pheromone-sprayed blanket with the distraction of treats, canned food and sometimes toys. Move slowly and quietly, as “less is always more”. Kittens, like children, have a short attention span, so do one procedure at a time with a short playtime in between. It is critical that both the kitten and the client have an excellent experience. So for example, when vaccinating kittens, use a new sterile 25G needle and inject in one of the AAFP recommended designated locations. As the injection is being administered, have an assistant gently steady the kitten while offering a treat or small amount of food in a little dish or a thumb depressor. If well distracted, the injection will go unnoticed by most kittens, and the client will be thrilled. All kittens can receive a nail trim at each visit, with the clients being taught and encouraged to do this routinely at home. Lastly, constant interruptions by team members must be avoided – personnel going in and out of the room will stop the kitten relaxing.

Educating kitten owners

The foundation for success begins with good communication and education, and the consult room is also an opportunity to create discussion topics with the client. For example, using food and other treats is a perfect time to discuss the importance of nutrition, and clients are often surprised that kittens and adult cats can have wet food as a major part of their daily diet. The author finds that these casual educative discussions during the appointment, as the kitten is playing, results in a lifetime of compliance, as clients are keen, excited and willing to commit to a future with their new family feline. However, the discussions should be structured. New kitten owners will usually have a long list of questions, often partly due to receiving confusing and conflicting advice from shelters, breeders, the internet, rescue groups, friends and neighbors, so the veterinary team needs to be flexible and answer the client’s priority questions first, but at the same time break through the clutter with a list of topics that should be covered at some point during the planned kitten visits.

A master list of topics is ideal so that nothing is omitted, and each appointment can cover different aspects. It can help to signpost what the owner can expect to cover at the next visit. For example, educating the keen new owner about teething, and mentioning that their kitten has 26 baby teeth which will soon be replaced with permanent dentition, starts the discussion about the importance of dental hygiene. It is very important that a cat owner understands the environmental needs of kittens and cats, so discuss types and locations of scratching posts, water bowls, sleeping areas, playtime and feeding times, and well as litterbox location, types, numbers and hygiene. Playtime is an environmental need for each feline. Encouraging clients to start using treats for training is very rewarding, and they will often come in on subsequent visits proudly showing their kitten “high fiving” or other tricks. Always remember to advise owners that no more than 10% of the kitten’s diet should be treats, and to

check the calorie count as well. Recommendations as to “Putting the Hunt in Mealttime” by using feeding puzzles and games of fetch are best started during kittenhood.

In addition to the welcome letter sent prior to the appointment, it is nice to send every kitten home with a welcome package. This can contain additional information and brochures, along with a report card or checklist of what was done at that visit and what still needs to be completed. Add the toy that the cat played with in the examination room – crinkle balls or similar are ideal – and other appropriate items. The team can have fun creating “gift bags” using various things such as breakaway collars, plastic fridge lids for canned food, treats, feeding puzzles, little blankets and suchlike, many of which are often donated by industry partners for this purpose.

As the kitten develops, health plans should be devised to prepare for the transition to adulthood. This will include a schedule for preventive broad spectrum parasiticides, and information as to what vaccinations and adult cat will require for the following and consecutive years. Closely monitoring the pet’s weight and body condition at each visit and sharing your findings with advice on what to feed now, what to feed as the cat gets older, and how much to feed, will be well received, and it is important not to neglect this topic at the spay/neuter discharge, which is an ideal time to reinforce the nutritional recommendations and advise the owner that this operation reduces the cat’s metabolic requirements by 25-30%.



CONCLUSION

The kitten life stage is the veterinary team’s opportunity to educate the client and to lay the foundation for a lifetime of preventive healthcare. It is also a fun and gratifying time for the team, so embrace and enjoy this experience. Cat clients are often not like dog clients; as with cats themselves, it is necessary to work hard to win their trust and gain their compliance. However, like cats, once you have won their trust and respect, it is in most cases yours forever.



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MATERNAL BEHAVIOR IN BITCHES



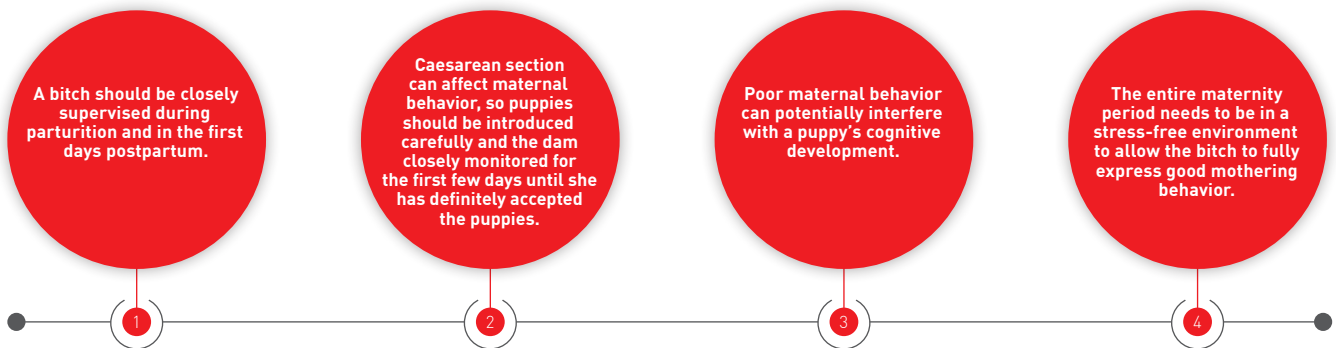
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Maternal behavior plays a major role in the survival of puppies during the first weeks of life, and it may also have a long-lasting effect on their cognitive development. This paper offers some cues and clues that could help the clinician when dealing with newborn puppies.

KEY POINTS



● ○ ○ ○ Introduction

Studying mammalian maternal behavior gives an idea of the necessary interactions between a mother and her offspring and the level of dependence between the two, and the behaviors will vary between precocial and altricial species. In the bitch, good maternal behavior is important for two major reasons. Firstly, since puppies are born helpless, deaf and blind, and have limited movement (*i.e.*, an altricial species), they are totally dependent on an external source to survive. For domestic dogs, in comparison to free-roaming dogs and some wild canids, parental care is performed mainly by the dam, so puppy survival is directly affected by the quality of the mothering abilities (assuming no human intervention). Secondly, the

mother's behavior can affect future development of her offspring; although recent studies are not conclusive, maternal quality seems to directly impact a puppy's cognitive development and performance (1-3).

Canine maternal behavior has been studied for many decades (4-6), and it is agreed that such behavior is a response to the needs of the neonates. The main aspects involve direct contact (for thermoregulation of the puppies), oral interaction (by licking), and nursing, playing with and disciplining the puppies. However, the impact of maternal care in the cognitive development of dogs is a recent concept, with various studies (1-3,7,8) attempting to understand and predict how

early interactions between a dam and her puppies can affect the latter's cognitive abilities, how long-lasting these effects are, and how great the impact is on the future performance and behavior of adult dogs. Consequently, poor maternal care could be the origin for later unwanted behaviors. This review will focus on the common aspects of maternal behavior around parturition and during the first weeks of life, and will discuss how maternal care may influence a dog's cognitive abilities and temperament.



Impending parturition

Behavior changes in the pregnant dam can appear one or two days before the due date [9], but the signs may or may not be obvious, depending on whether the bitch is primiparous or multiparous. In most cases she will be restless and have a reduced appetite 12-24 hours before whelping. Nesting and digging behavior is more variable and depends on both individual and environmental factors, and the level of human contact [10]. No correlation has been established between the intensity of preparation for whelping and the quality of maternal behavior. Other signs also described include inattention, drowsiness, aggression, anxiety, unpredictability, irritation, and an increased tendency to seek attention from the owner, although some bitches may prefer seclusion. As parturition approaches, the bitch will spend more time in the whelping area. A decrease in body temperature may cause shivering [9], and could explain other behavioral changes, but the use of this parameter as an indicator for parturition is still debatable. A drop of around 1.0°C has been used to indicate impending parturition [11], but vaginal temperature loggers have shown that this drop does not have a predictive value for the onset of whelping [12].



“It is important to monitor the process of parturition, in particular for nervous primiparous bitches, since the dam's inexperience can lead to her failing to display correct maternal traits.”

Natalia Ribeiro dos Santos



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Figure 1. Stage two parturition; the bitch should break the amniotic sac soon after birth to allow the puppy to breathe.



Parturition

Normal parturition (eutocia) is a combination of physiological, endocrinological and behavioral changes that culminate in delivery of the puppies. Whelping progresses in three stages with a distinct exhibition of behaviors. The first stage is the onset of subclinical uterine contractions, along with vaginal relaxation and cervical dilation, but with no indication of abdominal contractions. Some females will show no evident signs at this stage, but if seen, they mimic those described for impending parturition, such as rearranging the bedding material in an attempt to build a nest. The duration of this stage might be affected by parity of the bitch, and can be up to 36 hours in a nervous primiparous female [9], but usually lasts for 6-12 hours. The second stage is the active birthing process, and is characterized by strong and coordinated abdominal contractions, followed by vocalization of the bitch and release of fetal fluids. Once the cervix is fully dilated, the presence of the first puppy at the cervix initiates the Ferguson reflex and triggers oxytocin release, with contraction of the abdominal muscles that result in delivery.

Once the puppy is born, the bitch must break the amniotic sac (if it did not rupture during birth) (**Figure 1**); puppies that remain within the fetal membranes can die in a matter of minutes if not freed quickly. The bitch should also tear the umbilical cord and vigorously lick the newborn puppy [9], which is important both to stimulate respiration and to dry the puppy, and is essential to establish maternal bonding. Inexperience (in the primiparous bitch) and high levels of anxiety during parturition can disturb maternal behavior and lead to increased puppy mortality. The whole process will repeat until all puppies are born, and the bitch will interrupt the grooming of a newborn as contractions resume for the delivery of another puppy. In fact, a bitch may focus entirely on the whelping process, and may appear insensitive to the crying of the puppies [4], neglecting the litter until stage two is completed [5]. In general, the

first puppy will be born within 1-2 hours of the second stage commencing, although this can be up to 4 hours, and the overall duration of stage two varies depending on the size of the litter, but can last for up to 12 hours, and may possibly be delayed or arrested by any stress or disturbance (4,5).

The third stage is the expulsion of the fetal membranes, which may occur after each puppy or after two or three puppies have been born. If permitted, the bitch will eat the placentas, which in carnivores is important for several reasons; for hygiene, as a source of energy for the dam (4) and (possibly) to decrease the attraction of predators.

●●● Maternal behavior in the early postpartum period

Once whelping is complete, the bitch should display a set of behaviors that will allow the survival, growth and development of the puppies (13). Studies of maternal behavior tend to focus on easy-to-measure aspects, such as oro-nasal interactions (licking or poking the puppies), time spent with the litter (both in close contact and within the whelping area), and the duration and position of the bitch during nursing. Although maternal behavior is important until weaning, the neonatal and transition periods are emphasized here; this is when the puppies are most dependent on the dam, and these stages are crucial for how the mother's character and maternal abilities can affect the puppies' development. The neonatal period (defined as days 1-16) is the adaptation to extra-uterine life, whilst the transition period starts when the puppies open their eyes, and is characterized by the development of hearing capacity and neurological skills (10). At the end of this period a puppy's senses will be fully functional, and its levels of dependence start to decrease as its exploratory behavior increases.

Oro-nasal interaction

The first interaction of the bitch towards the newborn puppy is grooming (4,6,9). As discussed above, this is crucial not only to the puppy's survival but is fundamental to trigger the maternal connection. Licking is thought to initiate a puppy's urination and defecation in the first three weeks of life (6,9,14), and is also used by the dam to waken the puppies when she is ready to nurse them and to direct them towards the mammary glands. The dam will continue to lick the puppies at least until weaning, although this declines over time, and by around 21 days of age puppies are self-sufficient for toileting.

It is possible that the frequency and/or the time spent grooming the puppies can impact the cognitive behavior of dogs. Even though licking activity has been used to rank maternal behavior (1-3,7) no direct correlation has been established, although research in rodents has shown that offspring which are frequently licked

by their mother are better adapted to stress and have enhanced signaling of genes associated with learning and memory.

Contact time

Another important maternal behavior is to stay in close contact with the puppies, and a new mother will be reluctant to vacate the whelping area (**Figure 2**) until at least around three days postpartum (5,6,8,14), after which she will gradually resume her daily activities, leaving the puppies more often. She can be extremely protective at this point, especially against strangers (4). The close contact between dam and young puppies is very important to prevent hypothermia; since neonates have poor thermoregulation, it is crucial that they have a source of heat (from the dam and/or the environment) to keep them warm. Hypothermia in a newborn can suppress certain body functions, including digestion and breathing. There is a physiological drop in the body temperature of a puppy immediately after birth (15) before it gradually increases to 35-37°C, the normal range for newborn puppies at day 7. The dependence on external warmth decreases over time, but a heat source that allows puppies to maintain a stable body temperature appears to be important up until the 4th week of life (16).

Nurturing activity

For mammals, nurturing basically relies on the nursing behavior of the dam. Nursing and suckling are connected activities, whereby the dam performs the nursing and the puppy responds by suckling. This activity is essential for the survival of the offspring, providing both nourishment and (in the first 24 hours after birth) transfer of colostral antibodies. It is one manifestation of maternal care controlled both by hormonal status and by the central nervous system (17). Nursing can be initiated before parturition is finished, but feeding the puppies is not a priority for the bitch until whelping is completed (4). During the



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Figure 2. A bitch will remain with her puppies almost constantly in the first few days postpartum.



Figure 3. A bitch nursing in a sitting position, which is more commonly seen during the day.

first few days after parturition the bitch will nurse her puppies almost constantly (8,14). For the first 21 days postpartum, the bitch will lie down and lick the puppies to motivate nursing; this interaction is greatest at night-time (14). Once fully mobile, the puppies will initiate the suckling behavior (8,14), and the duration and frequency of nursing will gradually decrease. The bitch's preferred position for nursing will also change with time; a sitting position has been more commonly observed during the day (**Figure 3**), whilst a recumbent position is frequently seen at nighttime (**Figure 4**) (14). This appears to influence a puppy's development, although again more research is needed. Studies in

guide dogs showed that puppies from bitches that nursed more often lying down were less likely to be selected for training than those where the dam nursed primarily in a sitting or standing position (2).

The puppy regulates the frequency and duration of suckling, although an individual puppy's preference for a certain teat has not been identified. Once fed, the puppies will simply release the teats, but as long as they are attached a bitch will rarely leave the nest, at least in the early postpartum period. After around day 13, the bitch will start to actively interrupt the suckling activity (17).

●●● Timeline of maternal behavior

As the puppies develop, the frequency and intensity of the maternal behavior declines (3,4,11). The time spent in licking activity decreases as the puppies develop (6,17), as does the degree of contact – as there is less reliance on the mother for warmth, the bitch spends more time away from the puppies (14). The duration and frequency of nursing will also decrease gradually (1,14), and as the puppies become stronger and suckle more efficiently, the bitch will leave them more often.

A wet diet should be introduced at around 3-4 weeks of age to habituate the litter to solid food and to complement their diet, since the dam's milk production will start to reduce. The puppies are also capable of leaving the nest by this point, but although nursing may not be necessary from a nutrition standpoint, the puppies will continue to suckle, probably for emotional gratification (18).



Figure 4. A bitch nursing her puppies whilst lying down; this is typically noted at nighttime.



Neonate behavior toward the dam

During the neonatal period, a puppy's activities are predominantly suckling and sleeping. After birth, puppies seek a warm place, search for a mammary gland (olfactory cues seem to drive the attraction) and try to suckle as soon as possible. Newborn activity is minimal in the first two weeks of life, with puppies remaining close to the mother and each other (or an external heat source), presumably to maintain body temperature; as noted above, the interaction with the dam is normally initiated by the latter [14].

At the time the puppies open their eyes and their movements become more coordinated, the interaction between the dam and the littermates become more dynamic [6,8,14]. They begin to actively search for the dam [6], patterns of nursing are more variable [14] and they show increased interaction with different players (the dam, littermate, toys and humans). Whining and/or crying is an indication of distress (e.g., cold, hunger) and normally urges the dam to respond to the puppies' needs. Breeders will use the noise levels to rate a dam's level of serenity (**Figure 5**) [8], so if a litter is crying regularly it could be an indication of poor maternal behavior – for example, the bitch is not staying with the puppies enough, and/or the time spent nursing and licking them is insufficient.



Factors shaping maternal behavior

Maternal behavior can be defined in two phases. A critical or sensitive phase, associated with important hormonal changes during parturition, followed by a maintenance phase, with a more psycho-sensory component that lasts until weaning [19]. Although little information is available as to what elicits maternal behavior in dogs and how it differs amongst individuals, there are various possible factors involved.

Hormonal factors and stress

Various hormones are responsible for parturition in the bitch and they are probably also involved with maternal behavior, although how each hormone regulates this is poorly understood. The hormonal cascade will involve a drop in progesterone that initiates parturition, and an increase in the secretion of estrogens, oxytocin, relaxin, prolactin, prostaglandins and the down- and up-regulation of receptors. In particular, how prolactin and oxytocin regulate maternal behavior is still unclear. Oxytocin contributes to uterine contractions and seems to be important for maternal characteristics, with its influence well documented in other species, and low levels of the hormone have been associated with cannibalism in one canine study [20]. Oxytocin levels in the saliva are not a predictive factor of maternal quality in the bitch [21], but intranasal



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Figure 5. If a bitch displays good maternal behavior, the puppies should be calm and quiet.

oxytocin seems to help expression of maternal behavior after caesarean section [22]. However, no controlled studies have been conducted to establish the effects of the hormone and a timeframe for when it is effective. Prolactin, as well as being responsible for promoting lactation, probably also contributes to maternal behavior, although it is not clear how it acts. The progesterone drop seems to play a role as well, since it explains the behavioral changes seen in pseudopregnancy.

Parturition and the establishment of maternity can be perceived as a stress situation. Overstressed bitches seem to struggle more to adjust to motherhood and the changes it requires. Dog-appeasing pheromones can reduce the stress and can positively modulate maternal care; their use has been shown to increase the willingness of the bitch to stay with the puppies for longer, along with a better overall mother-offspring relationship [8].

Vaginal stimulation and amniotic fluid

Vaginal stimulation seems to be important for maternal behavior, since bitches that undergo a caesarean section without initiating parturition may have problems in displaying appropriate interactions with their puppies, although how important this stimulation is has yet to be proven (**Figure 6**).

Amniotic fluids also seem to play a fundamental role in directing a dam to accept her puppies [4,23]. A bitch will refuse a puppy removed at birth and washed, but if the newborn is covered in amniotic fluid, she will then accept it again [23], so using amniotic fluid before presenting a litter to a bitch after caesarean section may improve maternal recognition.

Parity and litter size

The effect of parity on behavior seems to be relatively unimportant, as no major differences have been observed when comparing primiparous and multiparous bitches [1,4]. The parturition experience improves a bitch's recognition of the



Figure 6. After a caesarean section, puppies should be presented to the dam as soon the anesthesia effects have worn off to improve the chances of normal maternal behavior.

needs of the newborn, and reduces apprehension from the physiological changes around parturition [1]. Multiparous bitches tend to show consistent maternal care, whereas primiparous improve in their maternal behavior over time [7]. A study of dog breeders reported primiparous bitches to be over-represented with maternal behavioral problems [24], so it is important to monitor the process of parturition, in particular for nervous primiparous bitches, since the dam's inexperience can lead to her failing to display correct maternal traits and even exhibit abnormal behavior such as cannibalism. Dams with small litter sizes have more contact with individual puppies and tend to rank better for mothering attributes [1].

Genetics and breed

Genetics may have an important role in maternal behavior, but it is poorly understood, and selecting for good maternal care is not a priority for many breeders. Human interference could negatively impact how the dam interacts with her puppies, but avoiding breeding from offspring of a dam with poor maternal behavior may be advisable. Although there are anecdotal reports on how mothering qualities can vary between breeds, this has not been investigated in depth, and in one study no specific breed was singled out as being particularly problematic with maternal behavior [24]. However, Golden Retrievers seemed to be better than German Shepherds in a study evaluating maternal behavior and success of puppy selection as guide dogs [2].

●●●● Inappropriate maternal behavior

The quality of maternal care may already be apparent during parturition. An inexperienced dam may not know what needs to be done to break the amniotic sac and tear the umbilical cord, increasing the chance of problems. Moreover, bitches that show little interest in licking their puppies may also have poor maternal behavior throughout the postpartum period. A bitch will normally choose a calm and safe environment to deliver her puppies, so if she feels threatened, she may become aggressive. Violence toward the puppies is rare and in general is towards strangers and other animals in the household. Even a very docile female can show signs of aggression if she perceives a situation to be a threat to her puppies. If aggressive behavior toward the puppies is observed, it is usually in the first days postpartum, typically in primiparous bitches, and may even lead to maternal cannibalism. Potential causes are excess stress, overcrowding and malnutrition, and low levels of oxytocin and blood lipids have been reported in the Kangal breed with a history of maternal cannibalism [20]. Alternatively, in the author's experience, a nervous primiparous bitch, when severing the umbilical cord, can unintentionally kill and eat her puppies. Lack of milk production (agalactia) can be also observed, typically in primiparous individuals, bitches that have undergone premature caesarean section, or have systemic illness, but no correlative studies have been done between agalactia and poor maternal behavior.

●●●● Maternal effects on cognitive development

Studies in rats confirm that the quality and quantity of interactions with the mother in the early postpartum period can influence the physiological, cognitive and behavioral development of the offspring. However, it is unclear if this can be extrapolated to a bitch and her puppies, and if so to what degree. The canine neonatal and transitional periods are characterized by rapid neurological development, and various studies looking at the impact of maternal behavior on an animal's development are contradictory [1-3], with the results to date apparently depending on the dog's breed and/or its prime functional aspect. So for military German Shepherd puppies, a high maternal score had a positive impact in the cognitive features required to perform their job [1], but when selecting guide dogs, puppies from mothers that showed greater levels of maternal behavior displayed characteristics that decreased their chances of selection. For example, they were more likely to have higher activity levels when left alone, they had a short latency period before vocalizing when presented with a novel object, and they showed low performance and perseverance in problem-solving



CONCLUSION

Many aspects of maternal behavior in the dog need still further consideration, but the veterinarian should be aware of certain factors that can, in particular, greatly influence the peripartum period. Perhaps most importantly, factors linked to the individual bitch and how they relate to her maternal behavior should be quantified. Anxious primiparous bitches, and any dog that has had a caesarean section, require closer attention in the first days of postpartum, and poor maternal behavior should be addressed as soon as possible in an attempt to avoid any long-lasting negative effects on the puppy and minimize unwanted behaviors later in life.

tasks (2). In addition, the results of testing young puppies (aged two months) to handle stress situations were also paradoxical; higher maternal care improved the ability of puppies in a laboratory environment (25) but had a negative effect in puppies raised in a home environment (3).

There is no doubt that early interaction between the dam and the puppies can affect their cognitive ability. However, there are various unknowns; when is the crucial window during the postpartum period, what is the long-term effect on the performance and behavior of the dogs, and is it possible to compensate at a later stage for poor maternal behavior – and if so, how effectively? The socialization period, which starts around 3 weeks of age and ends at approximately 12-14 weeks, may be of greater importance, since puppies are more mature at this stage, and therefore more susceptible to both positive and negative effects of interactions with the dam, their littermates, other dogs and humans. Due to the many factors involved, the effects of early life experiences require further study and observation to better understand their impact on a dog's development.

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