An adverse drug reaction (ADR) is an unfavorable and unintended effect that occurs after use of a medicinal product. Although awareness of some potential adverse drug reactions in veterinary medicine is widespread, others may not be promptly recognized by practitioners, either because they are rarely observed, because they are associated with newer pharmaceutical products and have not become entrenched in the literature, or because they mimic the clinical signs of other common diseases in dogs and cats. In human medicine, unrecognized adverse drug reactions may result in unnecessary patient morbidity and healthcare expense, and the term “prescribing cascade” has been coined to describe the situation of an unrecognized or misinterpreted adverse drug reaction resulting in the prescription of additional drugs to address the clinical signs.

Old age, chronic disease, and use of multiple drugs place a patient at risk for adverse drug reactions and a prescribing cascade in human medicine, and polypharmacy among elderly or critically ill hospitalized pets may create a similar scenario. Veterinary practitioners can avoid a prescribing cascade by increasing their awareness of potential adverse drug reactions (e.g. through periodic review of veterinary literature and perusal of package inserts for new products carried in their hospitals), and by considering that the cause of any new clinical sign in a pet receiving other medications could be a consequence of drug treatment. Examples of several veterinary adverse drug reactions that may initially be unrecognized for various reasons (some with the potential to trigger a prescribing cascade) are discussed below.

1. Phenobarbital and bone marrow toxicity
   Most veterinarians are familiar with the phenobarbital-associated side effects of polyuria, polydipsia, polyphagia, sedation/ataxia, and potential hepatotoxicity. Hepatotoxicity with phenobarbital is dose- and duration-dependent (more likely to occur when phenobarbital concentrations are >35-40 mcg/mL). A less common adverse effect of phenobarbital in dogs that may be less familiar to practitioners is idiosyncratic bone marrow toxicity. Reversible neutropenia, thrombocytopenia, and anemia have been reported in dogs on chronic phenobarbital therapy and after an acute overdose. If not suspected to be an adverse drug reaction, the presence of pancytopenia in a dog receiving phenobarbital may result in unnecessary prescription of immunosuppressive medications, which will not correct the problem. A diagnostic workup to rule out other causes is often appropriate, but discontinuation of phenobarbital as soon as possible and initiation of an alternative anticonvulsant is indicated if another cause of bone marrow disease is not identified. Recovery from phenobarbital-induced bone marrow toxicity usually occurs within 1-3 weeks of drug discontinuation.

   Phenobarbital has also been associated with dyskinesia (anxiousness and muscle twitching that appeared dose-dependent and resolved when the drug was discontinued), and superficial necrolytic dermatitis or hepatocutaneous syndrome.

2. Potassium bromide and coughing in cats
   Potassium bromide shares with phenobarbital the potential to cause polyuria, polydipsia, polyphagia, sedation, and ataxia in pets. However, an additional species-specific reaction to this drug is coughing in cats. Chronic cough occurs in up to 50% of cats receiving potassium bromide and is often associated with a diffuse bronchial pattern on thoracic radiographs. Because of the frequency of this side effect, potassium bromide is not generally recommended as an anticonvulsant in cats. However, it may still be prescribed by some practitioners, with the subsequent prescription of medications for feline lower airway disease (“feline asthma”) when a cough develops. An adverse drug reaction may ultimately be suspected when treatment is unsuccessful, as the cough generally does not resolve until the drug is discontinued.

3. Methimazole and lymphadenomegaly or pyogranulomatous folliculitis
   Gastrointestinal upset, facial excoriation, hepatotoxicity, and leukopenia are well-known as potential side effects of methimazole treatment, and some commercial laboratories offer hyperthyroid monitoring profiles specifically directed at detecting clinicopathologic changes associated with the latter two. However, rare cases of generalized lymphadenomegaly with or without concurrent cutaneous lymphoid hyperplasia have been described in both humans and cats receiving methimazole and may mimic lymphoma cytologically. In cats, the lymphadenomegaly resolves within a few days after discontinuation of the drug. Pyogranulomatous mural folliculitis was also diagnosed by skin biopsy in a cat receiving methimazole that developed non-pruritic alopecia with scales, crusts, and erythema.

4. Metoclopramide (or mirtazapine, or metronidazole) and neurologic signs
   Hospitalized patients with systemic illness causing inappetence, nausea, or decreased GI motility may be prescribed a combination of promotility agents, antiemetics, anti-diarrheals, and appetite stimulants. If neurologic signs appear in these patients, they may be
attributed to other possible disease sequelae (e.g. thrombosis, cerebral edema, electrolyte abnormalities). However, both infusion of metoclopramide and administration of mirtazapine can cause behavior changes and/or tremors, and recent medication history should be examined in patients exhibiting neurologic signs. Metronidazole can also cause vestibular and cerebellar signs in both dogs and cats at high concentrations. Either geriatric vestibular disease or primary neurological disease may be misdiagnosed if this is not realized.

5. Fluoxetine and weight loss
Fluoxetine may be prescribed to dogs and cats for various anxiety-related behavioral disorders. One of the most common side effects reported with a veterinary-labeled fluoxetine product in dogs was inappetence and weight loss (approximately 30% of dogs). This may trigger an extended diagnostic workup if it is not realized that the inappetence may be an adverse drug reaction. This scenario emphasizes the importance of educating oneself, other hospital veterinarians, and veterinary staff regarding potential adverse events associated with products prescribed or dispensed through the hospital. Package inserts are often a valuable source of information.

6. Any medication and adverse drug reactions involving the skin (e.g. erythema multiforme or toxic epidermal necrolysis)
Adverse drug reactions involving the skin are notorious for being attributed to other causes such as infection, allergy, or idiopathic immune-mediated disease. Drugs or classes of drugs that have been associated with cutaneous adverse reactions include antiparasitics (amitraz, metaflumizone, ivermectin), antibiotics (e.g. beta lactams, sulfonamides, tetracyclines), vitamin K, shampoos, contrast agents, NSAIDs, hydralazine, anticonvulsants, chemotherapeutic agents, griseofulvin, allopurinol, corticosteroids, and levothyroxine. A thorough drug history is important in any animal presenting with skin lesions and even drugs that the pet has received for many months should be considered as a potential etiology. More information about specific dermatologic syndromes and methods of diagnosis and treatment can be found in Reference 16.

Conclusion
The above are only a few examples of potential adverse reactions to veterinary drugs, and with the diversity of medications available in the human and veterinary marketplaces, it is not always possible for veterinarians to maintain full awareness of the occurrence of all potential adverse effects of all products used. However, recognition of adverse drug reactions and avoidance of an unneeded prescribing cascade can be facilitated by regular review of drug information (e.g. through regular perusal of package inserts and the veterinary literature, and utilization of product safety updates provided by the FDA and veterinary news sources). Veterinarians should also consider the possibility of an adverse drug reaction whenever new clinical signs appear in a patient receiving multiple medications, particularly geriatric or systemically ill patients. Involvement of the bone marrow, liver, or skin is also common with idiosyncratic adverse drug reactions and an adverse drug reaction should be on the differential list when these organs are affected. Whenever possible, polypharmacy should be avoided and the need for each medication re-assessed on a regular basis.

References
When selecting an antibiotic for use in dogs or cats, important considerations include the antibiotic’s spectrum of action (i.e. activity against likely pathogens) and its suitability for treatment of infections in a particular site (which may be affected by drug characteristics such as lipophilicity, degree of protein binding, and route of elimination). Details regarding antimicrobial spectrum and disposition may be easily recalled for frequently used antibiotics, but drug activity against emerging pathogens, or the spectra and pharmacokinetics of recently approved antibiotics, may not be as familiar. The goal of this presentation is to review the characteristics and spectra of action of different antibiotic classes, together with questions that may arise concerning their use in light of newer options.

**Antibiotics effective against gram-positive organisms**

Penicillins, first-generation cephalosporins, monobactams, glycopeptides, macrolides, and lincosamides have activity primarily against Gram-positive organisms. For penicillins, these organisms include include streptococci, enterococci, some staphylococci (those without beta-lactamases), Arcanobacter, Actinomyces, Listeria, and spirochetes such as Leptospira and Borrelia. The Gram-negative spectrum of penicillins is very limited but includes Pasteurella (the predominant pathogen in cat bite abscesses), and aminopenicillins and first-generation cephalosporins are effective against selected Gram-negative organisms (e.g. E. coli, Proteus mirabilis, Salmonella). Penicillins, aminopenicillins, and lincosamides have good anaerobic coverage except against Bacteroides fragilis.

Among beta lactams, activity against beta-lactamase producing staphylococci requires an antistaphylococcal penicillin (e.g. methicillin), addition of a beta-lactamase inhibitor, or the bulkier side chain of a cephalosporin (excluding carbapenems, which should be reserved for life-threatening resistant infections). Potentiated sulfonamides, tetracyclines, and chloramphenicol also have activity against Gram-positive organisms, including staphylococci.

**Q: Amoxicillin-clavulanate is often thought of as “broad-spectrum”. What does it NOT cover?**

Amoxicillin-clavulanate is not reliably effective against Bacteroides fragilis, Bordetella bronchiseptica, Enterobacter and Citrobacter spp, Klebsiella, non-mirabilis Proteus spp., Pseudomonas, and Serratia. In addition, it is not effective against organisms (generally Gram negative Enterobacteriaceae) that have acquired beta lactam resistance. Therefore, amoxicillin-clavulanate (or ampicillin-sulbactam) should not be selected as a sole or first choice for potentially life-threatening infections with suspected involvement of Gram-negative organisms.

**Q: What about MRSA/MRSP?**

Recently, there has been an increase in the incidence of infections involving multi-drug resistant staphylococci (methicillin-resistant Staphylococcus aureus or pseudintermedius). These pathogens tend to be resistant to all beta lactams and multiple other drug classes, and preferred antibiotics include doxycycline, fluoroquinolones (variably) and aminoglycosides. Rifampin may also be used in combination with other antibiotics.

**Q: Earlier generations of cephalosporins tend to have more Gram-positive activity, whereas later generations in general have greater Gram-negative at the expense of Gram-positive activity. How do the spectra of cefpodoxime and cefovecin compare with those of first-generation cephalosporins? Have they lost activity against common Gram-positive veterinary pathogens?**

Cefpodoxime, like the first-generation cephalosporins, is effective against streptococci and staphylococci (other than MRSA/MRSP). It also has efficacy against beta-lactamase negative E. coli, Klebsiella, Serratia, Proteus mirabilis and vulgaris, Providencia, and Salmonella. Approximately half of human isolates of beta-lactamase- producing E. coli, Enterobacter spp, Citrobacter spp., and Morganella are susceptible. Therefore, it has slightly expanded Gram-negative coverage compared with first-generation cephalosporins, but maintains some Gram positive activity (e.g. against opportunistic skin flora causing pyoderma in veterinary patients).

Cefovecin is also a third-generation cephalosporin and is more active with lower MICs for many bacteria than first-generation cephalosporins. In studies conducted by the sponsor of a long-acting veterinary formulation, the MIC<sub>90</sub> was 0.25 ug/mL for S. intermedius (vs. 2 ug/mL for cephalaxin), and it had an MIC<sub>90</sub> of 1 ug/mL (vs. 16 ug/mL for cephalaxin and cefadroxil) for many Gram-negative organisms and very low MICs for feline Pasteurella isolates and Streptococcus canis. However, as noted by the manufacturer, this antibiotic is heavily protein-bound and free concentrations may not be sufficient to reach an appropriate time above MIC for E. coli in the plasma in vivo. Therefore, single administration may be effective only for highly susceptible pathogens (Gram-positive and Pasteurella) and for urinary tract infection (as the drug is eliminated in the urine.) It is labeled for treatment of pyoderma,
bite wounds, and abscesses in the United States, and additionally for E. coli UTI in Europe. It is not effective against Pseudomonas or enterococci.

In both cases, amoxicillin for Pasteurella or susceptible UTI, or amoxicillin-clavulanic acid or cephalaxin for pyoderma, would be appropriate choices in lieu of third-generation cephalosporins unless compliance is an obstacle or Gram-negative involvement is suspected.

**Antibiotics effective against gram-negative organisms**

Aminoglycosides, fluoroquinolones, and parenteral third-generation cephalosporins (cefotaxime, ceftazidime) are generally used primarily for Gram-negative coverage. Aminoglycosides require oxygen-dependent transport into bacteria and are not effective against anaerobes, and among Gram-positive organisms, fluoroquinolones are effective against staphylococci but not streptococci. Fluoroquinolones (particularly enrofloxacin) have variable efficacy against Pseudomonas and antipseudomonal penicillins (e.g. ticarcillin) or selected third-generation cephalosporins (ceftazidime) might be preferable when fluoroquinolone resistance is encountered. Other options for treatment of Gram-negative infection include potentiated sulfonamides, tetracyclines, and chloramphenicol.

Pradofloxacin is a third-generation fluoroquinolone with expanded activity compared to other classes of fluoroquinolones. It is effective against a variety of Gram-positive, Gram-negative, and anaerobic pathogens and is labeled for treatment of dental as well as soft tissue infections in dogs.

**Anaerobes**

Drugs of choice for anaerobes include penicillins, clindamycin, metronidazole, and third-generation cephalosporins. Carbapenems and chloramphenicol also provide anaerobic coverage. Coverage is variable with tetracyclines.

**Q: Is there any rationale for using both a penicillin and metronidazole in animals with suspected anaerobic (e.g. clostridial) infections?**

Metronidazole’s coverage is exclusively anaerobic and in contrast to that of penicillins, it includes *Bacteroides fragilis*. However, the significance of this pathogen in veterinary medicine is questionable, and there is minimal difference in the effectiveness of metronidazole and penicillins against clostridia.
Can I Substitute? Ensuring Your Patients Get the Right Drugs in the Clinic or at the Human Pharmacy
Melissa Clark, DVM, PhD, DACVCP
Animal Medical Center
New York, NY

Because of the relatively small proportion of pharmaceuticals marketed for dogs and cats and the limited dispensary space in many veterinary hospitals, veterinarians frequently prescribe medications via an outside pharmacy (either human or veterinary). Confusion may arise during multiple steps in this process, e.g. during communication of the prescription (which often occurs via telephone), or during filling of the prescription and delivery of the medication to the client and ultimately to the pet. Veterinarians may also receive inquiries from clients about prescribed medications for which a seemingly comparable human or generic formulation is available.

The problem of prescribing confusion is not unique to veterinary medicine, and in human medicine, the nonprofit Institution for Safe Medical Practices (ISMP) has produced guidelines for hospitals and pharmacies to help reduce the likelihood of patient harm from medication errors. Application of these guidelines to veterinary prescribing can be helpful, as can an understanding of the distinctions between different formulations of human and veterinary drugs.

Accidental substitution during the prescription process: sources of error and measures to prevent them
“Look-alike/sound-alike” drugs
Considering the array of medications available for prescription through human pharmacies, it is not surprising that one drug may be inadvertently substituted for another based on a similar-sounding name, or a name with a similar written appearance. To prevent such a substitution, which can be life-threatening for the patient (e.g. azathioprine for azithromycin in a cat), the following (adapted from ISMP guidelines) are recommended.

1. Educate staff about common “sound-alike” drugs, and consider posting a list in an accessible area where telephone prescribing occurs. A list of “sound-alike” drugs from human medicine is periodically published by the ISMP and this can be reviewed to select those applicable to a particular veterinary practice. The list can be reviewed and renewed at least quarterly by a staff member.

2. The person placing a telephone prescription should either spell the name of the drug to the pharmacist for verification, or have the pharmacist spell it to the prescriber. The prescribing individual should also provide an indication for the drug, e.g. “for infection”. A drug indication that does not match the drug name will often trigger closer scrutiny.

3. When submitting a written prescription, be sure handwriting is legible, and, as for telephone prescriptions, be aware of drugs with similar-appearing names and provide an indication as part of the prescription. Do not abbreviate drug names.

4. If you routinely leave prescriptions on a pharmacy’s voicemail, make sure the client has the drug name (and potentially the strength and directions) in writing to verify at pickup.

Dosing errors
Dosing errors can result from incorrect interpretation of two similar-sounding numbers (e.g. “fifty” for “fifteen”), from illegible written prescriptions or incorrect placement of decimal points, from incorrect calculations, or from unfamiliar abbreviations. To avoid dosing errors:

1. When communicating a number over the phone, repeat numbers in digits, e.g. “one five” in addition to “fifteen.”

2. As for drug names, make sure drug dosages are legible, with no ambiguity surrounding numbers or decimal points (do not use trailing zeros, and place zeros before decimal points), and avoid abbreviations (particularly SID, which is not used in human medicine) where possible.

3. Double check all calculated drug doses.

General communication obstacles
For either a spoken or a written prescription, the prescriber should always 1) be willing to clarify the prescription to the pharmacist, and 2) maintain a courteous attitude. In a survey conducted among human healthcare workers by ISMP, 83% of pharmacists said they had encountered a reluctance or refusal to answer questions or return calls by prescribers, and 40% of respondents reported that they assumed a medication order they had concerns about was correct, rather than seeking clarification from the prescriber, if the prescriber was perceived as intimidating. 7% of these individuals also acknowledged that they had been involved in a medication error in which intimidation played a role within the previous year.

Potential sources of error when the prescription is filled
Human pharmacists reviewing veterinary prescriptions may note differences in the veterinary and human indications and dosing regimens for certain drugs. When this information is communicated to the client at pickup, it can cause confusion. For example, mirtazapine is an antidepressant in humans; and clients picking up benazepril for treatment of proteinuria may be told that it is for
blood pressure management. When a medication is prescribed, attention should be given by veterinary staff to educating clients about the drug’s purpose, directions, side effects, and any notable differences from use of the drug in humans.

**Substitutions among human formulations**

Clients or pharmacists may ask a prescribing veterinarian whether a substitution of one human drug or formulation for another is acceptable, or pharmacists may assume it is unless otherwise specified. Generic human drugs may be assumed to be equivalent to name-brand formulations, but this is not always the case in pets, as bioequivalence has been demonstrated between human name-brand and generic drugs in human populations, but not in canine and feline populations. If a drug has an easily monitored clinical effect (e.g. amlodipine), if the consequences of lack of efficacy are not serious or life-threatening, if there is not a body of veterinary data supporting a specific formulation only, or if the drug is not a biological product such as insulin or levothyroxine, substitution of a generic for a name-brand human formulation may be acceptable. Hormone-based medications are more difficult to standardize among patients and clients should be aware that substitution of one brand of insulin or levothyroxine for another may require re-regulation of the patient’s disease.

**Substituting a human drug for a veterinary drug**

In some situations, clients may ask if a human drug formulation or human drug from the same class can be substituted for a veterinary prescription, for cost or convenience reasons. Clients may not be aware that human and veterinary-labeled drugs may differ in effectiveness despite having the same active ingredient, as other components of the product (excipients, enteric coating) can affect absorption and bioavailability. The approval requirements for veterinary-labeled drugs require substantial evidence of safety and efficacy, which generally entails clinical trials in the species of interest documenting appropriate pharmacodynamics (with or without pharmacokinetic data) and information about the incidence of adverse events with that formulation specifically in that species. The same is not true of human formulations used in pets.

For several human drugs with veterinary analogues, however, a large body of literature describing efficacy and nature of adverse events to be expected with the drug exists, and efficacy is not restricted to a specific formulation (e.g. cephalexin, methimazole, amlodipine). Substitution of a human drug for the veterinary version in this case will likely result in similar efficacy, but may result in the loss of modifications specific to the veterinary product (most often improved palatability or precise dosage forms) and support from the veterinary sponsor in case of adverse reaction. With regard to drugs from the same class, substitution of ciprofloxacin for enrofloxacin is often requested by clients for financial reasons, but is not advised considering the wide variation in ciprofloxacin bioavailability among dogs, which has been demonstrated in multiple studies.

**Substituting veterinary generic drugs or compounded drugs for veterinary name-brand formulations**

Manufacturers of veterinary generic formulations are required to demonstrate bioequivalence of the generic product to the parent (name brand) drug. Generally, this means that the two products produced drug exposure (as assessed by maximum plasma concentration and area under the curve) that was similar enough it would not be expected to result in a clinical difference. Therefore, generic veterinary products can often be substituted for name-brand products with minimal repercussion, although for hormone-based formulations, re-regulation may then be necessary, as discussed above.

The same is not true of compounded products, for which no comparison with name-brand or generic products must be made and which are not subject to outside regulations regarding stability, efficacy, and safety. Although compounded products may be effective in some circumstances, they should be used only when approved alternatives are not available, and inquiries should be made of the compounding pharmacy regarding stability data and manufacturing practices for their products. Two recent veterinary studies have identified stability concerns and inadequate plasma concentrations with compounded doxycycline and itraconazole, respectively, in dogs, and numerous other examples exist.

**Additional notes on prescribing through an in-clinic pharmacy**

Several of the guidelines for avoiding communication errors with human pharmacies can be applied to medication orders within a veterinary hospital. Prescribing veterinarians can help to minimize medication errors by communicating medication orders clearly to staff, and by being courteous and receptive to questions. Additionally, “look-alike/sound-alike” drugs, especially injectable drugs, can be labeled as such and placed in different areas of the in-clinic pharmacy.

**References**


89


Puppies, Kittens, and Drugs: What’s Safe for Pediatrics
Melissa Clark, DVM, PhD, DACVCP
Animal Medical Center
New York, NY

Physiology of neonatal (0-2 weeks), infant (2-6 weeks), and pediatric (6-12 weeks) dogs and cats differs from that of adults in several important ways that can impact drug metabolism and disposition. Proportion of total body water is substantially higher in puppies and kittens, leading to a higher volume of distribution and lower than expected plasma concentrations of water-soluble drugs; the reverse is true for fat-soluble drugs. Renal and hepatic function are also immature until at least 3-6 weeks of age. In addition, young animals have slower gastrointestinal transit time and a more permeable blood-brain barrier than adults. Because of the latter and because certain systems are still developing (e.g. physes, tooth buds) younger dogs and cats may be more susceptible than adults to certain adverse drug reactions.

For some drugs (primarily antiparasitics), specific information exists to support safe use in puppies and kittens as young as 4 weeks. Other drugs have been demonstrated to have increased risk of toxicity in young compared with mature animals. However, for most drugs, neither of the above is true. Labels for veterinary products may include statements specifying that the product is approved only for use in animals above a certain age. In some cases, a particular adverse effect was noted during safety assessment. However, because most veterinary pharmaceuticals are not specifically designed for puppies and kittens, safety testing is often performed in “healthy young mature animals” as per FDA guidance. Consequently, the label recommendation to avoid use in animals younger than a certain age may simply mean that its safety in pets below that age has not been evaluated. Approval for younger animals may be sought later if they form a substantial portion of the use class after initial marketing (e.g. maropitant). Only a very few medications are approved for pregnant or lactating animals.

Consequently, recommendations for use of specific drugs in puppies and kittens are often based on an amalgam of information from other species, theoretical support or concerns, and clinical experience. A collection of these recommendations, by drug class, is discussed below.

Antibiotics
B-lactams (penicillins and cephalosporins) are often suggested to be safe in young animals because of their wide therapeutic index, which alleviates concern about a slower elimination rate. However, in neonates, penicillins may be associated with suppression of normal GI flora and colonization by pathogenic organisms. The same does not appear to be true of cephalosporins, several of which are active against common pathogens causing neonatal septicemia. Macrolides are not overtly toxic, but undergo hepatic recirculation and may disrupt GI flora. Trimethoprim-sulfonamide has also been recommended as an initial broad-spectrum choice for puppies and kittens, although it has been associated with immune-mediated drug reactions in adults. Chloramphenicol has caused blood dyscrasias in 8-12 week old puppies at 50 mg/kg twice a day, and causes cardiac depression in neonates of other species (e.g. humans). Aminoglycosides have a narrow therapeutic index and young age has been listed as a risk factor for nephrotoxicity; however, these agents may still be used if adequate hydration is ensured. If metronidazole is used, very young puppies and kittens should be closely monitored for neurotoxicity. Tetracycline-induced tooth staining (which appears less common with doxycycline but has still been reported to occur) and cartilage damage with fluoroquinolones in large-breed puppies up to 18 weeks of age are often cited as reasons not to use these drugs in young animals. However, if life-threatening infection is present, fluoroquinolones may be appropriate as a means of Gram-negative coverage.

Analgesics and sedatives
Based on human literature, short-term opioid use is likely to be safe in pregnant, nursing, and neonatal dogs and cats. NSAID use is to be avoided in pregnant animals based on numerous studies in other species documenting fetal nephrotoxicity (as COX-2 is important for the developing kidney) and teratogenesis. Because most NSAIDs are lipid-soluble and highly protein-bound, they may not be transferred in milk in sufficient concentrations to affect nursing animals; however, this has not been demonstrated in dogs or cats, and meloxicam concentrations in the milk of rats were higher than those in plasma. NSAIDs are not recommended for animals less than 6 weeks of age because of ongoing hepatic and renal maturation.

Benzodiazepines have a large margin of safety and are often recommended as components of sedative or preanesthetic protocols for young puppies. Opioids alone have a sedating effect in pediatrics (<4 mo). Acepromazine may cause CNS depression in young animals and dose reductions to 0.005-0.025 mg/kg have been recommended. Lidocaine can be used as a local anesthetic at 3-6 mg/kg in kittens (with the lower dose to be used in neonatal animals) and 6-10 mg/kg in dogs. Similarly, some authors recommend bupivacaine at 2 mg/kg in older puppies and kittens and half of this dose for patients <12 weeks.
Anticonvulsants
Both phenobarbital and potassium bromide have been used to manage seizures in young puppies. Potassium bromide does not require hepatic metabolism, which may be advantageous in animals with immature liver function. Phenobarbital use in human children and young rats has been shown to interfere with brain development, and some authors recommend reduction of the initial dose for animal younger than 6 months (e.g. 0.5 mg/kg once a day for animals less than 3 months old, 1 mg/kg twice a day for 3-6 month old animals, and 2 mg/kg twice a day for animals older than 6 months). Gabapentin and levetiracetam have not been evaluated in young dogs and cats.

Antiparasitics
Pyrantel has a wide safety margin and has frequently been used in animals as young as 2 weeks of age. Many other antiparasitics and flea/tick control products have been marketed by veterinary pharmaceutical companies, and age recommendations can be found on the product label.

References