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Which drug is associated with damage to articular cartilage in young growing animals?

Chloramphenicol	HIDE
Enrofloxacin	HIDE
Trimethoprim sulfa (TMS)	HIDE
Clindamycin	HIDE
Erythromycin	HIDE

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Correct:

Enrofloxacin is a Quinolone antibiotic which has been associated with damage to articular cartilage in young growing animals. Quinolones have also been associated with neurotoxicity (like convulsions) at higher doses.

Sulfonamides like trimethoprim sulfa are associated with HYPERSENSITIVITY (ie: allergic) reactions.

Clindamycin, a Lincosamide may be associated with GI upset and is CONTRAINDICATED IN HORSES because severe, even fatal colitis can occur.

Erythromycin, a macrolide does not have many side effects, but another macrolide, TILMICOSIN (Micotil®) can kill humans if accidentally injected.

Chloramphenicol has been associated with bone marrow suppression/aplastic anemia in exposed humans, and is CONTRAINDICATED IN FOOD ANIMALS.

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Which drug family is associated with ALL of the following side effects and toxicity issues?

Hepatotoxicity

Potential nephrotoxicity: contraindicated in renal insufficiency

Hypersensitivity (ie: allergy, "drug fever")

Can disrupt gastric and ruminal microflora

Causes swelling and discoloration at injection site

Sulfonamides	HIDE
Cephalosporins	HIDE
Aminoglycosides	HIDE
Tetracyclines	HIDE
Penicillins	HIDE

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Correct:

Tetracycline can cause hepatotoxicity and has potential nephrotoxicity: contraindicated in renal insufficiency. Some patients display hypersensitivity (ie: allergy, "drug fever"). Tetracyclines can disrupt gastric and ruminal microflora and also cause swelling and discoloration at injection site, which may mean that part of a food animal carcass gets discarded.

When you think of drugs with LOTS OF TOXIC EFFECTS, remember the TWO TOXIC Ts-Tetracycline and Trimethoprim-sulfa (TMS).

With TMS, think keratoconjunctivitis sicca, type 1 and 3 hypersensitivities, hepatitis, hemolytic anemia, urticaria, hematuria, hypothyroidism, bone marrow depression and that is just in DOGS.
Refs: Merck Veterinary Manual online edition.

1 ✓	2 ✓	3	4	5	6	7	8	9	10

Which of the following medications needs to have its dose gradually tapered prior to discontinuation in order to prevent the possible development of fatal cardiac arrhythmias?

Hydralazine	HIDE
Diltiazem	HIDE
Propranolol	HIDE
Lidocaine	HIDE
Quinidine	HIDE

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Overview   Lab Values   Definitions

Correct:

The dosing of propranolol (a beta-adrenergic blocker) must be gradually tapered prior to discontinuation because it leads to upregulation of beta receptors. This helps to prevent the development of potentially fatal cardiac arrhythmias.

Lidocaine and quinidine are sodium channel blockers. Diltiazem is a calcium channel blocker. Hydralazine is an arteriolar dilator that works on smooth muscle of the vascular system.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, pp. 1026–27; and Plumb's Veterinary Drug Handbook, 7th edition.

| 1 ✓ | 2 ✓ | 3 ✓ | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

Carprofen (Rimadyl ®) is a nonsteroidal anti-inflammatory (NSAID) commonly-used in dogs with arthritis. Which one of the following choices is an important potential side effect of carprofen?

Hypersensitivity	HIDE
Protein-losing nephropathy	HIDE
Hepatopathy	HIDE
Seizures	HIDE
Secretory diarrhea	HIDE

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Correct:

There is a reported incidence of <mark>hepatopathy</mark> in 0.05% of dogs treated with carprofen (Rimadyl®).

Geriatric dogs, or dogs with pre-existing chronic diseases like inflammatory bowel disease (IBD), renal or hepatic insufficiency may be at a greater risk of toxic side effects.

Carprofen is contraindicated in animals with bleeding disorders, like von Willebrand's disease.

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 204-10 and the Merck Veterinary Manual online edition.

Carprofen:

Carprofen is an NSAID of the arylpropionic acid class available in the USA in caplet and chewable tablet formulations. An injectable formulation is also available in the USA and Europe. Carprofen is approved by the FDA to manage pain and inflammation associated with osteoarthritis and acute pain associated with soft-tissue and orthopedic surgery in dogs. The recommended dosage is 4.4 mg/kg/day or divided bid, PO. In Europe and other countries, carprofen is also registered for use in horses and cattle and for short-term therapy in cats. In dogs, oral bioavailability is high (90%), and plasma concentrations peak ~2–3 hr after dosing. The elimination half-life is ~8 hr. As with other NSAIDs, carprofen is highly (99%) protein bound. Elimination is via hepatic biotransformation, with excretion of the resulting metabolites in feces and urine. Some enterohepatic recycling occurs. The exact mechanism of action of carprofen is unclear. Although it has greater selectivity for COX-2 over COX-1, carprofen is considered a weak COX inhibitor. In vitro assays with canine cell lines indicate that it is 129-fold more selective for COX-2, whereas in vitro assays with canine whole blood indicate that it is 7- to 17-fold more selective for COX-2. Equine whole blood assays indicate that it is 1.6-fold more selective for COX-2, and feline whole blood assays indicate it is >5.5-fold more selective for COX-2. Other mechanisms of action, including inhibition of PA_2, may be responsible for its anti-inflammatory effects. Carprofen has been used extensively in dogs since its introduction, and adverse events have been comparable to those of other NSAIDs (ie, ~2 events/1,000 dogs treated). Approximately one-fourth of the adverse reactions reported were GI signs, including vomiting, diarrhea, and GI ulceration. Renal and hepatic adverse effects are rare, as with other NSAIDs. Potentially serious idiosyncratic hepatopathies, characterized by acute hepatic necrosis, have been reported in some dogs. Approximately one-third of the dogs developing hepatopathies while receiving carprofen were Labrador Retrievers, although a true breed predisposition has not been established. As with any NSAID therapy, clinical laboratory monitoring for hepatic damage is advised, especially in geriatric animals that may be predisposed to more serious complications.

Inflammatory Bowel Disease in Small Animals

By **Alice Defarges, DVM, MSc, DACVIM, Assistant Professor in Internal Medicine, Ontario Veterinary College, Uni**

Idiopathic inflammatory bowel disease (IBD) constitutes a group of GI diseases characterized by persistent clinical signs and histologic evidence of inflammatory cell infiltrate of unknown etiology. The various forms of IBD are classified by anatomic location and the predominant cell type involved. Lymphocytic-plasmacytic enteritis is the most common form in dogs and cats, followed by eosinophilic inflammation. There are occasional reports of inflammation with a granulomatous pattern (regional enteritis). A neutrophilic predominance in the inflammatory infiltrate is rare. A mixed pattern of cellular infiltrate is described on many occasions. Certain unique IBD syndromes occur more often in some breeds, such as the protein-losing enteropathy/nephropathy complex in Soft-coated Wheaten Terriers, immunoproliferative enteropathy of Basenjis, IBD in Norwegian Lundehunds, and histiocytic ulcerative colitis in Boxers.

Etiology and Pathophysiology:

The etiology of IBD is unknown. Several factors may be involved, such as GI lymphoid tissue (GALT); permeability defects; genetic, ischemic, biochemical, and psychosomatic disorders; infectious and parasitic agents; dietary allergens; and adverse drug reactions. IBD may also be immune mediated. The intestinal mucosa has a barrier function and controls exposure of antigens to GALT. The latter can stimulate protective immune responses against pathogens, while remaining tolerant of harmless environmental antigens (eg, commensal bacteria, food). Defective immunoregulation of GALT results in exposure and adverse reaction to antigens that normally would not evoke such a response. Although dietary allergy is an unlikely cause of IBD (except in eosinophilic gastroenteritis), it may contribute to increased mucosal permeability and food sensitivity.

1 ✓	2 ✓	3 ✓	4 ✓	5	6	7	8	9	10

Which one of the following choices is a competitive antagonist for aldosterone that is sometimes used in treatment of congestive heart failure?

Hydrochlorothiazide	HIDE
Mannitol	HIDE
Acetazolamide	HIDE
Furosemide	HIDE
Spironolactone	HIDE

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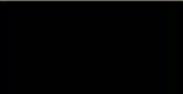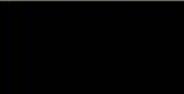
Correct:

Potassium-sparing diuretics (ie. spironolactone) are ==aldosterone antagonists== sometimes used with furosemide as part of the treatment plan for congestive heart failure (CHF).

Aldosterone, the mineralocorticoid produced in the ==adrenal cortex,== acts on the ==distal convoluted tubules== (and collecting ducts) of the nephron to retain Na+ and water, secrete K+ and increase blood pressure.

With CHF, aldosterone levels are **increased** due to activation of the renin-angiotensin-aldosterone system.

In contrast, see **decreased** aldosterone secretion (and decreased blood pressure) with hypoadrenocorticism.

Heart Failure, Congestive Heart Failure, and the Failing Heart

Systolic myocardial failure is described as reduced myocardial contractile function, characterized by a reduced force of contraction from any given preload. More objectively, a failing heart can be described as one with a reduced rate of liberation of energy from the breakdown of ATP, or with a reduced velocity of fiber shortening when the heart contracts during the imaginary situation of contracting against no load. It is difficult to directly measure myocardial contractility and to identify myocardial failure. Almost any animal with heart disease leading to chamber enlargement or increased wall thickness has a degree of myocardial failure on the cellular level, but such animals may remain compensated without clinical signs of heart failure for a prolonged time.

Low output heart failure and CHF (see Heart Disease and Heart Failure) are clinical syndromes in which an animal manifests signs referable to a complex interaction between a failing heart and the blood vessels. In low output heart failure, cardiac output is insufficient to perfuse organs with enough oxygenated blood for the organs to function properly either at rest or during periods of exertion. In CHF, blood dams up in or around organs—usually the lungs but occasionally in the systemic organs—and causes the congested organs to function abnormally, become edematous, or both. The functional classification of heart failure is expressed when, during graded exercise, the animal shows signs (eg, dyspnea, cough, collapse) due to the heart disease. There are several classifications of heart failure, the most recent and perhaps most practical of which is based on the course of heart disease expressed in four basic stages (A, B1, B2, C, D) described in the ACVIM Consensus Statement on canine chronic valvular heart disease (see ACVIM Consensus Statement).

| 1 ✓ | 2 ✓ | 3 ✓ | 4 ✓ | 5 ✗ | 6 | 7 | 8 | 9 | 10 |

Which one of the following is legal for appropriate use in food-producing animals?

Flunixin meglumine	HIDE
Chloramphenicol	HIDE
Diethylstilbesterol	HIDE
Furazolidone (nitrofuran)	HIDE
Estradiol cypionate	HIDE

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Correct:

Flunixin meglumine is labeled for use in dairy and beef cattle in the U.S. as long as appropriate withdrawal times are followed and there is a valid veterinary-client-patient relationship.

Always check out the Food Animal Residue Avoidance Databank (FARAD) for the most up-to-date info.

Diethylstilbesterol (DES) is banned for use in food-producing animals and should never be used.

Chloramphenicol has been associated with bone marrow suppression/aplastic anemia in exposed humans, and is contraindicated in food-producing animals.

According to the Food and Drug Administration (FDA) the use of ECP in animals is

According to the Food and Drug Administration (FDA) the use of ECP in animals is illegal. ECP has been used as an estrogenic hormone for reproductive therapy in food-producing animals, but even extra-label, this is not allowed.

Furazolidone a nitrofuran, is not allowed.

Refs: Update on drugs prohibited from extralabel use in food animals, Davis, et al., JAVMA, Vol 235, No.5, Sep 1,2009, Plumb's Vet Drug Handbook, 7th ed. pp. 426-8, 530-3, 853-7 and the Merck Veterinary Manual online edition.

FARAD Digest

Update on drugs prohibited from extralabel use in food animals

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Extralabel drug use encompasses the use of a drug in an animal in a manner that is not in accordance with the FDA-approved label. This includes use in a species or for a disease or condition not listed on the label; use at dosages, frequencies, or routes of administration that differ from those stated on the label; or deviation from the labeled withdrawal time. Extralabel drug use in veterinary species was made legal by the passage of AMDUCA in 1994.[1] However, there are restrictions to AMDUCA, particularly with reference to ELDU in food-producing animals.

The information reported here is intended to outline the guidelines pertaining to legal ELDU in food animals and to update readers on drugs that are prohibited by the FDA from ELDU in these species. Readers should use this information in conjunction with the information on prohibited drugs contained in a 1999 FARAD Digest.[2]

Guidelines for Legal ELDU

Limitations described in AMDUCA for ELDU in food animals include restrictions on which drugs can be used, the conditions for their use, and who can legally use them. When considering the need for ELDU, it must be remembered that the prime consideration should be to provide treatment to an animal in cases in which the health of the animal is endangered and suffering or death of the animal may result from lack of treatment. Also, there must be no licensed or marketed drug for that species that would be considered effective, and preference should be given for use of veterinary drug formulations, rather than human drug formulations.

A valid VCPR must exist prior to prescription of ELDU. This would assume that a veterinarian has examined the animal or group (herd or flock) of animals, has discussed the condition with the owner, and has sufficient information to make a preliminary diagnosis. Extralabel drug use by a layperson, such as a producer or farm worker, is prohibited, except when under the supervision of a licensed veterinarian.

ABBREVIATIONS	
CPG	Compliance Policy Guide
DES	Diethylstilbestrol
ECP	Estradiol cypionate
ELDU	Extralabel drug use
FARAD	Food Animal Residue Avoidance Databank
MUMS	Minor Use and Minor Species Animal Health Act of 2004
VCPR	Veterinarian-client-patient relationship
VRE	Vancomycin-resistant enterococci

Extralabel use of a drug for nontherapeutic purposes is not sanctioned under AMDUCA. This would include, but is not limited to, the use of drugs for growth promotion or reproductive purposes. Extralabel use resulting in any residue that may pose a risk to the public health or that is above an established tolerance is not allowed. In the case of extralabel use of a drug that is not licensed for any indication in that species, the established tolerance is zero or the lower limit of detection for the method used for residue analysis. Thus, any concentration detected in meat, milk, eggs, or honey would constitute a violative residue. Given the advanced methods currently available for detecting drug residues in food and food products of animal origin, miniscule amounts often can be detected.

The use of compounded drugs in food-producing species is allowed by AMDUCA; however, drugs can be compounded only when there is not an approved product available. Thus, compounded drugs, by definition, represent ELDU and are subject to the requirements set forth by AMDUCA. Because they are being used in an extralabel manner, all compounded formulations must have a withdrawal time stated on the label, and this withdrawal time must be specified by the veterinarian, not the compounding pharmacist. As a result of the variability of compounded products, it is difficult to determine an accurate, substantially extended withdrawal period supported by appropriate scientific information. Compounded products must not be used if there is a licensed veterinary drug formulation available, and the prescribing veterinarian must establish the need for the compounded product.

Compounding of drugs from bulk substances is illegal under FDA regulations; therefore, it is also not permissible by AMDUCA. There are a few important exceptions to this rule. One exception is antidotes for use in food animal medicine that would otherwise not

be available because of a lack of products approved for use in humans or other animals. The FDA has stated that regulatory discretion will be used for compounded antidotes, including ammonium molybdate, ammonium tetrathiomolybdate, ferric ferocyanide, methylene blue, pilocarpine, picrotoxin, sodium nitrite, sodium thiosulfate, and tannic acid.[3]

Consider the example of ECP. This drug was previously available for use as an estrogenic hormone for reproductive treatment in food animals, despite the fact that there are no FDA-approved products available for use in human or veterinary medicine.[4] Estradiol cypionate was used primarily for estrus synchronization in cattle. It was subsequently removed from the market, and the only way for practitioners to obtain ECP is through compounding from bulk substances. Although the drug is not specifically prohibited from use in food-producing animals, its use is illegal because it constitutes compounding of an unapproved animal drug and also extralabel use for nontherapeutic purposes. The example of ECP highlights the need for veterinary practitioners to understand the limitations involved in ELDU in food animals to protect themselves and their clients from regulatory actions.

In addition to these restrictions and guidelines, there are certain drugs and drug classes that the FDA has prohibited from use in food-producing animals, regardless of need or indication (**Table 1**). These are drugs for which no acceptable analytic method can be established or for which extralabel use poses a risk to public health. These prohibitions may be absolute or may be restricted to certain types of food-producing animals, such as dairy cows. For some drugs on this list, approved products are available, but there must be strict adherence to label directions.

A list of these drugs and the explanations behind their prohibition was published in a 1999 FARAD Digest.[2] However, in the past 10 years, several new drugs have been added to the list, and some of the previous prohibitions have been revised. A summary of these prohibitions with special emphasis on new and updated information is provided here.

Review of Prohibited Drugs or Drugs Prohibited From ELDU

The following section deals with drugs that have been on the FDA's prohibited drug list for > 10 years and have not had any revisions to the order of prohibition. A more complete summary can be found in the aforementioned FARAD Digest.[2]

Chloramphenicol—Chloramphenicol has been prohibited from use in food-producing animals since 1984 because of the potential development of an idiosyncratic, non–dose-dependent, irreversible, aplastic anemia that may develop in humans exposed to even small amounts of the drug.[2] The use of this drug in food-producing animals is not legal under any circumstance. Florfenicol is in the same class of antibiotics as chloramphenicol but is available for use in cattle, swine, and some aquatic species. Florfenicol has not been associated with aplastic anemia in humans, and therefore, extralabel use of florfenicol in food-producing animals is allowed.

DES—Diethylstilbestrol was once used as a treatment to prevent miscarriages; however, a link was found between the use of DES in pregnant women and the development of reproductive tract abnormalities and tumors in female offspring of DES-treated patients. Subfertility and infertility have also been detected in male and female offspring of DES-treated patients. Reproductive abnormalities have even been seen in granddaughters and grandsons of treated women.[5] The DES products are no longer marketed in the United States, and their use in food-producing species has been prohibited since 1979.

Nitroimidazoles—Members of this drug class, including metronidazole, dimetridazole, ipronidazole, ronidazole, and tinidazole, have in vitro and in vivo potential for carcinogenesis.[2] Some drugs in this drug class were labeled for the treatment of histomoniasis in turkeys and had been recommended as a treatment for trichomoniasis in bulls. However, approved products have been withdrawn from the market, and there are currently no nitroimidazole products approved for use in food animals. Therefore, any use would be in an extralabel manner and is prohibited in food-producing species.

Clenbuterol—Clenbuterol is a β_2-adrenergic receptor agonist that also has secondary anabolic effects. These anabolic effects have led to the illegal use of this drug in show and sale animals to increase lean body mass and weight gain. High doses of the drug are nec-

Table 1—Drugs currently prohibited from use or extralabel use in food-producing animals.

Drugs prohibited from use in food-producing animals	Drugs prohibited from extralabel use in food-producing animals
DES	Sulfonamides in adult dairy cattle*
Chloramphenicol	Fluoroquinolones
Nitroimidazoles (including metronidazole)	Medicated feeds†
Nitrofurans (including topical use)	Indexed drugs
Clenbuterol	
Dipyrone	
Glycopeptides	
Gentian violet	
Phenylbutazone in adult dairy cattle*	
Antiviral compounds in poultry (including adamantane and neuraminidase inhibitors)	

*Cattle > 20 months of age. †Exceptions may be made for minor species.

essary for these effects, which may have been one of the factors that led to the reported hospitalization of > 1,200 people and the death of 3 people in France and Spain that were linked to clenbuterol residues in the liver of illegally treated animals.[2,6] Similar outbreaks have been reported in other countries, including Italy and Portugal.[6–8] Although concentrations of drug are often highest in the liver, toxic amounts can also be found in non–liver-containing meat from treated cattle and lambs.[9]

Clenbuterol[a] is available in the United States only as an orally administered syrup for the treatment of horses with recurrent airway obstruction (ie, heaves). The FDA has never approved an injectable formulation of clenbuterol, so any importation or formulation of such a product would clearly be prohibited. Practitioners should be careful in prescribing this drug to horses that are housed on the same premises with food-producing animals and ensure that all labeling requirements are met. Albuterol, another β_2-adrenergic receptor agonist, is not strictly prohibited from ELDU; however, it is difficult to establish a withdrawal interval after extralabel use of albuterol because of a lack of pharmacokinetic data.

Dipyrone—Dipyrone is an anti-inflammatory, antipyretic, and analgesic drug previously licensed for use in humans. Concerns over an association with adverse effects in humans that ranged from non–dose-dependent teratogenic effects to prolonged bleeding times and agranulocytosis prompted the FDA to withdraw this drug from the market in 1977. Although no licensed products were available for use in animals, products were still marketed for use in non–food-producing animals, at the regulatory discretion of the FDA. However, the FDA received reports of extralabel use of dipyrone in food-producing species. Thus, since 1995, all dipyrone products have been withdrawn from the market until such time as a licensed product becomes available.[10] It is possible that dipyrone may not be included in official lists of prohibited drugs because there are no marketed products available. However, use of dipyrone in any food-producing animal is illegal.

Glycopeptides—Of the glycopeptide class of antimicrobials, vancomycin is the only one available in the United States. Although the authors are not aware of reports of the use of vancomycin in food-producing animals, it has been prohibited on the basis of its potential to cause development of resistant human pathogens.[11] Of particular concern with glycopeptides is the risk of development of VRE. Several studies[12,13] have revealed that VRE can be found in the feces of farm animals; however, there is little evidence of transmission of VRE from animals to healthy people.[14]

Sulfonamide use in dairy cattle—Sulfonamides have been banned from ELDU in adult dairy cows. For this purpose, adult dairy cows are defined as any dairy cow > 20 months of age, regardless of milking status.[15] This ban was instituted because of the concern over carcinogenic effects detected in laboratory animals, which coincided with reports of sulfonamide residues detected in up to 73% of commercial milk samples. There

currently is 1 sulfadimethoxine product marketed for use in dairy cows. Use of this drug in accordance with the label is permitted; however, ELDU is prohibited. Sulfadimethoxine is available to producers as over-the-counter products, and this can lead to extralabel use of a prohibited drug by a layperson. Veterinarians should educate their clients on the gravity and legal ramifications of this practice. Furthermore, veterinarians should be aware that they may still be listed as the veterinarian of record for any animals receiving over-the-counter sulfadimethoxine products and be held responsible for illegal residues. Extralabel use of all other sulfonamides and potentiated sulfonamide products is prohibited in adult dairy cattle.

Questions often arise regarding ELDU of sulfonamides in other dairy animals, such as goats or sheep used for milk production. Although this use is not expressly prohibited by the FDA, it is discouraged on the basis of the likelihood of violative residues in milk from these animals. Sulfonamides, similar to other drugs discussed in this report, are considered to be of high regulatory concern; therefore, use of these drugs in an extralabel manner is not advised.

Drugs with Updated Prohibition Orders

Several drugs discussed in the previous FARAD Digest on prohibited drugs[2] have had modifications to their prohibitions. These include the fluoroquinolones and nitrofurans as well as the ELDU of medicated feeds.

Fluoroquinolones—The fluoroquinolones were the first group of antimicrobials prohibited from extralabel use by the FDA because of their potential for creating antimicrobial-resistant strains that posed a threat to human health. Fluoroquinolones are commonly used as a treatment for multidrug-resistant *Salmonella* spp in humans; therefore, their use in food-producing species has been questioned. Consequently, the FDA banned the extralabel use of fluoroquinolones in 1997.[11] Use of marketed products was still allowed, providing label directions were followed. At the time of the prohibition, the use of these marketed products included sarafloxacin and enrofloxacin in poultry and enrofloxacin in beef cattle.

Surveillance of resistance to fluoroquinolones in bacteria isolated from food-producing animals was continued, and an increase in fluoroquinolone-resistant *Campylobacter* spp in poultry was linked to an increased incidence of infection with resistant *Campylobacter* spp in humans.[16,17] Therefore, the FDA proposed a withdrawal of fluoroquinolone products labeled for use in poultry on the basis of the proposed risk to human health, and sarafloxacin products were voluntarily withdrawn from the market by the sponsor. However, in 2005, the FDA withdrew the approval for enrofloxacin products in poultry and effectively made use of these drugs in poultry species illegal.[18] Despite the fact that fluoroquinolone products for poultry have not been available for several years, resistance to fluoroquinolones persists in *Campylobacter* spp and may actually be increasing.[19] In 1 study,[19] it was reported that fluoroquinolone resistance at 2 major US poultry production

operations increased from 13% in 2004 to 21% in 2006, despite discontinuing the use of these drugs.

Fluoroquinolone products are still available for other food-producing species, and these have not been removed from the market. These products include danofloxacin[b] and enrofloxacin.[c] Danofloxacin is labeled for use in beef cattle (excluding dairy cattle) and calves (excluding veal calves) for the treatment of respiratory disease associated with *Mannheimia haemolytica* and *Pasteurella multocida*. Enrofloxacin was originally approved for use in beef cattle for the treatment of respiratory disease associated with *M haemolytica*, *P multocida*, and *Histophilus somni*. Two times during the past year, the label for enrofloxacin has been expanded: first to add nonlactating dairy cattle and then to include swine for the treatment of respiratory disease associated with *Actinobacillus pleuropneumoniae*, *P multocida*, *Haemophilus parasuis*, and *Streptococcus suis*.

Practitioners are reminded that any use of fluoroquinolones that deviates from the label directions is expressly prohibited. Such prohibitions include use in lactating animals and veal calves and different nonlabeled conditions or diseases, dosages, frequencies, and routes of administrations. Fluoroquinolones must not be stored on dairy farms.[20]

Nitrofurans—Nitrofuran products for systemic administration were banned from use in food-producing species in 1991 because of concerns over carcinogenic effects in laboratory animals and a lack of a reliable detection method in food products. Products for topical use were still available with labels for food animals, which included treatment of surface wounds and infectious keratoconjunctivitis (ie, pinkeye). Studies reporting systemic absorption and detection of nitrofurazone residues in meat and milk from cows administered nitrofurans by the intramammary, intrauterine, or ocular routes prompted the FDA to prohibit topical use of these products.[21] Since 2002, all systemic and topical use of nitrofuran products has been prohibited.[22]

Extralabel use of medicated feeds—Extralabel use of medicated feeds by veterinarians and producers is prohibited. However, there are some exceptions to this rule, and these exceptions are published in the FDA's CPG on extralabel use of medicated feeds for minor species.[23] This policy was developed to aid practitioners in treating minor species that are difficult to medicate in any other way and that have few or no approved drug options for treatment. Although this does not legalize the extralabel use of medicated feeds, the FDA will exercise regulatory discretion with regard to the use of these feeds for minor species. Minor species are defined as any animal other than cattle, horses, swine, chickens, turkeys, dogs, and cats. Similar to AMDUCA, this policy has multiple limitations, including extralabel use of medicated feeds only for instances in which the health or life of an animal is in danger and use only in confined or farmed animals. Additionally, extralabel use of medicated feeds in accordance with the CPG is limited to products that have been approved for use in a major species; for aquaculture, extralabel use is limited to medicated feed products approved for use in aquatic species. These products must not be changed or adulterated in any way. All other tenets of AMDUCA must also be met, including prescription only under a valid VCPR, establishment of an appropriate withdrawal interval, and observance of all appropriate labeling and record-keeping duties. Veterinarians who treat minor species are referred to this CPG for complete details.

Many medicated feeds used for growth-promoting properties are actually subtherapeutic doses of antimicrobials. This restriction on extralabel use of medicated feeds is based on concerns about the development of resistant bacteria in animals exposed to subtherapeutic doses of antimicrobials. Along these lines, the European Union banned the use of all growth-promoting antimicrobials in 1995.[24] This included avoparcin, bacitracin, spiramycin, tylosin, and virginiamycin.

In the previous FARAD Digest on prohibited drugs,[2] it was stated that use of ionophore compounds in lactating dairy rations was prohibited. Although extralabel use of these compounds is still prohibited, a monensin-containing feed premix additive[d] has been approved for use in dairy cattle.

Gentian violet—Gentian violet is a xenobiotic dye that was originally added to poultry feeds as a growth promotant and was thought to increase dietary absorption of methionine and glucose.[25] It was determined that its main effect is more likely attributable to prevention of growth retardation secondary to aflatoxin; therefore, its primary use is as a mold inhibitor. However, the FDA has never approved the use of this product in feeds, and the impact of gentian violet residues on human health has not been fully assessed. As such, the use of gentian violet compounds in feeds constitutes extralabel use of a medicated feed and an unapproved new animal drug, and it is prohibited. Other compounds that are generally regarded as safe by the FDA are available for use as mold inhibitors in poultry feeds and should be used as an alternative. These include propionic acid and other organic acids.

The prohibition on gentian violet is not new. It was originally ordered in 1987, but gentian violet has not typically been specifically included on lists of prohibited drugs. Recently, however, topical products containing gentian violet have been found on the market, and the FDA has reiterated the prohibition order on this compound.[26]

Additions to the List of Prohibited Drugs

Since the publication of the previous FARAD Digest on prohibited drugs,[2] several new drugs or classes of drugs have been added to the prohibited drug list. A discussion of these is included in this section.

Phenylbutazone in adult dairy cattle—Use of phenylbutazone in dairy cattle > 20 months of age was prohibited in 2003.[27] This order was based on the detection of phenylbutazone residues in culled dairy cattle and the discovery of phenylbutazone products on dairy farms. This was of particular concern because there are no phenylbutazone formulations approved for use in any food-producing species.

Phenylbutazone has been used in human medicine as an NSAID in the past, but all human products were

withdrawn from the market for safety reasons. In particular, phenylbutazone at doses of 200 to 800 mg/d can induce blood dyscrasias (such as aplastic anemia, leukopenia, agranulocytosis, and thrombocytopenia) and cause death. It is also considered a carcinogen. Of more concern from a food residue standpoint are the reports of an idiosyncratic serum-sickness–type hypersensitivity reaction for which a threshold exposure concentration has not been determined.[27]

Currently, phenylbutazone use is strictly prohibited only in dairy cattle > 20 months of age; however, its use in other meat- and milk-producing species is discouraged for several reasons. The elimination half-life of phenylbutazone is greatly prolonged in ruminant species, compared with the half-life in monogastrics.[28] Residues may be detectable for extended periods after administration, which requires prolonged withdrawal times associated with its use.[29]

Another reason phenylbutazone should be avoided in food-producing animals is that its use is not covered by AMDUCA because there is an effective approved drug. Flunixin meglumine is an NSAID approved for IV administration to cattle (excluding veal calves) and swine. Phenylbutazone is preferred by some practitioners because of its slow elimination after oral administration, which allows for alternate-day administration. Ease of administration is not a viable reason for ELDU, unless it can be documented that no other route of administration is feasible. Therefore, it is difficult to justify the use of phenylbutazone over flunixin meglumine.

Similar to the situation with sulfonamide products, the use of phenylbutazone products in other milk-producing species is discouraged because of the high potential for residues in milk following administration. Although there are currently no NSAIDs labeled for use in small ruminants or other minor species, flunixin meglumine should be used preferentially over phenylbutazone in these animals because it is labeled for use in food animals in other major species. Phenylbutazone is considered to be a drug of high regulatory concern. As such, monitoring programs for residues of it and other NSAIDs in meat and milk are stringent.

Antiviral drugs in poultry—Two classes of antiviral drugs currently marketed for use in humans have been added to the list of prohibited drugs.[30] These are the adamantane inhibitors, rimantadine and amantadine, as well as the neuroaminidase inhibitors, oseltamivir and zanamivir. These antiviral drugs have been used in countries outside the United States to treat or prevent the development and spread of avian influenza in poultry. None of these drugs is labeled for animal use in the United States. The prohibition extends specifically to chickens, turkeys, and ducks; however, use of these drugs in other food-producing species is not recommended, and the prohibition order may be extended to other species in the future.

The prohibition order is based on the potential for the development of resistance to these compounds.[31–33] This potential is supported by the fact that countries that have made it a practice to use amantadine in poultry have detected the development of resistant strains of avian influenza, most notably the H5N1 subtype. Amantadine is used as a feed or water additive, often

for prolonged periods, with a median exposure time of 42 days.[32] Cross-resistance to rimantadine has also been reported.[31] In some countries, amantadine is available as an over-the-counter product and is easily obtained by producers without a veterinary prescription. In the United States, the drug is available (by prescription only) for use in humans for the treatment and prevention of influenza as well as the treatment of Parkinson's disease. Numerous adverse effects are associated with amantadine, including CNS effects and fatalities.

Because of the prohibitively high cost of the neuroaminidase inhibitors, they are not used in poultry; however, they currently remain as the last resort for treatment of adamantane-resistant influenza strains in humans. For this reason, the FDA has added this class of drugs to the prohibited list.

Indexed drugs—When dealing with drugs for use in minor species, the products can be approved, conditionally approved, or indexed. Under MUMS, indexing creates a new category of drug that the FDA allows to be marketed but which does not carry the FDA imprimatur of approval.[34] Drugs that have such a small market as to be added to the index are those not being administered to any animal that will enter the human food chain as well as prohibited from ELDU. An example of such a product is a combination product containing salmon gonadotropin–releasing hormone and domperidone.[e] This product can be legally marketed for use as a spawning aid in ornamental finfish,[35] but the product label clearly states that it is not intended for use in fish intended for human or animal consumption or in fish whose offspring may be consumed by humans or food-producing animals. It also expressly states that extralabel use of this product is prohibited.

The Issue of Cephalosporins

In July 2008, the FDA proposed an order of prohibition on the extralabel use of cephalosporins in food-producing animals. Cephalosporins were considered for prohibition because of the increased emergence of cephalosporin-resistant zoonotic foodborne pathogens, particularly *Salmonella* spp, believed to be associated with extralabel use of cephalosporins. A study[36] conducted as part of the US National Antimicrobial Resistance Monitoring System revealed an increase in resistance of *Salmonella* isolates from both humans and food-producing animals to ceftiofur, a third-generation cephalosporin drug marketed for use in cattle, sheep, dairy goats, and swine as multiple injectable formulations as well as intramammary preparations for lactating and nonlactating cows. Ceftiofur is not used in human medicine; however, concerns about the movement of foodborne bacteria between domestic animals and humans and evidence of cross-resistance among drugs in the cephalosporin class caused the FDA to consider the extralabel use of cephalosporins a risk to public health and safety.

Similar to the situation for other prohibited drugs, the FDA allowed a 60-day comment period before the rule would be in effect. In the case of the cephalosporins, a high response rate resulted in the comment period being extended an additional 60 days so that the

order of prohibition was expected to go into effect on November 30, 2008. Opposition to the order of prohibition was overwhelming, and the FDA opted to revoke the order of prohibition until it could adequately consider the comments received.[37] This should not be interpreted as the order being permanently revoked, however. The prohibition order may be reissued at any time if the FDA considers the evidence for prohibition stronger than the evidence against. We included this discussion of cephalosporins to highlight the process involved in drug prohibitions as well as to stress the need for responsible ELDU in animals.

Consequences of the Use of Prohibited Drugs in Food Animals

In the case of the detection of illegal residues for any drug, certain actions can be taken against the producers and any other individual that is held responsible for those residues, including the prescribing veterinarian.[38] These include condemnation of the animals or animal by-products (ie, milk) involved in the residue violation as well as detention of future shipments, on-site investigation of a suspect producer, and notification and reporting of abusers to state and federal agencies. After the initial violation, a warning letter is sent to the responsible persons. In the instance of repeated or flagrant abuse of the laws, an injunction is placed against the producer until such time as all animals on the premises can be shown to be free of residues. If the animals are not free of residues within 60 days, the injunction may become permanent.

In extreme cases, responsible persons may be fined or imprisoned. This involves cases in which blatant misuse of toxicologically important drugs results in residues substantially above tolerance, false guarantees are issued that animals with violative residues are free of drugs or the appropriate withdrawal period has been maintained, or there are multiple misdemeanor counts or 1 or more felony counts. These consequences also apply to cases in which the residues detected are for drugs prohibited from extralabel use in food animals. In these instances, a warning letter or injunction need not be filed prior to prosecution for criminal actions.[38]

In the case of purposeful or accidental exposure to prohibited drugs, FARAD will decline from providing withdrawal intervals for ELDU. It should be mentioned that FARAD is not a regulatory agency and will work with veterinarians and consumers to solve problems so that the human food chain is protected. If there is doubt as to whether a drug is prohibited, or if the use of a drug in an extralabel manner is covered by AMDUCA, practitioners are encouraged to contact FARAD via the Web submission form that can be found at the FARAD Web site (www.farad.org), via e-mail (usfarad@gmail.com), or via the FARAD hotline (1-888-873-2723). Information is also available at the FDA Center for Veterinary Medicine Web site (www.fda.gov/cvm/).

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b. A180, Pfizer Animal Health, New York, NY.
c. Baytril 100, Bayer Animal Health, Shawnee Mission, Kan.
d. Rumensin Type A medicated feed article, Elanco Animal Health, Greenfield, Ind.
e. Ovaprim injectable solution, Western Chemical Inc, Ferndale, Wash.

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1 ✓	2 ✓	3 ✓	4 ✓	5 ✗	6 ✓	7	8	9	10

Which drug is a calcium channel blocker?

Verapamil	HIDE
Propranolol	HIDE
Milrinone	HIDE
Enalapril	HIDE
Captopril	HIDE

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Overview   Mark this   Lab   Definitions   Report

Correct:

Verapamil is a calcium channel blocker. Calcium channel blockers are antiarrhythmic and have negative inotropic effects (decrease force of cardiac muscle contraction).

They are used to treat atrial fibrillation and supraventricular tachycardias, as well as hypertrophic cardiomyopathy (HCM) and hypertension. Amlodipine (used more for hypertension) and diltiazem are two other examples of calcium channel blockers.

ACE inhibitors like enalapril are vasodilators that help increase cardiac output.

Beta-blockers like propranolol and atenolol are used to treat arrhythmias, systemic hypertension, and HCM.

Positive inotropes increase the cardiac muscular contraction strength by making more intracellular calcium available for muscle proteins.

Examples of positive inotropes include:
Phosphodiesterase (PDE) inhibitors (amrinone, milrinone)
Beta-adrenergic agonists (dopamine, dobutamine, isoproterenol and epinephrine)
Cardiac glycosides (digoxin, digitoxin)

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 1379-82 and the Merck Veterinary Manual online edition.

| 1 ✓ | 2 ✓ | 3 ✓ | 4 ✓ | 5 ✗ | 6 ✓ | 7 ✓ | 8 | 9 | 10 |

Which one of the following choices correctly pairs the drug listed with its receptor and action?

Butorphanol - mu-activation	HIDE
Atipamezole - N-methyl-D-aspartate (NMDA) antagonist	HIDE
Detomidine - beta-1 stimulation	HIDE
Acepromazine - alpha-2 blockade	HIDE
Diazepam - gamma-amino butyric acid (GABA) agonist	HIDE

BACK   NEXT   LEAVE BLANK

Diazepam is an agonist at the GABA receptor.

Detomidine is a potent sedative used in horses that stimulates alpha-2 receptors.

Acepromazine is a sedative used in many animals that blocks alpha-1 receptors, producing vasodilation and sometimes hypotension.

Atipamezole is an antagonist at alpha-2 receptors; it is used to reverse alpha-2 agonists such as medetomidine, dexmedetomidine, or detomidine.

Ketamine is an antagonist at NMDA receptors.

Butorphanol is an opioid used in many animals; it activates kappa receptors but inhibits the mu receptor.

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Which of the following pharmaceutical agents has been shown to bind to endotoxin, which helps to minimize the effects of endotoxemia in horses?

Doxycycline	HIDE
Pentoxifylline	HIDE
Flunixin meglumine	HIDE
Polymyxin B	HIDE
Lidocaine	HIDE

BACK   NEXT   LEAVE BLANK

Overview | Mark this Question | Lab Values | | Report a Problem

Correct:

Polymyxin B is a polypeptide antibiotic that, at low doses, has been shown to bind endotoxin in horses' circulation, thus ameliorating its effects.

At higher doses polymyxin B can be nephro- and neurotoxic.

Topical applications are common due to low systemic absorption and thus, toxicity.

The other listed medications are used in various situations to combat endotoxemia, but none have the same mechanism of action in binding to endotoxin.

Pentoxifylline is a xanthine-derivative phosphodiesterase inhibitor with anti-tumor necrosis factor (anti-TNF) activity (among other anti-inflammatory and rheologic properties) also used to manage endotoxemic horses.

Flunixin meglumine is a nonsteroidal anti-inflammatory drug (NSAID) used at low doses to combat endotoxemia.

Lidocaine is a local anesthetic that acts as an anti-inflammatory when used as a continuous rate infusion.

Doxycycline is an antimicrobial that also inhibits matrix metalloproteinases.

Refs: Plumb's Veterinary Drug Handbook, 8th ed. and the Merck Veterinary Manual online edition.

Polymyxins

This group **of polypeptide antibiotics** includes **polymyxin B and polymyxin E, or colistin**. Because of **toxicity**, these drugs are most commonly **used topically**, **or PO for treatment of intestinal infections**. Colistimethate is a form of colistin intended for parenteral administration. **Polymyxins** are ==bactericidal==; they **interact** strongly with **phospholipids in bacterial cell membranes** and radically disrupt their permeability and function. The polymyxins are more ==effective against gram-negative than gram-positive bacteria==. Their rather **narrow spectrum**
includes ***Enterobacter, Klebsiella, Salmonella, Pasteurella, Bordetella, Shigella, Pseudo monas* spp, and *Escherichia coli***. Most *Proteus* or *Neisseria* spp are not susceptible. Although intrinsic bacterial resistance to polymyxins is recognized, resistance is uncommon and is chromosome-dependent only. Polymyxins act synergistically when **combined** with **potentiated** sulfonamides, tetracyclines, and some other antibacterials; they also ==reduce the activity of endotoxins in body fluids and may be beneficial in endotoxemia==. **Their action is inhibited by divalent cations, unsaturated fatty acids, and quaternary ammonium compounds.**

Polymyxins are **not absorbed after PO or topical administration**; plasma concentrations peak ~2 hr after parenteral administration. Blood concentrations usually are low, because polymyxins bind to cell membranes as well as tissue debris and purulent exudates. The polymixins undergo renal elimination mostly as degradation products, and their plasma half-lives are 3–6 hr. They are notably nephrotoxic and neurotoxic and, as such, systemic therapy at antimicrobial doses should be avoided. Neuromuscular blockade can be seen at higher concentrations. Intense pain at sites of injection and hypersensitivity reactions also can be expected. Polymyxin B is a potent histamine releaser. The main indication for parenteral use of polymyxins is life-threatening infection due to gram-negative bacilli or *Pseudomonas* spp that are resistant to other drugs. **Polymyxins are also used PO against susceptible intestinal infections**. Anti-endotoxin binding activity is an additional therapy via slow IV bolus. Topical application is common, eg, for otitis externa.

Recommended dose rates for polymyxins vary considerably. A general guideline is 20,000 U/kg, PO, bid; 5,000 U/kg, IM, bid; 50,000–100,000 U by intramammary infusion; 100,000 U intrauterine in cattle. IV administration of polymyxins is potentially dangerous

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11	12	13	14	15	16	17	18	19	20

Which one of the following choices is the mechanism of action of xylazine?

Blocks acetylcholine binding at sodium channels on nerve terminals, preventing transmission	HIDE
Antagonizes n-methyl-d-aspartate receptors, decreasing release of the excitatory neurotransmitter glutamate	HIDE
Dopamine receptor antagonist in the brain and alpha1-antagonist peripherally	HIDE
Inhibits release of norepinephrine at presynaptic alpha-2 receptors	HIDE
Stimulates GABA receptors resulting in the release of inhibitory neurotransmitters in the brain	HIDE

BACK   NEXT   LEAVE BLANK

Correct:

All the alpha-2 agonists (including xylazine) inhibit release of norepinephrine at presynaptic alpha-2 receptors both centrally and peripherally.

There are 3 subtypes of alpha-2 receptors (2A, 2B, 2C). Alpha-2 agonists also stimulate alpha-1 receptors at postsynaptic sites. Differences between specific drugs are due to their affinity for different alpha-2 subtypes and for alpha-1 vs. alpha-2 receptor affinity.

Here is a list of potency and cost, from highest to lowest, and ratio of alpha-1 to alpha-2 receptor action:

Medetomidine.......1:1620
Romifidine............1:340
Detomidine..........1:260
Xylazine...............1:160

The cardiovascular effects of alpha-2s are significant, including vasoconstriction, hypertension, bradycardia, and decreased cardiac output.

Refs: Grimm, Tranquilli, and Lamont's Essentials of Anes and Analgesia in SA, 2nd ed. pp. 44-7, Lumb & Jones Vet Anes, 4th ed., pp. 210-25, and Muir et al., Handbook of Vet Anes, 4thed., 36-41.

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11 ✗	12 ✓	13	14	15	16	17	18	19	20

Which one of the following treatments is indicated to mitigate gastrointestinal ulcerative effects of nonsteroidal anti-inflammatory drugs (NSAIDs)?

Sulfasalazine	HIDE
Tylosin	HIDE
Niacinamide	HIDE
Prednisone	HIDE
Misoprostol	HIDE

BACK   NEXT

Overview | Mark this Question | Lab Values | Definitions

Correct:

Misoprostol, a synthetic prostaglandin E1 analog, may be given concurrently with nonsteroidal anti-inflammatory drugs (NSAIDs) to decrease gastric acid secretion.

Other drugs that decrease gastric acid secretion include the H2-receptor antagonists (e.g., cimetidine, ranitidine, famotidine) and proton pump inhibitors (e.g., omeprazole).

Examples of NSAIDs include phenylbutazone, flunixin meglumine, carprofen, etodolac, deracoxib, meloxicam, and firocoxib.

Refs: Plumb's Veterinary Drug Handbook, 7th ed. pp. 942-5, Cote, Clinical Veterinary

11 ✗	12 ✓	13	14	15	16	17	18	19	20

Oral sulfonylurea is used in cats for which one of the following disorders?

Uncomplicated diabetes mellitus	HIDE
Urethral sphincter (urinary) incompetence	HIDE
Multicentric intestinal lymphosarcoma	HIDE
Hypertrophic cardiomyopathy	HIDE
Fungal choreoretinitis (Cryptococcosis)	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Uncomplicated diabetes mellitus. Sulfonylurea is an oral hypoglycemic agent (Glipizide) used in humans.

Glipizide is sometimes used with dietary therapy to manage cats with uncomplicated type 2 diabetes mellitus and NO history of ketoacidosis.

It is not a substitute for insulin therapy. Typically, diabetic cats whose owners refuse to give insulin injections are candidates for oral sulfonylurea therapy.

AAHA Diabetes Guidelines 2010 for dogs and cats

Refs: Plumb's Veterinary Drug Handbook, 7th ed. pp. 626-9, 710-8, Cote, Clinical Veterinary Advisor-Dogs and Cats, 3rd ed. pp. 271-2 and the Merck Veterinary Manual

AAHA Diabetes Management Guidelines for Dogs and Cats

Special Report

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Introduction

Diabetes mellitus (DM) is a treatable condition that requires a committed effort by veterinarian and client. This document provides current recommendations for the treatment of diabetes in dogs and cats. Treatment of DM is a combination of art and science, due in part to the many factors that affect the diabetic state and the animal's response. Each animal needs individualized, frequent reassessment, and treatment may be modified based on response.

In both dogs and cats, DM is caused by loss or dysfunction of pancreatic beta cells. In the dog, beta cell loss tends to be rapid and progressive, and it is usually due to immune-mediated destruction, vacuolar degeneration, or pancreatitis.[1] Intact females may be transiently diabetic due to the insulin-resistant effects of the diestrus phase. In the cat, loss or dysfunction of beta cells is the result of insulin resistance, islet amyloidosis, or chronic lymphoplasmacytic pancreatitis.[2]

Risk factors for both dogs and cats include insulin resistance caused by obesity, other diseases (e.g., acromegaly in cats, hyperadrenocorticism in dogs), or medications (e.g., steroids, progestins). Genetics is a suspected risk factor, and certain breeds of dogs (Australian terriers, beagles, Samoyeds, keeshonden[3]) and cats (Burmese[4]) are more susceptible.

Regardless of the underlying etiology, diabetic dogs and cats are hyperglycemic and glycosuric, which leads to the classic clinical signs of polyuria, polydipsia (PU/PD), polyphagia, and weight loss. Increased fat mobilization leads to hepatic lipidosis, hepatomegaly, hypercholesterolemia, hypertriglyceridemia, and increased catabolism. Eventually, hyperketonemia, ketonuria, and ketoacidosis develop and result in progressive compromise of the animal.

Diagnostic Criteria and Initial Assessment

Presentation

In this document, the authors describe different approaches to the animal depending on the level of hyperglycemia and severity of the clinical signs. Animals with DM may be presented with a variety of signs that are dependent, in part, on the time interval between onset of hyperglycemia and the client seeking veterinary help; the severity of hyperglycemia; presence and severity of ketonemia; and the nature and severity of concurrent disease, such as pancreatitis. Clinical signs of PU/PD do not develop until the blood glucose (BG) concentration exceeds the renal tubular threshold for spillage of glucose into the urine. In dogs and cats, glycosuria typically develops

when the BG concentration exceeds approximately 200 mg/dL and 250 mg/dL, respectively.

Clinical signs of DM are not generally present in dogs and cats with persistent fasting BG concentrations above the reference range but below the concentration that results in glycosuria (i.e., BG between the reference upper limit to 200 mg/dL in dogs and between the reference upper limit to 250 mg/dL in cats). BG concentrations in these ranges may occur for several reasons, including stress hyperglycemia (in cats), presence of an insulin-resistant disorder (e.g., obesity, hyperadrenocorticism), in association with medication (e.g., glucocorticoids), or as part of the early stage of developing DM.

Dogs and cats that are in the early stage of developing DM are classified as subclinical diabetics. Subclinical diabetics often appear healthy, have a stable weight, and are usually identified when routine laboratory work is performed for other reasons. A diagnosis of subclinical diabetes should only be made after stress hyperglycemia has been ruled out and hyperglycemia persists despite identification and correction of insulin-resistant disorders. Reassessing the BG at home or measuring serum fructosamine concentration may help differentiate between stress hyperglycemia and subclinical DM and help determine if further action is needed.

Clinical DM is diagnosed on the basis of persistent glycosuria and persistent hyperglycemia (>200 mg/dL in the dog and >250 mg/dL in the cat). Documentation of an elevated serum fructosamine concentration may be necessary to confirm the diagnosis in cats.[5]

Animals with clinical diabetes manifest PU/PD, polyphagia, and weight loss. Some animals present with systemic signs of illness due to diabetic ketoacidosis (DKA), such as anorexia, dehydration, and vomiting. Additional problems may include lethargy, weakness, poor body condition, cataracts (in dogs), and impaired jumping ability and abnormal gait (in cats).

Assessment

The initial evaluation of the diabetic dog and cat should:

- Assess the overall health of the animal (history, physical examination, medications, diet).
- Identify complications associated with the disease (e.g., cataracts in dogs, peripheral neuropathy in cats).
- Identify concurrent problems often associated with the disease (e.g., urinary tract infections, pancreatitis).
- Identify conditions that may interfere with response of the diabetic to treatment (e.g., hyperadrenocorticism, hyperthyroidism, renal disease).
- Evaluate for risk factors such as obesity, pancreatitis, insulin-resistant disease, diabetogenic medications, and diestrus (in the female dog).

The physical examination of the diabetic dog or cat can be relatively normal or may reveal dehydration, weight loss, dull coat, cataracts, or abdominal pain (if concurrent pan-

creatitis is present). A sweet odor may be noted on the breath if the animal is ketotic. Some cats with long-standing hyperglycemia may have a plantigrade stance secondary to a peripheral neuropathy.

Laboratory assessment should include the items in Table 1. Typical findings include a stress leukogram and increased glucose, cholesterol, and triglyceride concentrations.

Dogs often show increased alkaline phosphatase and alanine aminotransferase activity. In the cat, the stress leukogram and increases in alkaline phosphatase are variable. Cats with increased liver enzymes may have concurrent liver disease or pancreatitis and should be evaluated further.[6]

Dogs and cats with DKA may show very elevated BG concentrations, alterations in liver enzyme activity and electrolyte concentrations, azotemia, and decreased total carbon dioxide secondary to metabolic acidosis, osmotic diuresis, and dehydration.[7,8]

The urinalysis will reveal the presence of glucose and may reveal the presence of protein, ketones, bacteria, and/or casts. A urine culture should always be performed in glycosuric animals, as infection is commonly present.

If thyroid disease is suspected in a dog, it is best to perform thyroid testing after diabetes is stabilized because of the likelihood of euthyroid sick syndrome. All cats >7 years of age with weight loss and polyphagia should be tested for hyperthyroidism, as diabetes and hyperthyroidism cause similar clinical signs and can occur concurrently.

Treatment

The mainstay of treatment for clinical DM in both species is insulin, along with diet modification. However, insulin treatment is not indicated in dogs and cats with subclinical disease, unless hyperglycemia worsens and glycosuria is noted.

Veterinarians use a variety of insulin products, but only two are presently approved by the Food and Drug Administration (FDA) for use in dogs and cats. One of these is a **porcine lente** product (porcine zinc insulin suspension) that is approved for both dogs and cats.[9] If available, the authors' recommendation is to use this product in dogs. The other FDA-approved insulin is a longer-acting product (human recombinant **protamine zinc** insulin [PZI]) and is currently approved for use in cats.[10] For the majority of diabetic cats, insulin glargine (not veterinary approved) and PZI have appropriate duration of action.

Although bovine PZI is available from compounding pharmacies, its use is not recommended because of concerns about production methods, diluents, sterility, and the consistency of insulin concentration between lots. In addition, bovine insulin causes antibody production in dogs, which may impact control of DM.[11]

Initial Treatment and Monitoring of the Cat

Management of the cat with subclinical DM

Overall goals of treatment
- Prevent the onset of clinical DM.
- Address obesity and optimize body weight.

Table 1

Recommended Diagnostic Testing for Animals With Suspected or Confirmed Diabetes Mellitus

Test/Procedure*	Initial Workup and Regular Monitoring	If Ill/Troubleshooting, Consider These in Addition
CBC	Dog, Cat	
Serum biochemical analysis + electrolytes	Dog, Cat	
Urinalysis *with culture*	Dog, Cat	
T4	Cat	
Blood pressure	Cat	
Serum progesterone	Dog (intact female)	
Fructosamine	Dog, Cat	
FeLV/FIV	Cat, if status unknown	
Thyroid panel (T4/FT4 ± TSH)		Dog, Cat
TLI		Dog, Cat
PLI		Dog, Cat
Adrenal function testing		Dog, Cat
Cobalamin/folate		Cat
Abdominal ultrasound		Dog, Cat
Abdominal radiographs		Dog, Cat
Chest radiographs		Dog, Cat

* CBC=complete blood count; T4=thyroxine; FeLV/FIV=feline leukemia virus/feline immunodeficiency virus; FT4=free thyroxine; TSH=thyroid-stimulating hormone; TLI=trypsin-like immunoreactivity; PLI=pancreatic lipase immunoreactivity.

- Reverse or mitigate other causes of insulin resistance.
- To obtain normal BG concentrations without need for insulin.[12]

Cats with subclinical DM may attain euglycemia without the use of insulin. Begin management with diet change. Evaluate and manage body weight, identify and cease any existing diabetogenic drug therapy, and correct concurrent insulin-resistant disease. Perform a recheck examination with urine analysis and BG measurement every 2 weeks. If clinical DM occurs despite dietary intervention, initiate insulin therapy.

Diet therapy goals and management
- Optimize body weight with appropriate protein and carbohydrate levels, fat restriction, and calorie control.
  - Weigh at least monthly and adjust intake to maintain optimal weight.
  - Management goal of weight loss in obese cats: 1% to 2% loss per week[13] or a maximum of 4% to 8% per month (hepatic lipidosis risk is minimized with the recommended high-protein diet).
- Minimize postprandial hyperglycemia by managing protein and carbohydrate intake.
- Feed a high-protein diet (defined as >45% protein metabolizable energy [ME]) to maximize metabolic rate, improve satiety, and prevent lean muscle-mass loss.[14-17]
  - This is necessary to prevent protein malnutrition and loss of lean body mass.
  - Protein normalizes fat metabolism and provides a consistent energy source.
  - Arginine stimulates insulin secretion.
- Limit carbohydrate intake.[18-21]
  - Dietary carbohydrate may contribute to hyperglycemia and glucose toxicity in cats.
  - Provide the lowest amount of carbohydrate levels in the diet that the cat will eat.
  - Carbohydrate levels can be loosely classified as ultralow (<5% ME), low (5% to 25% ME), moderate (26% to 50% ME), and high (>50% ME).[22]

- Portion control by feeding meals.[23,24]
  - Allows monitoring of appetite and intake.
  - Essential to achieve weight loss in obese cats.
- Canned foods are preferred over dry foods. Canned foods provide:
  - Lower carbohydrate levels.
  - Ease of portion control.
  - Lower caloric density; cat can eat a higher volume of canned food for the same caloric intake.
  - Additional water intake.[25-28]
- Adjust diet recommendations based on concurrent disease (e.g., chronic kidney disease, pancreatitis, intestinal disease).

Management of the cat with clinical DM
In addition to diet therapy, insulin treatment is required for cats with clinical DM.

Overall goals of treatment
- Minimal to no clinical signs.
- Owner perceives good quality of life and is satisfied with treatment.
- Avoid or improve complications, specifically DKA and peripheral neuropathy.
- Avoid symptomatic hypoglycemia.

Management
- Feeding meals four times daily is ideal to prevent clinical hypoglycemia for cats on insulin. Timed feeders are useful for cats that require multiple meals per day to manage weight and control calories. Use of insulin glargine may reduce the need for timed feedings, as long as home monitoring of BG is being done. (See Insulin therapy in the cat.)
- Free-choice feeding is acceptable for underweight cats on insulin therapy.
- The sick diabetic, ketotic cat should be hospitalized to initiate aggressive therapy. If unable to provide 24-hour care, refer to an appropriate emergency or specialty hospital.
- Adjunct therapy includes environmental enrichment, particularly for obese cats.[29]
- Oral hypoglycemic drugs, combined with diet change, are only indicated if owner refuses insulin therapy or is considering euthanasia.[30] These agents are not considered appropriate for long-term use.

Insulin therapy in the cat
The insulin preparations with the appropriate duration of action in most diabetic cats are glargine (U-100) or the veterinary-approved human **protamine zinc** insulin (PZI U-40).[31]

This panel does not recommend the veterinary-approved **porcine zinc (lente)** insulin suspension as the initial treatment for the cat, because its duration of action is short and control of clinical signs is poor.[32] This insulin should be reserved for cats in which other insulin choices have not yielded satisfactory results.

Judicious dosing is recommended initially, given that diet change may alter food intake and impact the response to insulin. Likewise, with ongoing therapy and reversal of glucotoxicity, the pet's response to insulin will improve with time.[17] Use caution in increasing the insulin dose too soon. Increases should only be made once food intake has stabilized and only if clinical signs have not improved after 1 week of therapy.

Most cats are well regulated on insulin at 0.5 U/kg q 12 hours, with a range of 0.2 to 0.8 U/kg.[15,33] The panel recommends a starting dose of 0.25 U/kg q 12 hours, based on an estimate of the cat's **lean** body weight. This equates to 1 U q 12 hours in an average cat. Even in a very large cat, the starting dose of insulin should not exceed 2 U per cat q 12 hours.

Initiating insulin therapy
Outline of initial approach
- Initiate insulin therapy with PZI or insulin glargine at a starting dose of 1 U per cat q 12 hours.
- The decision to monitor BG on the first day of insulin treatment is at the discretion of the veterinarian.
- The goal of monitoring is solely to identify hypoglycemia. The insulin dose should **not** be increased based on first-day BG evaluation.
  - If monitoring is elected, measure BG every 2 to 3 hours for cats on PZI and every 4 hours for those on insulin glargine, for 10 to 12 hours following insulin administration.
  - Decrease insulin dose by 0.5 U if BG is <150 mg/dL any time during the day.
  - Treat as an outpatient and plan to reevaluate in 7 days regardless of whether BGs are monitored on the first day.
  - Immediately reevaluate if clinical signs worsen; if clinical signs suggest hypoglycemia; or if lethargy, anorexia, or vomiting is noted.

Precautions and details
- Home monitoring of BG is ideal and strongly encouraged to obtain the most accurate interpretation of glucose relative to clinical signs.[34] Most owners are able to learn to do this with a little encouragement, and interpretation of glucose results is much easier for the clinician. See Table 2 for web links to client educational materials.
- The pressing concern for cats at this stage is identifying impending hypoglycemia, since cats often do not show overt signs until the BG is dangerously low.
- Use extreme caution when interpreting a "high BG" in the cat. It is important to discern between stress hyperglycemia and hyperglycemia that needs treatment. Use all laboratory findings and the clinical examination when evaluating response to insulin.
- Be aware that chronic insulin overdose may not only result in clinical hypoglycemia (seizures, coma), but also the development of sustained hyperglycemia and insulin ineffectiveness following secretion of insulin antagonists (catecholamines, glucagon, cortisol, growth hormone) that combat hypoglycemia.[35]

Table 2

Web Links for Staff and Client Education

Title	URL
AAHA/AAFP Feline Life Stage Guidelines	www.aahanet.org and www.catvets.com
ACVIM referral resources	www.acvim.org
University of Queensland diabetes information for veterinarians	http://www.uq.edu.au/ccah/index.html?page=41544&pid=42973
Canine diabetes site for owners	www.caninediabetes.org
Washington State University client information	http://www.vetmed.wsu.edu/ClientEd/diabetes.aspx
Winn Feline Foundation information on cats	http://www.winnfelinehealth.org/Health/Diabetes.html?gclid=CK3R9__T8p4CFQkIswodAhcdLA

- In-clinic blood glucose curves (BGCs) are more likely to be affected by stress hyperglycemia than BGCs generated at home. Veterinarians should be cautious of high glucose results and subsequent overzealous increases in dose.
- Regardless of the approach, it is important to remember that a BGC performed at the time insulin is initiated is intended mainly to detect and avoid dangerous hypoglycemia.

Ongoing Monitoring of the Cat

Monitoring strategies may be influenced by persistence or resolution of clinical signs. The pressing concern for the newly diagnosed and treated cat is the development of hypoglycemia in individuals that may quickly go into remission. Cats on long-acting insulin may not show overt signs of hypoglycemia until the BG is dangerously low, so it is important to identify impending hypoglycemia by home glucose testing whenever possible.

If BG monitoring is not possible, close attention and documenting changes in clinical signs are imperative. Likewise, urine glucose testing using glucose-detecting crystals in the litter can be helpful for detecting diabetic remission.[17]

Ongoing home monitoring for all cats
- Log food, water, and appetite daily.
- Log insulin dose daily.
- Note any signs suggestive of hypoglycemia; contact veterinarian if persistent.
- Periodically test urine, looking for negative glycosuria (suggestive of hypoglycemia or diabetic remission) or positive ketonuria (suggestive of substantial hyperglycemia).

At 1 week after initiating insulin treatment
- If clinical signs have improved, and no ketonuria is present:
  - Continue present insulin dose.
  - Introduce home monitoring if not already done.

- If a spot check on the BG is possible, assess for hypoglycemia at 6 to 8 hours following insulin administration.
- If BG is <150 mg/dL, either decrease insulin dose to 0.5 U q 12 hours, consider dosing q 24 hours, or suspend insulin treatment and wait for clinical signs and glycosuria to recur before restarting insulin at 0.5 U q 12 hours.
- If clinical signs have persisted or worsened:
  - Evaluate client compliance and dosing technique (see Client Education).
  - If adherence is good, consider increasing the dose to 2 U q 12 hours.
  - If the cat is ketonuric, has developed peripheral neuropathy, or does not have a good appetite, evaluate for DKA and rule out complicating disease (e.g., pancreatitis) that may be worsening the diabetic state.

During the first month after initiating insulin treatment
- In-clinic (only if home monitoring is not possible)
  - Every 1 to 2 weeks:
    - Spot checks of BG at 6 to 8 hours following insulin administration.
      - Decrease insulin dose if BG is <150 mg/dL.
      - Cautiously increase insulin dose if clinical signs persist or worsen or ketonuria is noted. Do not exceed 3 U per injection.
    - Urinalysis (to detect glycosuria, ketonuria, or infection).
    - Consider BGC if clinical signs persist or worsen and insulin dose is at 3 U per injection.
- Home
  - Weekly:
    - Spot checks of BG at 6 to 8 hours following insulin administration (more often if hypoglycemia is suspected).

- Increase dose if necessary based on BG results.
- Urine dipsticks for glucose and ketones (particularly useful if BG measurements are not possible).
  ○ Every 2 weeks:
    - Perform BGC (see protocol for BGC).
    - Utilize urine dipstick or litter glucose-detecting crystals.
    - Adjust insulin as discussed previously.
    - Consider insulin overdose and/or possible diabetic remission if three consecutive negative urine glucose results are obtained.
    - If ketones or persistently high urine glucose are noted, a clinic evaluation is in order; consider the need for dose increase.

At 1 month after initiating insulin treatment
- In-clinic examination recommended for all cats:
  ○ Thorough history, physical examination, weight, and urinalysis.
  ○ Measure fructosamine unless detailed home-monitoring records are available.
  ○ Additional laboratory analysis if indicated by examination [Table 1].
  ○ Adjust insulin **if** needed; insulin dose should not be increased more than 1 unit at a time.
  ○ The cat must be reevaluated if clinical signs persist at 3 U *q* 12 hours. Consider problems with insulin duration or action, concurrent conditions, or medications causing insulin resistance. The majority of cats on insulin glargine or PZI do not need >3 U of insulin *q* 12 hours to control diabetes.

Long-term monitoring of insulin treatment
- Advise clients to monitor and record the following:
  ○ Daily: Clinical signs, food/water intake, insulin dose.
  ○ Weekly: Body weight.
  ○ Monthly: BG spot checks (twice monthly if practical).
    - If on insulin glargine, evaluate BG prior to insulin administration and at 8 hours following.
    - If on PZI, evaluate BG prior to insulin administration and 3, 6, and 9 hours later.
  ○ Twice monthly: Urine glucose and ketones.
    - If urine glucose is consistently negative, consider diabetic remission.
- In-clinic:
  ○ Any items listed above that client cannot perform.
  ○ If the cat is doing well, don't make changes based on increased BG measurements alone, especially if measured at the clinic.
  ○ Every 3 months: Examination, including weight.
  ○ Every 3 to 6 months: Serum fructosamine concentration.
    - If at the lower end of the reference range or below the reference range, consider chronic hypoglycemia and diabetic remission.
    - Consider monitoring BG or urine glucose at home, or decrease insulin dose and recheck in 4 weeks.

- If BG is consistently <150 mg/dL or urine is persistently negative for glucose, or both, consider decreasing the insulin dose, switching treatment to *q* 24 hours, or stopping insulin and monitoring response. In cats, glucose toxicity suppresses beta cell function, and with control of hyperglycemia and resolution of glucose toxicity, the remaining beta cells become functional again and start secreting insulin.
  ○ Every 6 to 12 months: Full laboratory analysis [Table 1].

Initial Treatment and Monitoring of the Dog

Management of the dog with subclinical DM
- Investigate and address causes of insulin resistance
  ○ Obesity.
  ○ Medications.
  ○ Intact female in diestrus.
  ○ Hyperadrenocorticism.
- Initiate diet therapy to limit postprandial hyperglycemia.
- Evaluate closely for progression to clinical DM.
- Subclinical diabetes is not commonly identified in the dog. Most dogs in the early stages of naturally acquired diabetes (i.e., not induced by insulin resistance, per se) quickly progress to clinical diabetes and should be managed (using insulin) as described in that section.

Diet therapy
Evaluate and recommend an appropriate diet that will correct obesity, optimize body weight, and minimize postprandial hyperglycemia. Dogs with DM can do well with any diet that is complete and balanced, does not contain simple sugars, is fed at consistent times in consistent amounts, and is palatable for predictable and consistent intake.
  Dietary considerations include:
- The use of diets that contain increased quantities of soluble and insoluble fiber or that are designed for weight maintenance in diabetics or for weight loss in obese diabetics.[36,37]
  ○ May improve glycemic control by reducing postprandial hyperglycemia.
  ○ May help with caloric restriction in obese dogs undergoing weight reduction.
  ○ In underweight dogs, the priority of dietary therapy is to normalize body weight, increase muscle mass, and stabilize metabolism and insulin requirements. Underweight dogs should be fed a high-quality maintenance diet or a diabetic diet that has mixed fiber and is not designed for weight loss.
- Modify the diet based on other conditions (e.g. pancreatitis, kidney disease, gastrointestinal disease) and needs of the dog.

Adjunctive treatment
- Initiate a consistent, moderate daily exercise program to help promote weight loss and lower BG concentrations secondary to increased glucose utilization. Exercising

twice daily after feeding is ideal to minimize postprandial hyperglycemia.
- Oral sulfonylurea drugs work by stimulating insulin secretion and are not effective in the dog.

Management of the dog with clinical DM

Treatment of clinical DM in the dog always requires exogenous insulin therapy. The U-40 pork lente (porcine zinc insulin suspension) has been the first-choice recommendation for dogs. The duration of action is close to 12 hours in most dogs, and the amorphous component of the insulin helps to minimize postprandial hyperglycemia.[38] However, according to the FDA, that product has recently had "problems with stability," and while the manufacturer is "working with FDA on resolving this issue, supplies may be limited" (http://www.fda.gov/AnimalVeterinary/NewsEvents/CVM Updates/ucm188752.htm; accessed 4/14/2010). If it again becomes consistently available, it will remain a great option for dogs. In the meantime, diabetic dogs should be started on a different insulin.[39]

When porcine zinc insulin is not available, U-100 human recombinant Neutral Protamine Hagedorn (NPH) insulin is a good initial alternative, although its duration of action is often <12 hours in many dogs.[40]

As a third option, human PZI is likely to be a better choice for dogs than is insulin glargine. There are no studies showing effective use of either of these products in dogs, however, glargine would likely require concurrent use of a short-acting insulin due to its slow release from subcutaneous tissues.

Overall goals of treatment
- Resolve PU/PD.
- Optimize weight, activity level, and body condition.
- Avoid hypoglycemia.
- Avoid DKA.
- Minimize complications (e.g. urinary tract infections, cataracts).
- Owner-perceived good quality of life and owner satisfaction with treatment.

Initiating insulin therapy

Outline of initial approach
- Administer the first insulin dose (0.25 U/kg) and feed in the morning.
- Perform BGC with samples every 2 hours for at least 8 and preferably 12 hours, or until the nadir can be determined.
- If BG remains >150 mg/dL, send dog home and repeat BGC in 1 week.
- If BG becomes <150 mg/dL, decrease the next dose by 10% to 25% rounded to the nearest unit based on dog body weight and severity of glucose nadir. If possible, hospitalize dog to monitor response to the lower dose.
- Repeat BGC in 1 week (or sooner if concerns for hypoglycemia exist based on results of initial BGC).

Precautions and details
- Most dogs are well controlled on insulin at 0.5 U/kg q 12 hours, with a range of 0.2 to 1.0 U/kg.[14,41] The authors recommend a starting dose of 0.25 U/kg q 12 hours, rounded to the nearest whole unit.
- Feed equal-sized meals twice daily at the time of each insulin injection. Maintain a schedule to achieve a consistent amount of food at the same time, and thus consistent insulin needs.
- A critical initial goal of treatment is avoidance of symptomatic hypoglycemia, which may occur if the dose is increased too aggressively.
- Be cautious with adjustments until the dog and client are used to their new regimen (diet, insulin, etc). With stabilization of BG levels, reversal of hyperglucagonemia, and reduction in hepatic gluconeogenesis, insulin sensitivity is likely to improve during the first month of therapy. Once the routine is set, then adjustments in insulin can be made to maximize benefit and minimize risk.
- If problems attaining diabetic control persist despite adjusting the insulin dose, and the duration of effect of the insulin is found to be inappropriate (e.g., <10 hours or >14 hours), consider a different insulin type.
- In contrast with cats, diabetic remission does not occur in dogs with naturally acquired diabetes. Hypoglycemia in dogs results from excess insulin caused by an insulin overdose, excessive exercise, or inappetence, and not from diabetic remission.
- Tailor treatment and monitoring to the individual case, using a combination of in-clinic evaluation and phone consultation. Monitoring of BG can be done in the clinic, at home, or both.
- Strenuous and sporadic exercise can cause severe hypoglycemia and should be avoided.
- Note that the BGC in established cases differs slightly from the initial protocol.

Ongoing Monitoring and Treatment of the Dog

Always tailor the monitoring and treatment to the dog. See Client Education for links to how-to videos and information.

During first month after initiating insulin
- Weekly (every 7 to 10 days):
  ○ Recheck examination and BGC.
  ○ Adjust insulin (as listed under Interpretation of the Glucose Curve).
  ○ Continue until clinical signs are controlled, body weight is trending toward optimal, and results of BG testing suggest control (see section on BGCs).

Long-term monitoring
- Tailor monitoring to the dog. Focus on weight, history, physical examination, and client observations regarding thirst, urine output, energy level, and behavior.[42] Treat the dog, not the BG results. Always repeat the BGC 2 weeks after any insulin dose adjustment.

- In-clinic
  - Every 3 months:
    - Examination, including weight and ocular examination.
    - Measure BG.
    - Measure fructosamine if the dog is doing well clinically and if a spot-check glucose (prior to dose and at anticipated nadir) is satisfactory. If fructosamine concentration is abnormal, proceed with BGC.
    - Perform a BGC if the examination or clinical history suggests any problems, if the fructosamine level is abnormal, or if the insulin dose has recently been adjusted.
  - Every 6 months:
    - Full laboratory work, including urinalysis and urine culture [Table1].
- At home
  - Advise clients to monitor and record the following:
    - Daily: Clinical signs, food/water intake, insulin dose.
    - Weekly: Body weight.
    - Monthly: Home BGC.

Indications, Method, and Interpretation of the BGC in the Dog and Cat

BGCs are part of the long-term monitoring plan. Create a BGC when:

- PU/PD persists.
- Signs of hypoglycemia are reported.
- 2 weeks after any change in insulin dose.
- Clinical history or physical examination suggests poor control (weight loss, neuropathy, etc.).

Use results to measure the nadir and to calculate the average BG over a roughly 12-hour period (average equals sum of all measurements divided by number of measurements). The BGC is the optimal way to assess:

- Duration of insulin action; the ideal duration is 12 (10-14) hours.
- The glucose nadir (to avoid hypoglycemia); approximately 8 hours postinjection is ideal.
- The average BG concentration throughout the day (indicates overall glycemic control).

Protocol for BGC in Established Diabetic Cases

Initial BG measurements are performed as described under Initial Treatment. This is the protocol for the BGC in established diabetic animals.

If the BGC is performed at home, have client measure BG before insulin or food is given. In free-fed cats, measure BG before insulin is given.

Dogs

1. Feed and administer insulin as usual.
   a. Feeding at home ensures that pet eats all of its food.

2. Once food is consumed, transport pet to hospital for the duration of the day or continue BGC at home.
3. Test BG every 2 hours until next dose of insulin.
   a. Repeat BG within 1 hour if any glucose value is <100 mg/dL.

Cats

1. At-home monitoring is strongly encouraged, as results are more reliable.
2. On PZI: Measure BG every 2 hours until next dose of insulin.
3. On insulin glargine: Measure BG prior to dose, 4 and 8 hours following insulin administration, and prior to next dose.

Target results[43]

- Nadir: 80 to 150 mg/dL.
- Time of nadir: 8 hours after insulin injection (a nadir may not be easily identified if using insulin glargine).
- Average BG <250 mg/dL; ideally no single BG >300 mg/dL.

Action plan: If nadir is

- <80 mg/dL, decrease insulin approximately 25% in dogs and 0.5 U per injection for cats or decrease to q 24 hours dosing if on 1 U q 12 hours.
- >150 mg/dL, increase insulin.
  - Cats: 0.5 to 1 U per injection based on severity of hyperglycemia.
  - Dogs: 10% to 20% to nearest unit.
- 80 to 150 mg/dL, and
  - Average glucose is <250 mg/dL: no change.
  - Average glucose is >250 mg/dL:
    - Glucose nadir ≤6 hours after insulin, change to a longer-acting insulin.
    - Glucose nadir ≥10 hours after insulin, change to a shorter-acting insulin. Consultation with a specialist on suitable insulin choices is advisable at this time.

Troubleshooting of the Dog and Cat

The "uncontrolled diabetic" is one with poor control of clinical signs. This may include hypo- and hyperglycemic pets, those with insulin resistance (decreased responsiveness to the insulin, defined by >1.5 U/kg per dose), or those with frequent changes (up or down) in insulin doses. Any dog or cat with persistent BG >300 mg/dL despite receiving >1.5 U/kg per dose should be reevaluated [Table 1], as insulin resistance or insulin overdosage causing the Somogyi response is likely.

1. Rule out client and insulin issues first.
   a. Observe client's administration and handling of insulin, including type of syringes used.
   b. Assess insulin product and replace if out of date or if the appearance of the insulin changes (i.e., becomes flocculent, discolored, or—in the case of glargine—cloudy).

2. Review diet and weight loss plan.
3. Perform a BGC (at home for cats).
4. Perform laboratory analysis [Table 1].
   a. Repeat basic laboratory testing.
   b. Conduct additional testing to evaluate for endocrine disease, infection, pancreatitis, and neoplasia.
   c. Rule out causes of continued insulin resistance (obesity, steroid use).
5. Consult with a specialist if you are unable to regulate your animal. This paper does not go into detailed management of the challenging diabetic or the animal with DKA.

Client Education

Give clients a realistic idea of the commitment involved, along with positive encouragement that it is possible to manage this disease. Provide access to trained veterinary support staff and helpful web links. Stress the importance of appropriate nutrition and weight management. Table 2 provides web resources for education of staff and clients. Inform clients about the following:

Insulin Mechanism, Administration, Handling, and Storage

- Explain how insulin works and its effects on glucose.
- Roll, don't shake, bottles (PZI, lente/zinc insulin, NPH).
- Wipe bottle stopper with alcohol prior to inserting syringe needle.
- Do not freeze.
- Do not heat; avoid prolonged exposure to direct sunlight.
- Recommend storage in refrigerator for consistency in environment.
- Recommend new bottle if insulin changes in appearance or becomes out of date.
- Refer to package insert for instructions about shelf life after opening.

Types of Syringes

- Always use a U-40 insulin syringe with U-40 insulin and a U-100 insulin syringe with U-100 insulin.
- 0.3 and 0.5 mL insulin syringes are best to facilitate accurate dosing, especially in cats and dogs getting <5 U per dose.
- Syringes are for single use.
- Do not use "short" needles. A standard 29-g, half-inch length needle is recommended.

Troubleshooting and Action

- If the pet does not eat:
  ◦ Educate owners to measure BG, to not administer insulin, and to contact veterinarian.
- Help clients with recognition and treatment at home for low BG.
  ◦ Signs include lethargy, sleepiness, strange behavior, abnormal gait, weakness, tremors, and seizures.
  ◦ If conscious, feed high-carbohydrate meal (e.g., rice/chicken, regular diet with added corn syrup).

◦ If pet is poorly responsive or has tremors, rub 1 to 2 teaspoons of corn syrup onto gum tissue. Feed if animal responds within 5 minutes; otherwise, take to veterinarian.
- Home BG monitors should be veterinary-approved products calibrated for dogs and cats.[44]
- Dosing increases to be made only after consulting with doctor. Client is empowered to decrease or skip an insulin dose if hypoglycemia is noted.

Summary

Management of the diabetic animal requires commitment and excellent communication between veterinarian and client about the treatment, follow-up appointments, associated costs, and home care. Diabetes is a dynamic disease, and successful management requires frequent client education and communication with the veterinary team. With appropriate client commitment, monitoring, and a firm understanding of the variables that are within our control, DM can be well managed.

Important differences exist between the development of canine and feline DM, and understanding these differences will help predict management success. The recommendations made in this manuscript are intended to guide medical decisions and treatment choices, with the recognition that within each animal, variations in response will exist and no two cases are alike. In difficult-to-manage cases, you may consider consulting with or referring to an internal medicine specialist.

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< PREV

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| 11 ✕ | 12 ✓ | 13 M ✓ | 14 | 15 | 16 | 17 | 18 | 19 | 20 |

Which drug is associated with increased risk of esophageal strictures in the feline patient?

Triamcinalone	HIDE
Methimazole	HIDE
Taurine	HIDE
Doxycycline	HIDE
Metacam	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Doxycycline may cause esophageal strictures in feline patients and is best administered with food or followed with 6 cc of water.

Don't dry-pill doxycycline in cats.

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 486-92 and the Merck Veterinary Manual online edition.

| 11 ✗ | 12 ✓ | 13 M ✓ | 14 ✓ | 15 | 16 | 17 | 18 | 19 | 20 |

A 4-year old female, spayed, feline leukemia positive domestic shorthair cat is diagnosed with atopic dermatitis.

Which one of the following therapies for atopic dermatitis is contraindicated in this patient?

Oatmeal shampoo	HIDE
Cyclosporine (Atopica™)	HIDE
Cetirizine (Zyrtec®)	HIDE
Diphenhydramine (Benadryl®)	HIDE
Amoxicillin-clavulanic acid (Clavamox®)	HIDE

BACK   NEXT   LEAVE BLANK

Correct:

Cyclosporine (Atopica™), is CONTRAINDICATED in cats infected with feline leukemia virus, feline immunodeficiency virus and *Toxoplamsa* and in cats with malignancies.

Cyclosporine acts as an immunosuppressant, primarily by inhibiting the cell-mediated response. It also blocks cytokine production and release, which interferes with the function of inflammatory cells.

Cyclosporine (Atopica™) is frequently used in the management of canine and feline atopic dermatitis.

Refs: Cote, Clinical Veterinary Advisor–Dogs and Cats, 3rd ed. pp. 98-100, Plumb's Veterinary Drug Handbook, 8th edition, *Cyclosporine (Systemic)*, and Merck Veterinary Manual online edition

MERCK MANUAL

Veterinary Manual

Veterinary / Integumentary System / Atopic Dermatitis

Feline Atopic Dermatitis

By **Karen A. Moriello, DVM, DACVD, Professor of Dermatology, Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison**

Feline AD is similar to canine AD. It is a pruritic disease in which affected cats have a hypersensitivity reaction to inhaled or contacted environmental allergens. The age of onset is variable but generally is <5 yr. The signs may be seasonal or nonseasonal. Purebred cats may have a higher risk than domestic shorthaired cats. As in dogs, pruritic cats may have several clinical presentations (eg, miliary dermatitis, symmetric alopecia, eosinophilic granuloma complex, head and neck pruritus) that are consistent with a diagnosis of AD but that must be differentiated from other diseases with similar clinical signs. Differential diagnoses include flea allergy, various mite infestations (eg, *Cheyletiella, Demodex, Notoedres, Sarcoptes, Otodectes*), mosquito bite hypersensitivity, food allergy, autoimmune disease (eg, pemphigus foliaceus), dermatophytosis, and cutaneous neoplasia. A thorough review of the cat's history and complete dermatologic and physical examination, along with the standard flea combing, skin scrapings, and fungal cultures, are mandatory first steps. The diagnosis of AD is made when the other differential diagnoses have been eliminated. Response to glucocorticoids is excellent initially but decreases over time.

Intradermal allergy testing and hyposensitization procedures in cats are similar to those used in dogs, but the intradermal test results are more difficult to read because the reactions are less dramatic and dissipate more rapidly in cats. The same avoidance recommendations made for dogs apply to cats. Symptomatic therapy includes control of secondary infections and use of antipruritic drugs. The approved formulation of cyclosporine for use in cats is liquid; the dosage is 7 mg/kg, and it can be administered PO or in food. After 30 days, the dosage can be tapered to every other day in ~70% of cats and to twice a week in ~50% of cats. Response to immunotherapy is similar to that in dogs (see above); owners are advised to commit to 1 yr of therapy before deciding its usefulness.

11 ✕	12 ✓	13 M ✓	14 ✓	15 ✓	16	17	18	19	20

A 3-week-old Thoroughbred foal in Kentucky is presented with clinical signs of trembling, weakness, inability to stand for longer than a few minutes, and stilted gait.

The foal is unable to nurse, is tachycardic, and is beginning to become dyspneic.

Botulism ("shaker foal syndrome") is suspected.

Abnormal lung sounds are heard on thoracic auscultation and aspiration pneumonia is suspected, so the clinician wants to include a parenteral antimicrobial in the initial therapy.

Which one of the following antimicrobials should be avoided?

Metronidazole	HIDE
Ceftiofur	HIDE
Potassium penicillin G	HIDE
Gentamicin	HIDE
Ampicillin	HIDE

Correct:

Gentamicin should be avoided in cases of botulism due to its association with the adverse effect of neuromuscular blockade. Other adverse effects of aminoglycosides include nephrotoxicity and ototoxicity.

This foal likely has toxicoinfectious botulism or "shaker foal syndrome." The best way to protect foals in endemic areas is by vaccination of the dams.

Affected foals require intensive supportive care, with about 50% needing ventilatory support for successful treatment.

Botulism is seen in wild water fowl>chickens>horses and cattle.

Refs: Wilson, Clinical Vet Advisor: The Horse (Botulism) and Merck Veterinary Manual online edition.

■■■■ MEDICINE I

Botulism in Foals: A Survivable Disease

Pamela A. Wilkins, DVM, PhD, and Jonathan E. Palmer, VMD

Botulism in foals less than 6 mo of age is readily treated, and the survival rate is more than 95% in foals receiving appropriate treatment. Nursing care, IV fluid support, nasogastric or nasoesophageal tube feeding, broad-spectrum antimicrobial coverage (excluding aminoglycoside and tetracycline classes), oxygen therapy, and the administration of botulism antitoxin are important therapies. Approximately 33% of affected foals may require positive pressure mechanical ventilation. Authors' address: Graham French Neonatal Intensive Care Unit, University of Pennsylvania, School of Veterinary Medicine, New Bolton Center, Kennett Square, PA 19348.© 2002 AAEP.

1. Introduction

Botulism toxin causes a widely recognized potentially fatal disease of horses. Botulinum toxin has three primary means of entering the horse: intestinal toxicoinfection, ingestion of preformed toxin, and absorption of toxin from wounds infected with *Clostridium botulinum*. The toxin affects the neuromuscular junction and results in weakness that progresses to flaccid paralysis. The initial manifestation in foals and adults is generally dysphagia, with increased muscular trembling and recumbency occurring with larger doses of the toxin. Progression of the disease can result in respiratory failure caused by respiratory muscle weakness. The diagnosis of botulism is primarily clinical, after exclusion of other causes of generalized flaccid paralysis and dysphagia in horses. Affected animals will have poor tongue, anal, tail and eyelid tone, dysphagia, and decreased pupillary reflexes. Attempts at isolation of the toxin from blood and feces can confirm the clinical diagnosis but may be negative. The prognosis for adults is guarded to poor for horses that become recumbent, even if appropriate antitoxin therapy and supportive care measures are initiated. There are no large retrospective studies evaluating the outcome of appropriately treated botulism in foals. The objective of this study was to retrospectively evaluate the outcome in foals less than 6 mo of age presenting to the Graham French Neonatal Intensive Care Unit between the years 1989 and 2001 and having a final diagnosis of botulism.

2. Materials and Methods

The Medical Records System at New Bolton Center, University of Pennsylvania School of Veterinary Medicine was searched for all cases with a final diagnosis of botulism in horses less than 1 yr of age. The medical records were retrieved and all horses older than 6 mo of age were eliminated. Data from the case records were then entered into a statistics program (Minitab, version 12.1) for descriptive (continuous data) and summary (categorical data) investigation. Student's t tests were employed to evaluate differences between groups where applicable.

NOTES

Proceedings of the Annual Convention of the AAEP 2002

3. Results

Twenty-eight cases with complete medical records were recovered. The age at presentation was 1.92 ± 0.29 mo (mean $\pm$ SE). The age distribution was bimodal, however, with 16 foals presenting at 1.5 mo of age or less and 8 foals presenting between 2.5 and 3 mo of age. Three foals presented at 5 mo of age. There was no apparent sex bias with 13 males and 15 females presenting. There were 10 Thoroughbred foals, 8 Standardbred, 3 Arabian, 2 Warmblood, 2 Quarter Horses, and 1 each of Appaloosa, Morgan, and Paint breeds. Foals weighed 232 ± 20 lbs at presentation. Five cases were identified where the dam had been vaccinated against botulism; in 20 cases the dam had not been vaccinated and a vaccination history was not recorded in 3 cases. Twenty-five foals survived to discharge, one foal died while being treated, and two foals were euthanatized shortly after admission for economic reasons. Length of hospitalization was 15.3 ± 1.5 days, with euthanatized foals being hospitalized for less than 1 day. Temperature ($100.7 \pm 0.2°F$) and heart rate (86 ± 4 bpm) were generally within normal limits. Respiratory rate was significantly increased at admission (52 ± 11 bpm).

Sixteen foals were treated with intra-nasal insufflation of oxygen for 4.4 ± 1.0 days. Nine foals were treated with mechanical ventilation, average duration 7.4 ± 1.4 days. Eight foals treated with intra-nasal oxygen insufflation also received mechanical ventilation. Ten foals did not receive either intra-nasal oxygen insufflation or mechanical ventilation. Pa_{O_2} at admission was not significantly different between foals receiving intra-nasal oxygen therapy at some point during hospitalization (75.7 ± 6.7 mm Hg) and those not placed on intra-nasal oxygen therapy (72.4 ± 7.6 mm Hg). However, in five cases, the initial arterial blood gas was obtained with the foal already receiving intra-nasal oxygen insufflation. Pa_{O_2} in these 5 cases was 103.3 ± 14.9 mm Hg at admission, whereas average Pa_{O_2} in the 16 cases not receiving oxygen at the time the initial blood gas was obtained 64.6 ± 4.4 mm Hg. In seven cases the initial respiratory management was not recorded. Pa_{CO_2} was increased at admission (56.6 ± 2.8 mm Hg) and tended to be larger in foals receiving oxygen therapy (58.4 ± 3.2 mm Hg) than in those not receiving oxygen therapy (52.6 ± 5.5), although the difference was not statistically significant ($p = 0.36$). Foals requiring mechanical ventilation had significantly greater ($p = 0.009$) Pa_{CO_2} values at admission (67.4 ± 5.2 mm Hg) than foals not requiring mechanical ventilation (49.7 ± 1.3 mm Hg). Pa_{O_2} tended to be less in foals requiring mechanical ventilation (64.4 ± 5.8 mm Hg) than in those not requiring mechanical ventilation (79.1 ± 5.8 mm Hg), although this difference was not statistically significant ($p = 0.26$). Foals requiring ventilation were significantly ($p = 0.011$) more acidemic (7.25 ± 0.04) than foals not requiring ventilation

(7.39 ± 0.01). No other significant abnormalities were consistently present on hematology or serum clinical chemistry evaluation. One foal presenting at 7 days of age had partial failure of passive transfer (serum IgG < 800 mg/dl).

Additional therapies provided included intravenous fluid support (24 of 28), nasogastric or nasoesophageal tube feedings (25 of 28), and broad-spectrum antimicrobial therapy (28 of 28). Twenty-five of 28 foals survived; all surviving foals were treated with botulism antitoxin[a] shortly after arrival. One foal died while receiving therapy because of respiratory, and subsequent cardiac, arrest. Two foals were euthanatized for purely economic reasons, and treatment was minimal in these cases, usually aimed at stabilization for initial diagnosis.

4. Discussion

Botulism has been supposed by some authors to be an almost uniformly fatal problem of the young foal.[1] Our experience has been different, and this study was undertaken to show the efficacy of rapid institution of appropriate therapy for this potentially fatal disease. Foals affected by botulism can be found dead in the field, can present initially as colic, or can present with the classic "Shaker Foal" signs of muscular trembling and weakness.[2–5] Our study identified at least five cases where the dam had been vaccinated against botulinum toxin, one of which had failure of passive transfer. The bimodal distribution of age at presentation suggests that younger foals are at increased risk if they are born to unvaccinated dams or fail to ingest sufficient colostrum from the vaccinated dam. Foals presenting at greater age seem to be most at risk before their own vaccination, when maternal antibody is waning. Type B botulism is most common in this geographic area.

Standard therapy at our hospital includes administration of botulism antitoxin as soon as possible after diagnosis, nutritional support, antimicrobial coverage, IV fluid administration as necessary, scrupulous nursing care, and ventilatory management. Ventilatory management generally falls into one of three categories: doing nothing specific but monitoring arterial blood gas parameters, administration of oxygen by intra-nasal insufflation, and mechanical ventilation. Approximately one-third of foals with botulism in our case population received mechanical ventilation at some point during their disease course. Tracheal intubation, with or without mechanical ventilation, is frequently part of the management of botulism in humans, particularly in infants where airway protection is important.[6] Acute respiratory failure (defined for our purposes as Pa_{CO_2} > 50 mm Hg with HCO_3 < 28 mEq/l and some degree of hypoxemia) is commonly reported in human infants and adults with botulism[6–8] and was present in 13 of the foals included in this report. Not all foals with increased Pa_{CO_2}

received mechanical ventilation, and these cases were managed more conservatively.

Outcome was uniformly excellent in treated foals, and length of hospitalization was less than that reported for human infants and adults.[6,7] There were no reported long-term or career-limiting problems. Recognition of the severity of respiratory compromise is essential for appropriate management of these cases and requires the ability to obtain reliable arterial blood gas data. The degree of respiratory distress and respiratory effort is an unreliable indicator of respiratory compromise in this group of patients, given that muscular weakness and paralysis prevent the usual responses. The availability of "bedside" blood-gas monitors should allow the practitioner to manage many of these cases in field situations, given the ability to administer botulism antitoxin, to provide supplemental oxygen by intra-nasal insufflation, and to recognize when respiratory failure is severe enough to warrant referral and more extensive respiratory therapy.

Botulism in foals less than 6 mo of age is readily treated, and the survival rate is more than 95% in foals receiving appropriate treatment. Nursing care, IV fluid support, nasogastric or nasoesophageal tube feeding, broad-spectrum antimicrobial coverage (excluding aminoglycoside and tetracycline classes), oxygen therapy, and the administration of botulism antitoxin are important therapies. Ap-proximately 33% of affected foals may require positive pressure mechanical ventilation, whereas the majority may require supplemental oxygen therapy. Cost for treatment depends on length of hospitalization and required therapies and will, of course, vary by institution or referral facility. Foals requiring parenteral nutrition or mechanical ventilation will be significantly more expensive to treat. The cost of treatment with antitoxin is less in these patients than in adults because of their smaller body size.

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[a]Polyvalent botulism antiserum. Dr. R H Whitlock, University of Pennsylvania, New Bolton Center, Kennett Square, PA 19348.

11 ✕	12 ✓	13 M ✓	14 ✓	15 ✓	16 M ✓	17	18	19	20

Which one of the following drugs should not be administered to lactating dairy cattle?

Penicillin G	HIDE
Thiabendazole	HIDE
Sulfamethazine	HIDE
Oxytetracycline	HIDE
Pirlimycin	HIDE

BACK   NEXT   LEAVE BLANK

Overview | Mark this Question | Lab Values | Definitions | Report a Problem

==Correct.==

==Sulfamethazine cannot be used in lactating dairy== cattle and there is no exception for extralabel use. Basically, almost all sulfonamides are banned from use in lactating dairy cows.

Click here to see a list of <u>drugs prohibited for extra-label use</u> in food animals. Here is an FDA summary on the <u>Ins and Outs of Extra-Label Drug Use in Animals</u>.

<u>Oxytetracycline</u>, ==penicillin G, and pirlimycin== either ==have labeled indications== for treatment of dairy cattle or can be used extralabel if warranted in the opinion of the attending veterinarian. Be aware that just because something makes medical sense does not mean it is legal for use in food producing animals.

Refs: Giguere S, Prescott JF, Baggot JD, Antimicrobial Therapy in Vet Med. 4th ed., Sulfonamides, Diaminopyrimidines and Their Combinations, p. 254 and the Merck Veterinary Manual online edition.

☐ **FDA** U.S. FOOD & DRUG
ADMINISTRATION

☐ back to Resources for
You

The Ins and Outs of Extra-Label Drug Use in Animals: A Resource for Veterinarians

| ☐ SHARE | ☐ TWEET | ☐ LINKEDIN | ☐ PIN IT | ☐ | ☐ EMAIL | ☐ PRINT |

As a practicing veterinarian, you've likely prescribed a drug for an extra-label use. What does that mean? What gives you the legal ability to do so? What conditions must you meet? By explaining FDA's requirements for extra-label drug use in animals, this article answers these questions and more.

In 1994, Congress added provisions to the Federal Food, Drug, and Cosmetic Act (FD&C Act) that give veterinarians the legal ability - with certain restrictions - to use approved human and animal drugs in an extra-label manner. This means, in some cases, you can use an approved drug in a way that isn't listed on the drug's labeling. Extra-label drug use is sometimes called off-label because the use is "off the label."

To prescribe drugs in an extra-label manner, you need to follow FDA's requirements for extra-label drug use, as stated in the FD&C Act and FDA regulations. You should also educate your clients, particularly food animal producers, on these requirements and on FDA's recommendations for the judicious use of antimicrobials.

Extra-Label Drug Use in Animals

Before Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) in 1994, federal law did not permit extra-label drug use in animals. The AMDUCA provisions amended the FD&C Act to allow veterinarians to prescribe approved human and animal drugs for extra-label uses in animals under

specified conditions. The key points are:

- Valid Veterinarian-Client-Patient Relationship

- General Conditions for Extra-Label Drug Use

- Conditions for Extra-Label Drug Use in Food-Producing Animals

- Compounding

- Drugs Prohibited from Extra-Label Uses in Animals

We'll look at each point separately as well as touch on how FDA's judicious use recommendations affect extra-label use of antimicrobials in food-producing animals.

Valid Veterinarian-Client-Patient Relationship

The AMDUCA provisions of the FD&C Act allow extra-label drug use only on the lawful order of a licensed veterinarian in the context of a valid veterinarian-client-patient relationship. A valid veterinarian-client-patient relationship has three parts:

- You have assumed responsibility for making medical judgments about the health of an animal, or animals, and the need for medical treatment. In turn, the client (the owner or other animal caretaker) has agreed to follow your instructions;

- You have sufficient knowledge of the animal, or animals, to develop a general or preliminary diagnosis of the medical condition; and

- You are readily available for follow-up in case of adverse drug reactions or treatment failure.

Such a relationship can exist only when you have recently seen and are personally acquainted with the keeping and care of the animal or animals. This means you have recently examined the animal or animals, made "medically appropriate and timely visits" to the premises (usually the case for food-producing animals), or done both.

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General Conditions for Extra-Label Drug Use

The purpose of FDA's requirements for extra-label drug use in animals is to limit this use to situations where an animal's health is threatened or where the animal may suffer or die without treatment. In addition, one of the following general conditions must be met before you can legally prescribe an approved human or animal drug for an extra-label use:

- There is no animal drug approved for the intended use; or

- There is an animal drug approved for the intended use, but the approved drug does not contain the active ingredient you need to use; or

- There is an animal drug approved for the intended use, but the approved drug is not in the required dosage form (for example, you need a liquid dosage form, but the approved drug is only available as a tablet dosage form); or

- There is an animal drug approved for the intended use, but the approved drug is not in the required concentration (for example, you need 5 mg, but the approved drug is only available at 50 mg); or
- You have found, in the context of a valid veterinarian-client-patient relationship, that the approved drug is clinically ineffective when used as labeled.

In companion (non-food-producing) animals, you can prescribe an approved human drug for an extra-label use even if an approved animal drug is available. This is not the case for food-producing animals. For these animals, FDA's requirements for extra-label drug use prohibit you from prescribing an approved human drug if there's a drug approved for food-producing animals that you can prescribe instead. For example, if a drug approved for chickens is available, you must first use that drug to treat a sick cow before reaching for a drug approved for people.

Thorough recordkeeping is vital. You must maintain records that identify the treated animal or animals. For food-producing animals, this can be done on a group, herd, flock, or per-client basis. The records must include the:

- Established name of the drug including its active ingredient, or if formulated from more than one active ingredient, the established name of each active ingredient. Ordinarily, the established name of the drug is the name listed in the United States Pharmacopeia (USP) and is made up of the active ingredient, route of administration, and dosage form (for example, "fenbendazole oral suspension");
- Condition treated;
- Animal species treated;
- Dosage administered;
- Treatment duration; and
- Number of animals treated.
- For food-producing animals, the records must include the withdrawal, withholding, or discard period for food products, such as meat, milk, or eggs, made from treated animals.

You must keep these records for two years or as otherwise required by federal or state law, whichever is longer. The records must be made available to FDA-designated personnel, at all reasonable times, for copying and verifying.

Thorough labeling is critical. The labeling for a drug dispensed on your order for an extra-label use must state your name and address. If the drug is dispensed by a pharmacy on your order, the labeling must state your name, and the name and address of the dispensing pharmacy. The labeling must also include information similar to what is required in the record:

- Established name of the drug or, if formulated from more than one active ingredient, the established name of each active ingredient. As mentioned above, the established name of the drug typically is the name listed in the USP and is made up of the active ingredient, route of administration, and dosage form (for example, "fenbendazole oral suspension");
- The class/species or identity of the treated animal. Animals should be identified individually (usually for companion animals) or by herd, flock, pen, or lot (usually for food-producing animals);

- Directions for use, including dosage, frequency, route of administration, and duration of therapy; and

- Any cautionary statements (for example, "Not for use in veal calves").

- For food-producing animals, the drug labeling must also include the withdrawal, withholding, or discard period for food products, such as milk, meat, or eggs, made from treated animals.

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Conditions for Extra-Label Drug Use in Food-Producing Animals

If you're a food animal veterinarian, you should be aware of the additional requirements for extra-label drug use in food-producing animals. Before prescribing any approved human or animal drug for an extra-label use in food-producing animals, you must:

- Carefully diagnose and evaluate the condition for which you are prescribing the drug;

- Make sure procedures are in place so your client maintains the identity of the treated animal or animals;

- Establish a substantially extended withdrawal period supported by appropriate scientific information. You may get this information from such sources as scientific literature, academia, or the [Food Animal Residue Avoidance Databank (FARAD)](#); and

- Take measures to assure that no illegal drug residues occur in the treated animal or animals. Your client must follow your established withdrawal period.

If you want to use a drug approved for people or a drug approved only for companion animals in food-producing animals, you must also have an appropriate medical rationale for using the drug. In addition, if scientific information is unavailable on the safety of food products made from animals treated with the particular drug, you must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

Remember, you may not prescribe an approved human drug for food-producing animals if there's an animal drug approved for food-producing animals that you can prescribe instead.

The FD&C Act doesn't allow the extra-label use of any drug in animal feed. However, for some [minor species](#), you may determine that extra-label use of a drug in animal feed is needed to prevent suffering and death in these animals. (Minor species are all animals that aren't one of the seven major species: cattle, horses, swine, chickens, turkeys, dogs, and cats.) Please refer to FDA's [Compliance Policy Guide](#) on extra-label use of medicated feeds for minor species.

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Compounding

Under the FD&C Act, an animal drug that is compounded using an unapproved drug or bulk drugs as the starting material is adulterated. An animal drug that is compounded using an approved human or animal drug as the starting material is not adulterated, and using such a drug is considered a legal extra-label

use as long as all other conditions required by law are met. You can find these requirements in:

- Sections 512(a)(4) and (5) of the FD&C Act [Sections 360b(a)(4) and (5) of Title 21 of the United States Code (New Animal Drugs, 2017)] and;

- Section 530.13 of Title 21 of the Code of Federal Regulations(Extra-label use from compounding of approved new animal and approved human drugs, 2017).

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Drugs Prohibited from Extra-Label Uses in Animals

Under the AMDUCA provisions, FDA has the right to prohibit extra-label uses of certain drugs in animals. The following drugs (both human and animal), families of drugs, and substances are prohibited from extra-label uses in all food-producing animals, including horses intended for human food:

- Chloramphenicol

- Clenbuterol

- Diethylstilbestrol (DES)

- Dimetridazole

- Ipronidazole and other nitroimidazoles

- Furazolidone and nitrofurazone

- Sulfonamide drugs in lactating dairy cattle, except for the approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine

- Fluoroquinolones

- Glycopeptides

- Phenylbutazone in female dairy cattle 20 months of age or older

- Cephalosporins (not including cephapirin) in cattle, swine, chickens, or turkeys:

  - For disease prevention purposes;

  - At unapproved doses, frequencies, durations, or routes of administration; or

  - If the drug is not approved for that species and production class.

The following drugs, or classes of drugs, that are approved for treating or preventing influenza A are prohibited from extra-label uses in chickens, turkeys, and ducks:

- Adamantane

- Neuraminidase inhibitors

The above list can be found in Section 530.41 of Title 21 of the Code of Federal Regulations(Drugs prohibited for extra-label use in animals, 2017). Currently, no approved drugs are prohibited from extra-label uses in companion animals.

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Judicious Use of Medically Important Antimicrobials and Extra-Label Drug Use in Food-Producing Animals

FDA's Guidance for Industry #209 discusses the agency's concerns about antimicrobial resistance and recommends the following judicious use principles in food-producing animals:

- Limit medically important antimicrobials to uses that are necessary for assuring animal health (in other words, therapeutic uses to treat, control, or prevent specific diseases); and

- Limit medically important antimicrobials to uses that include veterinary oversight or consultation.

(The term "medically important antimicrobials" generally refers to antimicrobials that are important for therapeutic uses in people.)

In light of the public health risk posed by antimicrobial resistance, FDA stated in this guidance document that the agency doesn't think using medically important antimicrobials for production purposes in food-producing animals is a judicious use of these drugs. Animal drugs currently approved for production purposes, such as increased rate of weight gain and improved feed efficiency, are typically given in feed or water on a herd- or flock-wide basis.

FDA's Guidance for Industry #213 discusses the agency's recommendations for drug sponsors to align with the judicious use principles outlined in Guidance for Industry #209. (A drug sponsor is the entity that owns the right to market a particular drug. Any organization, or even one person, can be a drug sponsor, but typically, the drug sponsor is a drug company.) The process of implementing Guidance for Industry #213 began in December 2013 when FDA recommended that drug sponsors voluntarily phase out the use of medically important antimicrobials for production purposes in food-producing animals. [By January 2017, this phase-out was complete](#)—the drug sponsors voluntarily removed all production claims from the approved labeling of medically important antimicrobials for use in food-producing animals in or on feed or water or the sponsors voluntarily withdrew the approvals. Continued use of such a drug in animal feed or water for a production purpose is an illegal extra-label use.

Let's say a medically important antimicrobial is approved for a therapeutic use in food-producing animals, such as to treat bovine respiratory disease in cattle. Prescribing this drug in an extra-label manner for a production purpose, such as to increase rate of weight gain in cattle, goes against FDA's judicious use principles. It also doesn't comply with FDA's requirements for extra-label drug use in animals. These requirements state that for extra-label drug use in food-producing animals, you must carefully diagnose and evaluate the condition for which you are prescribing the drug. This means you must diagnose a medical condition and any drug you prescribe in an extra-label manner must be for a therapeutic use, which wouldn't include increased rate of weight gain (or any production claim).

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Conclusion

The Animal Medicinal Drug Use Clarification Act of 1994 added provisions to the Federal Food, Drug, and Cosmetic Act legalizing the extra-label use of approved human and animal drugs in animals under

certain conditions. You can ensure proper extra-label use by complying with FDA's requirements and by understanding what's allowed and what's not under the law.

For more information, please call FDA's Center for Veterinary Medicine at 240-402-7002, or email AskCVM@fda.hhs.gov.

FDA's Guidance Documents on Judicious Use

- Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals.

- Guidance of Industry #213: New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209.

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Food Animal Residue Avoidance Databank

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One-page PDF

Prohibited and Restricted Drugs in Food Animals

Under provisions of the *American Medicinal Drug Use Clarification Act* (AMDUCA) and
21 CFR part 530, FDA can prohibit use of an entire class of drugs in selected animal
species if FDA determines that: (I) an acceptable analytical method needs to be
established and such a method has not or cannot be established; or (II) the extra-label
use of the drug or drug class presents a public health risk. FDA can also limit the
prohibition on extra-label use to specific species, indications, dosage forms, routes of
administration, or a combination of these.

GROUP I. Drugs with No Allowable Extra-Label Uses in Any Food-Producing Animal Species

- CHLORAMPHENICOL
- CLENBUTEROL
- DIETHYLSTILBESTEROL (DES)
- FLUOROQUINOLONE–CLASS ANTIBIOTICS

- **GLYCOPEPTIDES** – all agents, including **VANCOMYCIN**
- **MEDICATED FEEDS**
- **NITROIMIDAZOLES** – all agents, including **DIMETRIDAZOLE**, **IPRONIDAZOLE**, **METRONIDAZOLE** and others
- **NITROFURANS** – all agents, including **FURAZOLIDINE**, **NITROFURAZONE** and others

GROUP II. Drugs with Restricted Extra-Label Uses in Food-Producing Animal Species

- **ADAMANTANE & NEURAMINIDASE INHIBITORS** – Extra-label use (ELDU) of these drugs is **prohibited** in poultry including chickens, turkeys and ducks in the United States. Although these drugs are **not approved for use in animals in the United States**, some of these drugs are used in other countries for the treatment or prevention of avian influenza in chickens, turkeys and ducks.
- **CEPHALOSPORINS**
  - – ELDU of all cephalosporin antibiotics, except CEPHAPIRIN, is **restricted** in the United States.
  - – ELDU restrictions differ for Major vs. Minor Food Animal Species as noted below:
    1. **Major Food Animal Species** (Cattle, Pigs, Chickens and Turkeys): ELDU is permissible only for therapeutic indications that are not included on the product label. However, ELDU of cephalosporin antibiotics is **prohibited** in all of the following situations:
       a) the intended use of the product deviates from the approved dose, treatment duration, frequency or administration route on the product label,
       b) the intended use of a product in an unapproved major species or animal production class,
       c) the intended use of the product for the purpose of disease prevention.
    2. **Minor Food Animal Species** (all species that are not major species): ELDU of cephalosporin antimicrobial agents is permitted in these species.
- **GENTIAN VIOLET** – use is **prohibited** in food or feed of all food-producing animal species (details)
- **INDEXED DRUGS** (view here) – ELDU of these drugs is **prohibited** in all food producing animals, with some exceptions for minor-use animal species that are not used as food for humans or other animals.
- **PHENYLBUTAZONE** – all uses of this drug is **prohibited** in female dairy cattle greater than 20 months of age.
- **SULFONAMIDE–CLASS ANTIBIOTICS**
  - – ELDU of all sulfonamides and potentiated sulfonamides is prohibited in adult lactating dairy cattle or dairy cattle greater than 20 months of age.
  - – only labeled uses of approved sulfonamides are allowed.
  - – ELDU of sulfonamides in milking sheep and goats is discouraged but not prohibited.

GROUP III. Drugs with Special Restrictions for Grade "A" Dairy Operations

Based upon recommendations by the National Conference on Interstate Milk Shipments (NCIMS), the FDA publishes a set of minimum standards and requirements for the production of Grade "A" milk. These standards, which are published collectively as the **Grade A Pasteurized Milk Ordinance** (Grade "A" PMO), provide applicable CFR references and can be used as an inspectional guide to cover specific operations in the dairy industry, including pasteurization equipment, packaging, quality control and record keeping requirements. Although the PMO does not have the force of regulations, it provides procedures and standards of general applicability that are acceptable to FDA. Owing to human food safety concerns, certain drugs including non-medical grade dimethylsulfoxide (DMSO), dipyrone and colloidal silver, are not to be used or not to be stored on dairy operations or fed to lactating dairy cattle.

Updated 07-16-2018

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Clindamycin (ie: Antirobe) is in which family of antibiotics?

Lincosamides	HIDE
Sulfonamides	HIDE
Tetracyclines	HIDE
Aminglycosides	HIDE
Macrolides	HIDE

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Correct:

Clindamycin is a lincosamide. According to the Merck Veterinary Manual, 9th edition, lincosamides should NOT be used in neonates because of their limited ability to metabolize drugs.

DO NOT to use Clindamycin (Antirobe®) in rabbits, guinea pigs, chinchillas, hamsters, horses, and ruminants. May be associated with GI upset.

CONTRAINDICATED IN HORSES because a severe, even fatal colitis can occur.

Refs: Plumb's Veterinary Drug Handbook, 7th ed. pp. 309-13 and the Merck Veterinary Manual online edition.

| 11 ✗ | 12 ✓ | 13 M ✓ | 14 ✓ | 15 ✓ | 16 M ✓ | 17 ✓ | 18 ✓ | 19 ✗ | 20 |

Which one of the following drug choices can predispose an animal to develop Tyzzer's disease?

Phenylbutazone	HIDE
Sulfonamides	HIDE
H-2 antagonists (Ranitidine, Cimetidine)	HIDE
Albendazole	HIDE
Avermectins (Ivermectin, Moxidectin)	HIDE

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Correct:

Immunosuppressive drugs and sulfonamide antibiotics predispose to Tyzzer's disease caused by *Clostridium piliforme*.

Think of sporadic fatal infection in well-nourished but stressed young foals and acute fatal epidemics in lab animals. Rare in dogs, cats and calves.

Refs: Pasquini's Guide to Eq Clin, 3 rd ed. pp. 87 and the Merck Veterinary Manual online edition.

Clostridium piliforme , silver stain, liver 🖨
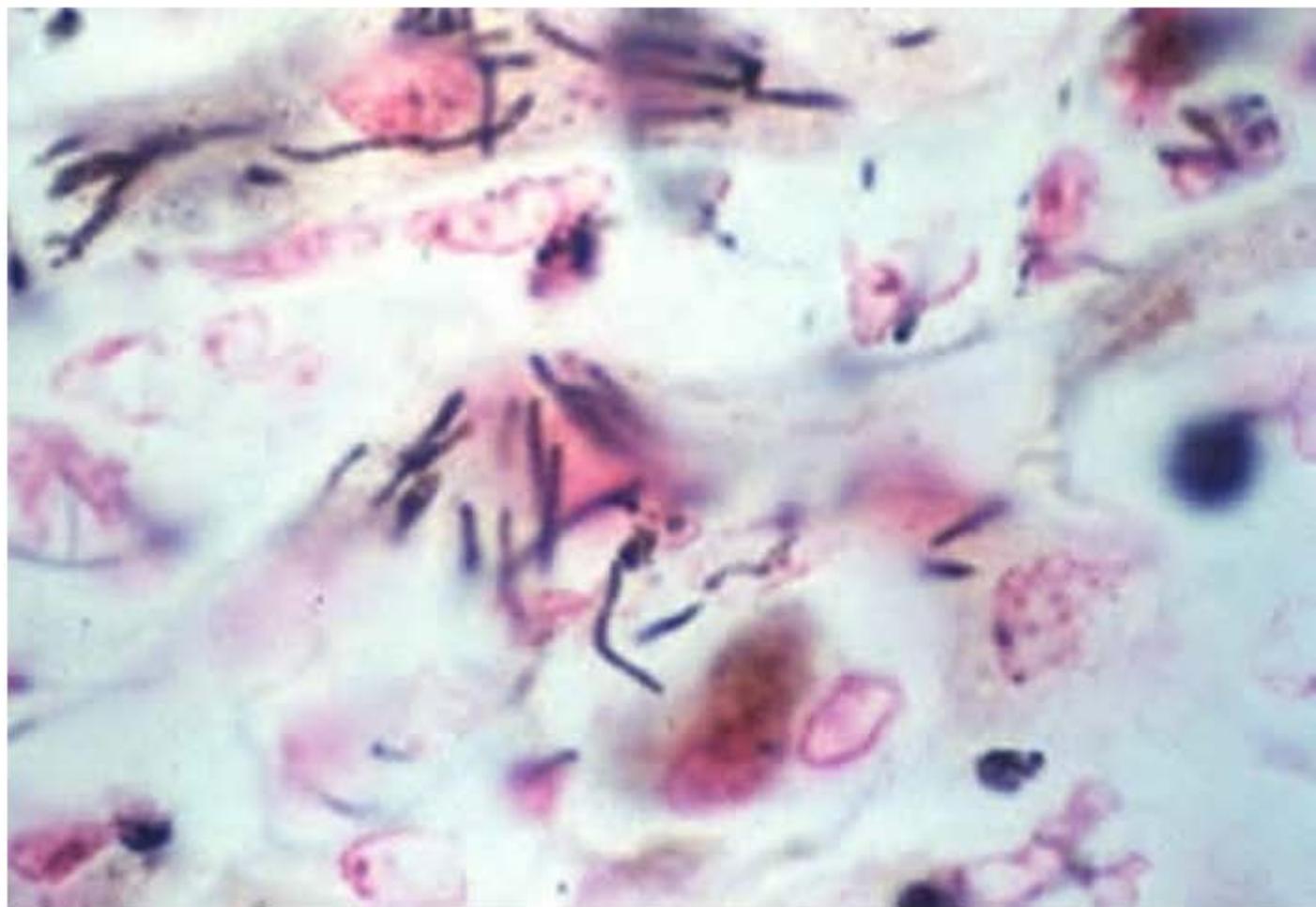
Note the characteristic bundling of the black, silver-stained *Clostridium piliforme* rods in this liver section (silver stain, high power).

Courtesy of Dr. John Prescott.

Overview of Tyzzer Disease

By **Thomas W. Swerczek, DVM, PhD, Professor, Department of Veterinary Science, University of Kentucky**

Tyzzer disease is an enterohepatic syndrome of a wide range of animals (also see Tyzzer Disease in rabbits) and is seen worldwide. Tyzzer disease was first described in mice in 1917. Several years later, it was reported in laboratory rabbits and then in other small laboratory mammals, including guinea pigs, hamsters, gerbils, and rats. It is a highly fatal disease of young foals. The disease is rare in other domestic animals, including dogs, cats, and calves. It has been reported in a variety of wildlife, including muskrats, cottontail rabbit, coyote, gray fox, lesser panda, snow leopard, raccoon, marsupials, and white-tailed deer.

The disease primarily affects young, well-nourished animals, especially those fed high-protein diets, during periods of stress. Some species appear resistant unless stressed or immunosuppressed, whereas others appear to be susceptible without immunosuppression. Dietary factors, including excessive nitrogenous diets fed to laboratory animals and to nursing mares, seemingly may cause immunosuppression and may predispose susceptible animals to the disease. Other immunosuppressive agents and drugs and some antibacterials, especially sulfonamides, may also predispose animals to the disease.

Under laboratory conditions, stress is created by immunosuppressive drugs or other factors that can be easily identified. With many experiments, stress may be involved as part of the protocol, and when the disease develops, it is devastating.
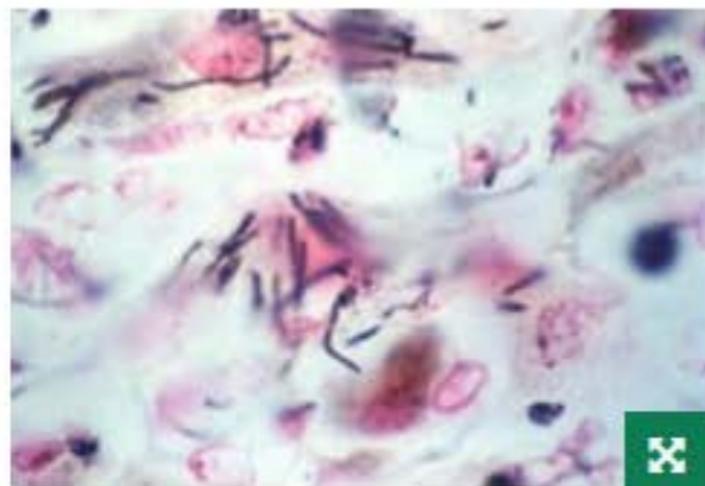
Tyzzer Disease

Overview of Tyzzer Disease

Etiology and Pathogenesis:

The disease is caused by *Clostridium piliforme*, a motile, spore-forming, rod-shaped, flagellated, obligate, intracellular bacterium. It does not grow in cell-free media but can be cultured in the yolk sac of chick embryos or tissue culture cells. The vegetative phase is very labile; spores may survive in soiled bedding at room temperature for >1 yr and are resistant to heating up to 60°C for 30 min, or exposure to 70% ethanol, 3% cresol, 4% chlorhexidine, and 0.037% formaldehyde; however, they are sensitive to 0.4% peracetic acid, 0.015% sodium hypochlorite, 1% iodophor, and 5% phenol.

C piliforme appears to be common in the environment, but because it is difficult to culture, very little knowledge has been accumulated on the epidemiology, pathogenesis, and immunity. Infection most likely results from oral exposure to spores from the environment. The feces of infected and carrier animals are the primary source of spores that contaminate the environment.

C piliforme infections are often subclinical or asymptomatic but may be severe in many animal species. There may be differences in susceptibility within animal species. B lymphocytes, T lymphocytes, and natural killer cells may play a role in mediating strain susceptibility. Seroanalysis using monoclonal antibody-based competitive inhibition ELISA suggests that Tyzzer disease may be relatively common in horses, which are susceptible to at least two distinct strains.

Clostridium piliforme , silver stain, liver

Courtesy of Dr. John Prescott.

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A 7-year old female spayed Border Collie is presented with two very goopy, gunk-covered eyes.

A Schirmer tear test reveals less than 10 mm/minute of wetting [N= 15mm or more/ minute].

The owner reports that the dog has been on "some kind of medicine" for the last 10 days, but it is not his dog, and he doesn't know what the medicine is.

Keratoconjunctivitis sicca (KCS) secondary to the drug is suspected.

Which one of the following drugs may be causing the KCS?

Trimethoprim-sulfa	HIDE
Amitraz	HIDE
Prednisolone	HIDE
Itraconazole	HIDE
Griseofulvin	HIDE

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Correct:

Systemic sulfonamides like ==trimethoprim-sulfa== have been associated with keratoconjunctivitis sicca (KCS), sometimes irreversibly.

Another drug-associated cause of TRANSIENT KCS is the combination of recent general anesthesia and atropine.

==Other causes of KCS include==: distemper, immunologic (think ATOPY), breed (Pugs, Yorkies), and trauma (proptosed eyeball).

Refs: Plumb's Vet Drug Handbook, 8th ed., *Trimethoprim/sulfadiazine*, Cote, Clin. Vet Advisor-Dogs and Cats, 3rd ed. keratoconjunctivitis sicca (online edition)

Nasolacrimal and Lacrimal Apparatus

By **Kirk N. Gelatt, VMD, DACVO, Emeritus Distinguished Professor, Department of Small Animal Clinical Scie Medicine, University of Florida**

Lacrimal apparatus, dog

Lacrimal apparatus, dog. Illustration by Dr. Gheorghe Constantinescu.
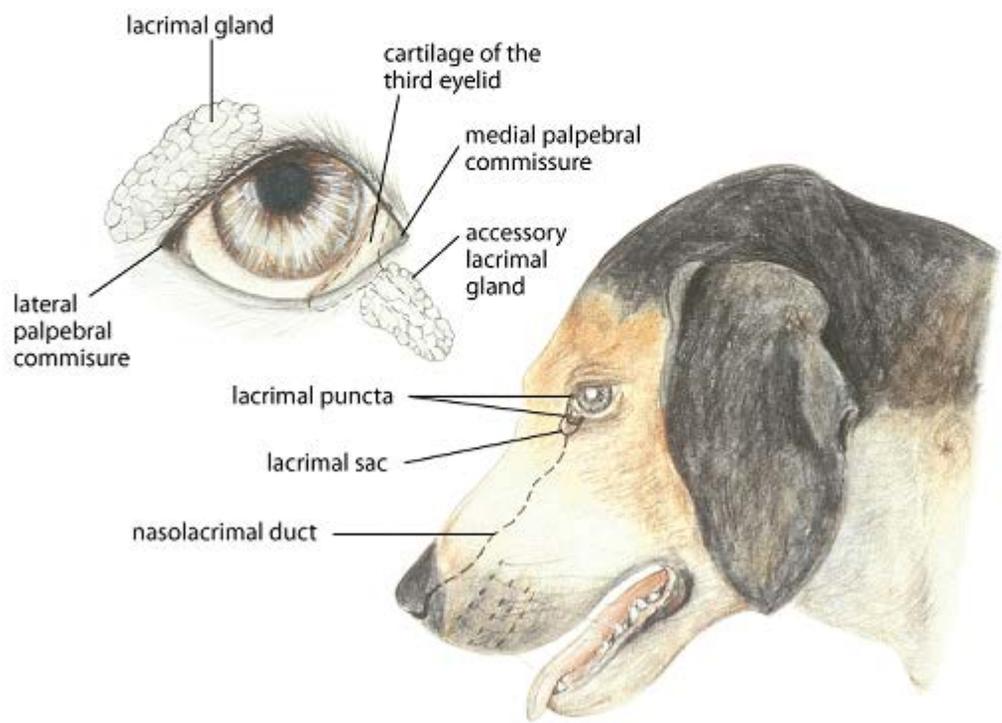
Keratoconjunctivitis sicca (KCS) is due to an aqueous tear deficiency and usually results in persistent, mucopurulent conjunctivitis and corneal ulceration and scarring. KCS occurs in dogs, cats, and horses. In dogs, it is often associated with an autoimmune dacryoadenitis of both the lacrimal and nictitans glands and is the most frequent cause of secondary conjunctivitis. Distemper, systemic sulfonamide and NSAID therapy, heredity, and trauma are less frequent causes of KCS in dogs. KCS occurs infrequently in cats and has been associated with chronic feline herpesvirus 1 infections. In horses, KCS may follow head trauma.

Topical therapy consists of artificial tear solutions, ointments, and, if there is no corneal ulceration, antibiotic-corticosteroid combinations. Lacrimogenics such as topical cyclosporin A (0.2%–2%, bid), tacrolimus (0.02%, bid), or pimecrolimus (1%) may increase tear production; cyclosporine increases tear formation in ~80% of dogs with Schirmer tear test values ≥ 2 mm wetting/min. Ophthalmic pilocarpine mixed in food may be useful for neurogenic KCS (dogs 20–30 lb [10–15 kg] should be started on 2–4 drops of 2% pilocarpine, bid). Mucolytic agents (eg, 10% acetylcysteine) lyse excess mucus and restore the spreading ability of other topical agents. In chronic KCS refractory to medical therapy, parotid duct transplantation is indicated. In general, canine KCS requires longterm (often for life) topical lacrimogenic therapy.

Alpha1 adrenergic blockers as prazocin, acepromazine, Phenoxybenzamine which Decrease peripheral vasoconstriction & promote digital circulation

Acepromazine (Phenothiazine tranquilizer)

1- Penis protrusion in large animals

2-**No analgesic** effect

3-Sedative & anti-emetic in dog, cat

4- **Contraindicated** in Organophosphate (opp) toxicity

5-May cause **Hypotension**

6-Dibliating and Geriatric animals need decrease dose

7- Sight hounds dog and Giant dog overly sensitive

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Which of the following choices are effects of acepromazine in dogs and cats?

Sedation, piloerection	HIDE
Prevent vomiting, vasodilation	HIDE
Increase blood pressure, muscle tremors	HIDE
Anti-arrhythmic, hypertension	HIDE
Muscle relaxation, analgesia	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

Correct:

Acepromazine is a phenothiazine that causes vasodilation and acts as an anti-emetic, sedative, muscle relaxant, and anti-arrhythmic.

Acepromazine blocks peripheral alpha-1 receptors, which produces vasodilation and hypotension.

Acepromazine also blocks dopamine receptors in the brain, which produces sedative, anti-emetic, and anti-arrhythmic effects, as well as causing muscle relaxation.

It does NOT provide analgesia or cause vasoconstriction.

Refs: Tranquilli, Thurmon, and Grimm's Lumb & Jones Veterinary Anesthesia, 4th ed. pp. 207-9, and Muir, Hubbell, Bednarski, and Skarda's Handbook of Veterinary Anesthesia, 4th ed. pp. 29-34.

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Which drugs are both contraindicated in horses because of potential to cause a severe, even fatal colitis?

Enrofloxacin, erythromycin	HIDE
Clindamycin, lincomycin HCl	HIDE
Ceftiofur, enrofloxacin	HIDE
Chloramphenicol, lincomycin HCl	HIDE
Trimethoprim sulfa, chloramphenicol	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

Correct:

Clindamycin and lincomycin HCl are lincosamide antibiotics contraindicated in horses because a severe, even fatal colitis can occur.

Remember that macrolides like erythromycin should be used with caution in adult horses because of GI problems. Erythromycin is often used as part of combination therapy with rifampin in foals with *Rhodococcus equi* pneumonia. The mares can develop colitis after ingesting tiny amounts of erythromycin during contact with the foal's mouth, coprophagia, or from contaminated feeders or water sources.

Note that the use of enrofloxacin in young horses is controversial because quinolones have potential to cause cartilage abnormalities.

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Which drugs can depress T3/T4 levels?

Azathioprine, doxycycline, enalapril	HIDE
Fenbendazole, acyclovir, barium	HIDE
Furosemide, prednisone, phenobarbital	HIDE
Propofol, pyrantel pamoate, cyclosporine	HIDE
Phenoxybenzamine, omeprazole, selamectin	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct: Furosemide, prednisone, phenobarbital

Many drugs can depress T3/T4 hormones. Think of:

Glucocorticoids, anabolic steroids
Anticonvulsants (phenytoin, phenobarbital)
Phenylbutazone
Ipodate (radiographic contrast agent)
Furosemide
Anesthetics (thiopental, methoxyflurane, halothane)
Mitotane (o,p DDD)

Euthyroid sick syndrome in dogs occurs when a non-thyroidal illness causes a decrease in T3/T4 hormones. Not to be confused with true hypothyroidism.

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What is the best method to terminate a potential pregnancy in a cow that has just been mis-mated by semen from the wrong bull?

Prostaglandin F2alpha 7 to 9 days post-insemination	HIDE
Human chorionic gonadotropin (HCG) 24 hours post mis-mating	HIDE
Estradiol cypionate (ECP) at the time of mis-mating	HIDE
Dexamethasone 21 days post mis-mating	HIDE
Diethylstilbesterol (DES) at the time of mis-mating	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

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Correct:

The easiest way to stop the pregnancy is to regress the corpus luteum using prostaglandin F2-alpha. Resumption of the estrus cycle prevents fetal implantation.

Diethylstilbesterol (DES) is banned for use in food-producing animals and should never be used.

Human chorionic gonadotropin (HCG) is luteotrophic. It possesses LH activities, and thus would not terminate the pregnancy.

Dexamethasone will initiate abortion in late-term cows, but is not indicated in very early pregnancies. Typically, use dexamethasone in cattle to induce parturition (20-30 mg, IM, given within 2 wk of normal term).

==Estrogenic== therapy may be teratogenic in pregnant animals and has been associated in dogs and cats with cystic endometrial hyperplasia, pyometra, bone marrow suppression and potentially fatal aplastic anemia. According to the Food and Drug Administration (FDA) the use of ECP in animals is **illegal**. ECP has been used as an estrogenic hormone for reproductive therapy in food animals, but even extra-label, this is not allowed.

Here is a statement from the FDA regarding estradiol cypionate (ECP) and food-producing animals.

"The Animal Medicinal Drug Use Clarification Act (AMDUCA) amended the Federal Food, Drug, and Cosmetic Act to allow licensed veterinarians to prescribe extra-label uses of approved animal drugs and human drugs in animals. However, under AMDUCA extra-label use is limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat. The extra-label use of ECP for reproductive purposes does **not** qualify under these provisions."

Pyometra, cat (ultrasound) 🖨
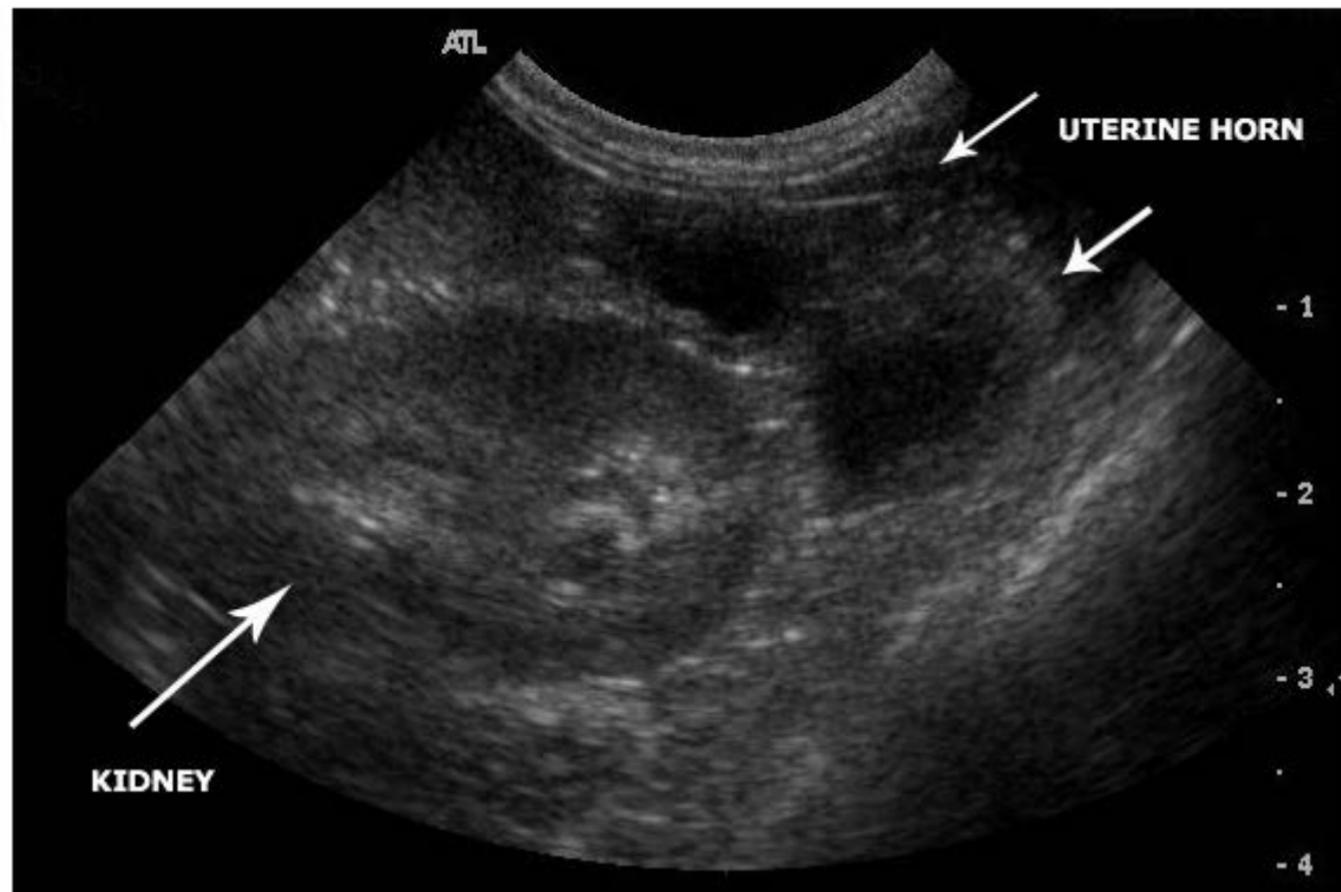
Pyometra in a cat (ultrasound).

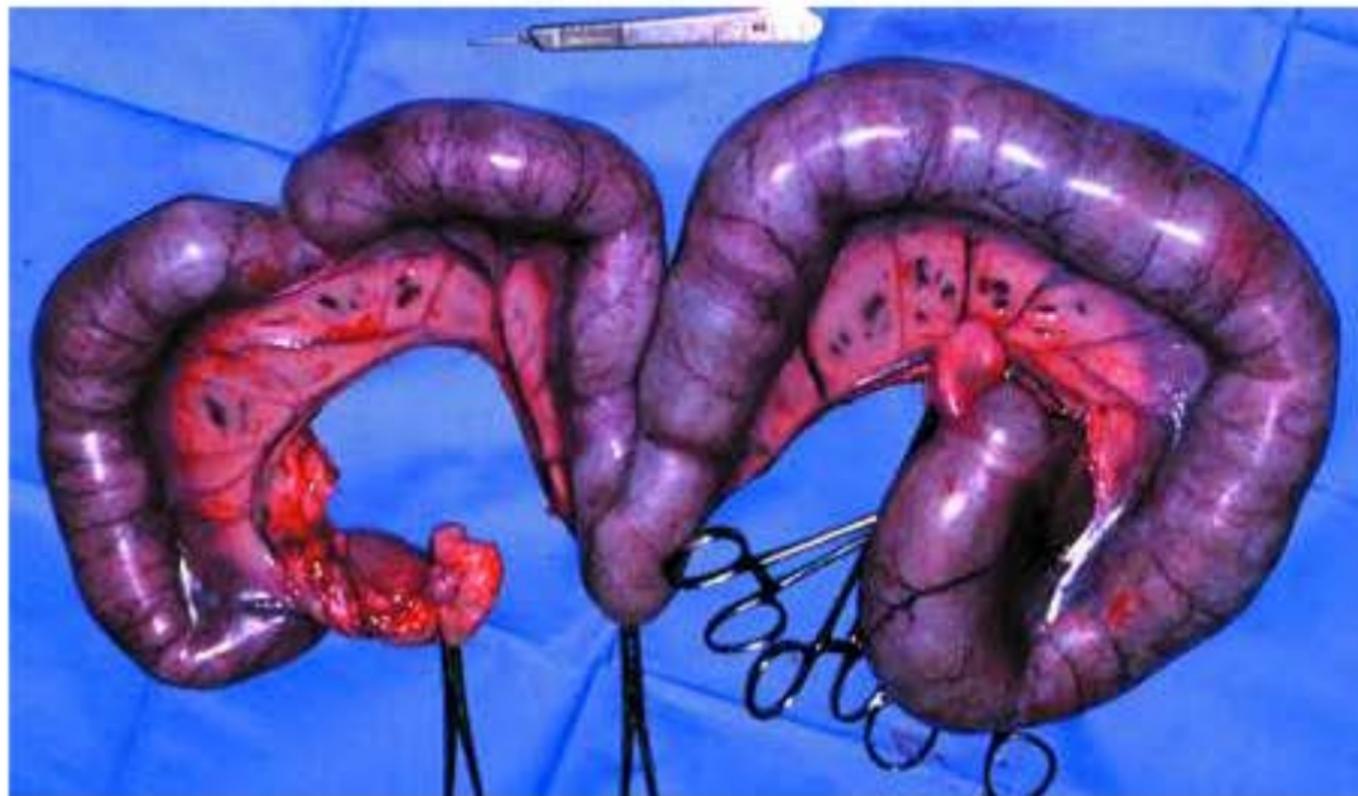*Courtesy of Dr. Autumn P. Davidson.*

Pyometra, radiograph, Norwegian Elkhound 🖨

Pyometra in a 10-yr-old Norwegian Elkhound, lateral projection.

Courtesy of Dr. Ronald Green.

Uterus with pyometra, dog 🖨

Uterus with pyometra removed by ovariohysterectomy from a 7-yr-old Golden Retriever with a history of anorexia and vaginal discharge that began 4 wk after breeding.

Courtesy of Dr. Mushtaq Memon.

MERCK MANUAL

Veterinary Manual

Veterinary / Reproductive System / Reproductive Diseases of the Female Small Animal

Pyometra in Small Animals

By **Mushtaq A. Memon, BVSc, PhD, DACT, Theriogenologist, Department of Veterinary Clinical Sciences, Washington State University**

Pyometra is a hormonally mediated diestrual disorder characterized by cystic endometrial hyperplasia with secondary bacterial infection. Pyometra is reported primarily in older bitches (>5 yr old), 4–6 wk after estrus.

Etiology:

Factors associated with occurrence of pyometra include administration of longlasting progestational compounds to delay or suppress estrus, administration of estrogens to mismated bitches, and postinsemination or postcopulation infections. Progesterone promotes endometrial growth and glandular secretion while decreasing myometrial activity. Cystic endometrial hyperplasia and accumulation of uterine secretions ultimately develop and provide an excellent environment for bacterial growth. Progesterone may also inhibit the WBC response to bacterial infection. Bacteria from the normal vaginal flora or subclinical urinary tract infections are the most likely sources of uterine contamination. *Escherichia coli* is the most common bacterium isolated in cases of pyometra, although *Staphylococcus*, *Streptococcus*, *Pseudomonas*, *Proteus* spp, and other bacteria also have been recovered.

Because queens require copulatory stimulation to ovulate and produce progesterone from corpora lutea, pyometra is less common in queens than in bitches. Administration of medroxyprogesterone and other progestational compounds has been associated with development of pyometra in bitches and queens. Pyometra can develop in uterine tissue left after ovariohysterectomy (stump pyometra). It can also occur secondary to postpartum metritis.

By itself, estrogen does not contribute to the development of cystic endometrial hyperplasia or pyometra. However, it does increase the stimulatory effects of progesterone on the uterus. Administration of exogenous estrogens to prevent pregnancy (ie, "mismate shots") during diestrus greatly increases the risk of developing pyometra and should be discouraged.

Clinical Findings:

Clinical signs are seen during diestrus (usually 4–8 wk after estrus) or after administration of exogenous progestins. The signs are variable and include lethargy, anorexia, polyuria, polydipsia, and vomiting. When the cervix is open, a purulent vulvar discharge, often containing blood, is present.

When the cervix is closed, there is no discharge and the large uterus may cause abdominal distention. Signs can progress rapidly to shock and death.

Physical examination reveals lethargy, dehydration, uterine enlargement, and if the cervix is patent, a sanguineous to mucopurulent vaginal discharge. Only 20% of affected animals have a fever. Shock may be present.

The leukogram of animals with pyometra is variable and may be normal; however, leukocytosis characterized by a neutrophilia with a left shift is usual. Leukopenia may be found in animals with sepsis. A mild, normocytic, normochromic, nonregenerative anemia (PCV of 28%–35%) may also develop. Hyperproteinemia due to hyperglobulinemia may be found. Results of urinalysis are variable. With *E coli* uterine infection, isosthenuria due to endotoxin-induced impairment of renal tubular function or to insensitivity to antidiuretic hormone (or both) may develop. A glomerulonephropathy caused by immune-complex deposition may result in proteinuria. These renal lesions are potentially reversible once the pyometra is resolved.

Diagnosis:

Pyometra should be suspected in any ill, diestrual bitch or queen, especially if polydipsia, polyuria, or vomiting is present. The diagnosis can be established from the history, physical examination, abdominal radiography, and ultrasonography. Vaginal cytology often helps determine the nature of the vulvar discharge. A CBC, biochemical profile, and urinalysis help exclude other causes of polydipsia, polyuria, and vomiting; they also evaluate renal function, acid-base status, and septicemia. The uterine exudate should be cultured and sensitivity tests performed. Differential diagnoses include pregnancy and other causes of vulvar discharge, polyuria and polydipsia, and vomiting.
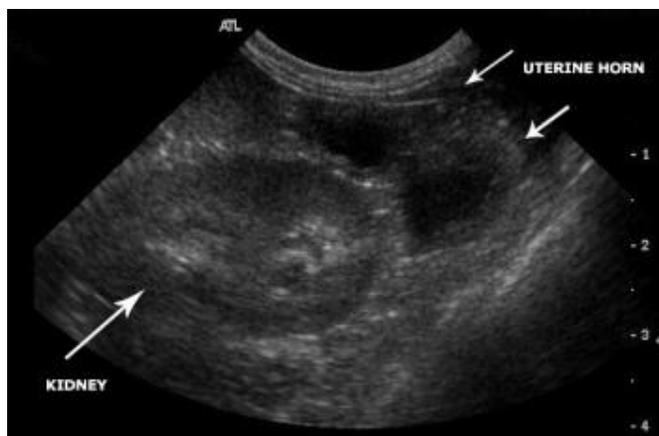
Pyometra, cat (ultrasound)

Courtesy of Dr. Autumn P. Davidson.
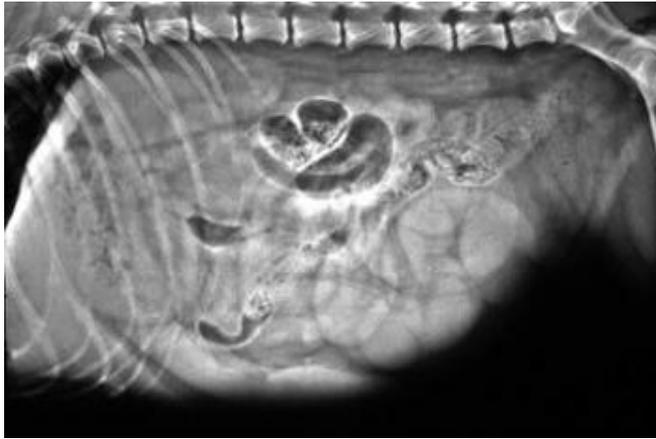
Pyometra, radiograph, Norwegian Elkhound

Courtesy of Dr. Ronald Green.

Treatment and Prognosis:

Ovariohysterectomy is the treatment of choice for pyometra. Medical management could be considered if preserving the reproductive potential of the bitch or queen is desired. Fluids (IV) and broad-spectrum, bactericidal antibiotics should be administered. Fluid, electrolyte, and acid-base imbalances should be corrected as quickly as possible, before ovariohysterectomy is performed. The bacterial infection is responsible for the illness and will not resolve until the uterine exudate is removed. Oral antibiotics (based on the results of the culture and sensitivity) should be continued for 7–10 days after surgery.
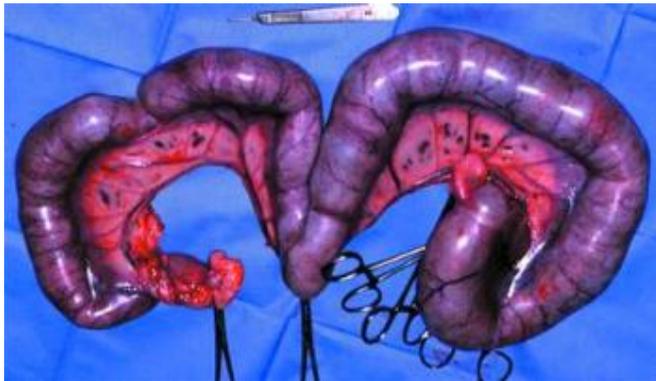
Uterus with pyometra, dog

Courtesy of Dr. Mushtaq Memon.

Medical therapy with prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) can be used for animals to be bred in the future, although prostaglandins are not approved in the USA for use in cats or dogs. $PGF_{2\alpha}$ causes luteolysis, contraction of the myometrium, relaxation of the cervix, and expulsion of the uterine exudate. They should probably not be used in animals >8 yr old or in those not intended for breeding. The delay

before clinical improvement and the many adverse effects of $PGF_{2\alpha}$ preclude its use in a severely ill animal. $PGF_{2\alpha}$ also should be used with caution in bitches or queens with a closed-cervix pyometra because of increased risk of uterine rupture. Pregnancy must be excluded, because prostaglandins can induce abortion.

Naturally occurring $PGF_{2\alpha}$ (0.25 mg/kg/day, SC, for 5 days) is commonly used. Synthetic analogues (eg, cloprostenol, fluprostenol, and prostalene) are much more potent than natural $PGF_{2\alpha}$ and have been used to treat pyometra in dogs. Broad-spectrum, bactericidal antibiotics, chosen on the basis of culture and sensitivity tests, should be given for ≥2 wk.

The adverse effects of $PGF_{2\alpha}$ include restlessness, anxiety, panting, hypersalivation, pacing, tachycardia, vomiting, urination, and defecation. In cats, vocalization and intense grooming behavior also may be seen. These reactions disappear within 2 hr of the injection. The LD_{50} of $PGF_{2\alpha}$ in dogs is 5.13 mg/kg. Severe ataxia, respiratory distress, and muscle tremors may be seen in queens given 5 mg/kg. If adverse effects are severe, IV fluids at rates appropriate for treatment of shock are indicated. Uterine evacuation after an injection is variable.

Other antiprogestins (eg, aglepristone) are available in some European countries. Clinicians using aglepristone report virtually no adverse effects as compared with prostaglandins. Aglepristone is also used to treat bitches with closed-cervix pyometra. In one study, a dosage of 10 mg/kg given on days 1, 2, and 8 in 15 bitches with closed pyometra led to opening of the cervix after 26±13 hr in all treated animals.

Animals should be reexamined 2 wk after completion of medical therapy. If a sanguineous or mucopurulent vulvar discharge or uterine enlargement is still present, $PGF_{2\alpha}$ therapy, using the same protocol, may be repeated; however, the prognosis for recovery is much worse. After medical therapy, the prognosis for initial resolution of the pyometra is good if the cervix is open but guarded to poor if closed. Of those animals that respond, as many as 90% of bitches and 70% of queens with open-cervix pyometra may be fertile. Recurrence is likely; 70% of bitches treated medically for pyometra had recurrence within 2 yr. Therefore, the animal should be bred on the next and each subsequent cycle until the desired number of puppies or kittens has been produced, and then spayed. Prostaglandins should not be dispensed for owner administration because of the narrow safety index and the potential to trigger asthmatic events and pregnancy loss in people.

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21 ✓	22 ✓	23 M ✗	24 ✓	25	26	27	28	29	30

Which one of the following choices is the mechanism of action of omeprazole?

Proton pump inhibitor	HIDE
Cyclooxygenase blocker	HIDE
Synthetic prostaglandin E1 analog	HIDE
H_2-receptor antagonist	HIDE
Beta-adrenergic receptor agonist	HIDE

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Overview | Mark this Question | | | Report a Problem

Correct:

Omeprazole is a proton pump inhibitor that decreases gastric acid secretion. Omeprazole inhibits the sodium/potassium proton pump at the luminal surface of parietal cells.

Parietal cells normally secrete hydrogen ions into the stomach, a key component of acidic HCl.

Other drugs that decrease gastric acid secretion include the H$_2$-receptor antagonists cimetidine, ranitidine, and famotidine and a synthetic prostaglandin E1 analog called "misoprostol."

Carprofen, etodolac, deracoxib, meloxicam and firocoxib are all nonsteroidal anti-inflammatory drugs (NSAIDS) that may CAUSE gastric acid secretion.

| 21 ✓ | 22 ✓ | 23 ᴹ ✗ | 24 ✓ | 25 ✓ | 26 | 27 | 28 | 29 | 30 |

You decide to **treat a cat** with severe chin acne with a trial course of **isotretinoin.**

What should you tell the owner?

Men should not handle the pills	HIDE
Keep medicine bottle refrigerated	HIDE
Must feed before treatment to avoid GI upset	HIDE
Keep medicine bottle separate from human meds	HIDE
Must give 6 cc water after pill to prevent esophageal stricture	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Keep medicine bottle separate from human meds.

Severe cases of feline acne may need a trial of isotretinoin or cyclosporin. Must **warn owner**, if you prescribe isotretinoin, a powerful teratogen.

Best practice is to clearly label medicine bottle "For animal use only" and to keep it separate from human meds. Pregnant women (and animals) should avoid it.

Oral doxycycline has been implicated in cases of esophageal stricture in cats.

Plumb's recommends giving 6 cc water after pilling with doxycycline. Do not dry pill.

Refs: Blackwell's 5-Min. Vet Consult, 4th ed. p.14, Plumb's Vet Drug Handbook, 7th ed. pp. 486-92, 744-6 and the Merck Veterinary Manual online edition.

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| 21 ✓ | 22 ✓ | 23 M ✗ | 24 ✓ | 25 ✓ | 26 ✓ | 27 | 28 | 29 | 30 |

Medetomidine acts upon which one of the following receptors?

Cholinergic	HIDE
Sympathetic	HIDE
Dopamine	HIDE
Alpha-2	HIDE
Gamma amino butyric acid	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

Correct:

Alpha-2 receptors. Medetomidine acts at both alpha-1 and alpha-2 receptors, but its affinity for alpha-2 is much, much greater; the ratio of activity for alpha-1 vs. alpha-2 sites has been measured at 1:1620. The important clinical effects result from inhibition of the release of norepinephrine from presynaptic alpha-2 sites.

Click here to see an image of a dog with a painful cruciate injury sedated with medetomidine for radiographs.

A potent sedative used in human and veterinary medicine, medetomidine has recently been largely replaced by dexmedetomidine, the dextro-rotary isomer component of racemic medetomidine.

Metomidine causes profound sedation and muscle relaxation. It also causes significant analgesia but this subsides before sedative effects.

Cholinergic receptors are normally activated by acetylcholine; atropine and glycopyrrolate block this receptor.

Dopamine is a neurotransmitter and a receptor. Dopamine receptors are present in many tissues, especially the brain, lung, and kidney.

The gamma amino butyric acid (GABA) receptor is a complex unit with many sites for several anesthetics, sedatives, and other drugs, including propofol, benzodiazepines, barbiturates, inhalant anesthetics, steroids, ethanol, and GABA.

Sympathetic refers to the sympathetic nervous system, which has both alpha and beta receptors.

Refs: Grimm, Tranquilli, and Lamont's Essentials of Anes and Analgesia in SA, 2nd ed. pp. 44-7, Tranquilli, Thurmon, and Grimm's Lumb & Jones Veterinary Anesthesia, 4th

| 21 ✓ | 22 ✓ | 23 M ✗ | 24 ✓ | 25 ✓ | 26 ✓ | 27 ✓ | 28 | 29 | 30 |

What is amprolium typically used for in veterinary medicine?

Treat coccidiosis	HIDE
Treat thiamine deficiency	HIDE
Growth promoting feed additive	HIDE
Treat amoebiasis	HIDE
Ionophore-containing feed additive	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Use amprolium to treat coccidiosis, most commonly in cattle, pigs, chickens. Sometimes used (off label) as a preventive and treatment in dog kennel situations.

Follow this link to see coccidian oocysts.

Typically asymptomatic in cats and dogs, but young, stressed animals and the immunocompromised may show clinical signs.

Because amprolium mimics thiamine's structure, it competitively inhibits thiamine utilization of the host. Because of this, prolonged dosages can cause thiamine deficiency. Usually do not treat more than 14 days.

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 97-9 and the Merck Veterinary Manual online.

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| 21 ✓ | 22 ✓ | 23 M ✕ | 24 ✓ | 25 ✓ | 26 ✓ | 27 ✓ | 28 ✓ | 29 | 30 |

What category of drug is enalapril?

Calcium channel blocker	HIDE
Beta blocker	HIDE
Negative inotrope	HIDE
Angiotensin-converting enzyme (ACE) inhibitor	HIDE
Positive chronotrope	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

Correct:

Enalapril is an Angiotensin converting enzyme (ACE) inhibitor. ACE inhibitors are basically vasodilators that help increase cardiac output. They stop formation of angiotensin II, prevent vasoconstriction and reduce the retention of Na+ and water in animals with congestive heart failure (CHF).

Angiotensin-converting enzyme (ACE) is produced in vascular endothelial cells of the lung, primarily. It converts angiotensin I to angiotensin II. Angiotensin II causes retention of Na+ and water, in part by stimulating synthesis and release of aldosterone by the adrenal cortex. Angiotensin II also causes vasoconstriction.

ACE inhibitors are also used in conjunction with diuretics (like furosemide) and beta blockers (like atenolol) to treat systemic hypertension.

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| 21 ✓ | 22 ✓ | 23 M ✗ | 24 ✓ | 25 ✓ | 26 ✓ | 27 ✓ | 28 ✓ | 29 ✓ | 30 |

Which of the following is true about drug absorption?

Charged (or ionic) drugs more readily move into cells	HIDE
Hydrophilic medications are easily absorbed after oral administration	HIDE
Lipophilic drugs readily cross cell membranes	HIDE
Oral drugs are 100% bioavailable	HIDE
Absorption is promoted when the concentration of drug is higher inside the cell	HIDE

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10/24/2018

Correct: **Lipophilic drugs readily cross cell membranes**

Lipophilic drugs readily cross cell membranes whereas hydrophilic drugs do not. Therefore, lipophilic drugs typically have good absorption after oral administration and hydrophilic drugs typically need to be administered by injection.

Uncharged (nonionic) drugs are also more readily absorbed. Absorption requires a concentration gradient – the concentration of the drug needs to be higher outside of the cell as compared to inside the cell.

Drug bioavailability depends on the absorption of the drug into circulation. Intravenous drugs are 100% bioavailable because all the drug is being put directly into the bloodstream. Oral drugs have varying bioavilability.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, p. 1011.

31	32	33	34	35	36	37	38	39	40

Which of the following opioids is more potent than morphine, given most often via continuous intravenous infusion and can be administered via transdermal patch?

Buprenorphine	HIDE
Fentanyl	HIDE
Oxymorphone	HIDE
Tramadol	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Fentanyl is very lipophilic, so it is absorbed and eliminated quickly. It is therefore not useful for pain control via single doses given intramuscularly (IM) or intravenously (IV).

However, it produces good analgesia when given continuously via intravenous infusion and, in many patients, via a transdermal patch. Serum levels can be variable in some patients with patches.

Absorption is affected by temperature; the use of heating blankets can increase levels, hypothermia will decrease levels.

Fentanyl is less likely to cause nausea and vomiting compared to morphine and other mu-agonist opioids. It does cause respiratory depression and dysphoria in some

Other analgesics that can be administered via transdermal patches are lidocaine and buprenorphine.

Use of patches in patients at home must be evaluated carefully – toxicity and death has been seen in children and small animals that have ingested fentanyl patches.

See very nice articles on pain management and opioids in small animals: Murrell J. Clinical use of opioids in dogs and cats: Part 1. *Companion Animal* 2011; 16(4): 35-8, and Part 2, 16(5): 44-9.

Refs: Gaynor & Muir Handbook of Vet Pain Mgt 2nd ed. pp. 118-9, 244-5, 169, 348, 422, Greene, Vet Anes & Pain Mgt Secrets pp. 78-9, 336-7, Riviere & Papich Vet Pharm & Therapeutics, 9th ed. pp. 320-2 and the Merck Veterinary Manual online edition.

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31	32	33	34	35	36	37	38	39	40

What category of drug is verapamil?

Phosphodiesterase (PDE) inhibitor	HIDE
Calcium channel blocker	HIDE
Beta blocker	HIDE
Positive inotrope	HIDE
Angiotensin-converting enzyme (ACE) inhibitor	HIDE

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Overview   Lab Values   Definitions   Report a Problem

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Correct:

Verapamil is a calcium channel blocker. Calcium channel blockers are antiarrhythmic and have ==negative inotropic effects== (decrease force of cardiac muscle contraction).

They are used to ==treat atrial fibrillation and supraventricular== tachycardias, as well as hypertrophic cardiomyopathy (HCM) and hypertension. Amlodipine (used more for hypertension) and diltiazem are two other examples of calcium channel blockers.

ACE inhibitors like enalapril are vasodilators that help increase cardiac output.

Beta-blockers like propranolol and atenolol are used to treat arrhythmias, systemic hypertension, and HCM.

Positive inotropes increase the cardiac muscular contraction strength by making more intracellular calcium available for muscle proteins.

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31

What cat

Phospho

Calcium

Beta blo

Positive

Angiotensin converting enzyme (ACE) inhibitor

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Beta-blockers like propranolol and atenolol are used to treat arrhythmias, systemic hypertension, and HCM.

Positive inotropes increase the cardiac muscular contraction strength by making more intracellular calcium available for muscle proteins.

Examples of positive inotropes include:
Phosphodiesterase (PDE) inhibitors (amrinone, milrinone)
Beta-adrenergic agonists (dopamine, dobutamine, isoproterenol and epinephrine)
Cardiac glycosides (digoxin, digitoxin)

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 1379-82, and the Merck Veterinary Manual online edition.

31

What cat

Phosph

Calcium

Beta blo

Positive

Angiotensin converting enzyme (ACE) inhibitor

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31 ✗	32 ✓	33 ✓	34	35	36	37	38	39	40

What adverse effect will azathioprine have on feline patients?

Bone marrow suppression	HIDE
Acute hepatic toxicity	HIDE
Anorexia	HIDE
Hemorrhagic gastroenteritis	HIDE
Renal toxicity	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Azathioprine is a chemotherapeutic agent, contraindicated in feline patients due to the likelihood for <mark>bone marrow suppression</mark>.

Refs: Cote, Clinical Veterinary Advisor-Dogs and Cats, 3rd ed. pp. 62-3, **1515**, Plumb's Vet Drug Handbook, 7th ed. pp. 97-9 and the Merck Veterinary Manual online.

31 ✗	32 ✓	33 M ✓	34 ✗	35	36	37	38	39	40

Which one of the following choices would be contraindicated for treatment of a calf with a bleeding abomasal ulcer?

Magnesium oxide after copper sulfate solution, PO	HIDE
Blood transfusion	HIDE
Intravenous fluids	HIDE
Broad-spectrum antibiotic therapy	HIDE
Non-steroidal anti-inflammatory drugs	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Abomasal ulcer, lesions.

Courtesy of Dr. Sameeh M. Abutarbush.

Correct:

Non steroidal anti inflammatory drugs should be avoided in animals with pre-existing gastric ulcers.Click here to see abomasal ulcers

Antacids can effectively increase abomasal pH in milk-fed calves when administered at 4- to 6-hr intervals to stimulate esophageal groove closure (which shunts the antacid directly into the abomasum.

Some references suggest giving copper sulfate solution per os to stimulate gastric groove closure, then giving magnesium oxide. Antacid efficacy is questionable in adult cows due to ruminal dilution.

Blood transfusion would be a desirable treatment in a severely anemic animal.

Sarcina lutea, and *Clostridium perfringens* type A have been isolated from the edges of ulcerated abomasums. Antibiotics in the form of penicillin G or a macrolide should be given.

Intravenous fluids are important for correction of dehydration and maintenance of circulation to the ulcerated tissues.

Refs: Fecteau, M-E, Whitlock, R, *Abomasal Ulcers*, in Current Veterinary Therapy 5 Food Animal Practice 2009, pp. 29-34, Pasquini's Guide to Bov Clin, 4 th ed. p. 31, Plumb's Vet Drug Handbook, 7th ed. pp. 1059-64 and the Merck Veterinary Manual online edition.

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| 31 ✕ | 32 ✓ | 33 M ✓ | 34 ✕ | 35 ✓ | 36 | 37 | 38 | 39 | 40 |

In which category of drugs are isoproterenol and dobutamine classified?

Beta-adrenergic agonists	HIDE
Angiotensin-converting enzyme (ACE) inhibitors	HIDE
Phosphodiesterase (PDE) inhibitors	HIDE
Negative chronotropes	HIDE
Calcium channel blockers	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Isoproterenol and dobutamine are <u>beta-adrenergic agonists</u> and positive inotropes (increase cardiac contraction strength). Dopamine and epinephrine are also beta-agonists.

Two other categories of positive inotropes are:
<u>Cardiac glycosides</u> (digoxin, digitoxin)
<u>Phosphodiesterase (PDE) inhibitors</u> (milrinone and amrinone)

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 431-6, 740-2 and the Merck Veterinary Manual online edition.

31 ✗	32 ✓	33 M ✓	34 ✗	35 ✓	36 ✓	37	38	39	40

Which drug should not be used as an injectable in swine?

Erythromycin	HIDE
Oxytetracycline	HIDE
Trimethoprim sulfa (TMS)	HIDE
Tilmicosin (Micotil®)	HIDE
Lincomycin	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Tilmicosin (Micotil®) is a macrolide contraindicated in pigs (injection may kill them. May kill YOU too). Note though, that tilmicosin is approved for use as a feed additive in swine.

Erythromycin is a macrolide you CAN use in pigs, usually for respiratory infections.

Lincomycin can be used in pigs. Typically used to treat *mycoplasma* pneumonia. May be associated with GI upset. CONTRAINDICATED rabbits, hamsters, guinea pigs, ruminants and horse because of serious gastrointestinal side effects, including death.

Trimethoprim sulfa (TMS), is a sulfonamide that is ok to use in pigs.

Oxytetracycline is used to treat pigs, and is specifically mentioned in Plumb's Veterinary Drug Handbook 7th ed. as a treatment against Anthrax.

| 31 ✗ | 32 ✓ | 33 M ✓ | 34 ✗ | 35 ✓ | 36 ✓ | 37 ✓ | 38 | 39 | 40 |

Which diuretic acts on the distal convoluted tubule in the nephron?

Furosemide	HIDE
Osmotic diuretics (Mannitol, DMSO)	HIDE
Carbonic anhydrase inhibitors (Acetazolamide)	HIDE
Thiazides (chlorothiazide, hydrochlorothiazide)	HIDE
Angiotensin	HIDE

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Overview   Mark this Question   Definitions   Report a Problem

Thiazide diuretics like chlorothiazide, hydrochlorothiazide act on the proximal part of the distal convoluted tubule to inhibit sodium reabsorption and promote potassium excretion.

Note that aldosterone, the mineralocorticoid produced in the adrenal cortex, also acts on the distal tubules (and collecting ducts) to retain Na+ and water, secrete K+ and increase blood pressure.

Clinically, look for increased aldosterone secretion (increased blood pressure) with congestive heart failure.

Potassium-sparing diuretics (spironolactone, amiloride) are aldosterone antagonists sometimes used to treat CHF.

See decreased aldosterone secretion (and decreased blood pressure) with hypoadrenocorticism.

| 31 ✕ | 32 ✓ | 33 ✓ | 34 ✕ | 35 ✓ | 36 ✓ | 37 ✓ | 38 ✓ | 39 M ✕ | 40 |

What is the function of lysine in the treatment of a kitten or young cat with signs of a probable herpes viral upper respiratory infection (rhinitis, sneezing, conjunctivitis, ulcerative keratitis)?

Loosens/liquifies nasopharyngeal secretions	HIDE
Interferes with viral replication	HIDE
Potentiates bronchodilators	HIDE
Nasal decongestant	HIDE
Nutritional support	HIDE

BACK   NEXT   LEAVE BLANK

Overview   Mark this   Lab

Correct:

Lysine is an amino acid that interferes with herpetic viral replication in patients infected with feline viral rhinotracheitis (FVR, herpes virus, common).

Refs: Cote, Clinical Veterinary Advisor-Dogs and Cats, 3rd ed. pp. 482-3, Plumb's Vet Drug Handbook, 7th ed. pp. 824-6 and the Merck Veterinary Manual online.

Feline Respiratory Disease Complex

By **Ned F. Kuehn, DVM, MS, DACVIM, Section Chief, Internal Medicine, Michigan Veterinary Specialists**

Feline respiratory disease complex includes those illnesses typified by rhinosinusitis, conjunctivitis, lacrimation, salivation, and oral ulcerations. The principal diseases, feline viral rhinotracheitis (FVR; feline herpesvirus type 1), feline calicivirus (FCV), *Chlamydia felis*, *Mycoplasma felis*, or combinations of these infections, affect exotic as well as domestic species. Feline pneumonitis (*Chlamydia psittaci*) and mycoplasmal infections appear to be of lesser importance. Feline infectious peritonitis (see Feline Infectious Peritonitis) typically causes a more generalized condition but may cause signs of mild upper respiratory tract infection.

FVR and caliciviruses are host-specific and pose no known human risk. Human conjunctivitis caused by the feline chlamydial agent has been reported.

Etiology:

Most acute feline upper respiratory infections are caused by FVR virus, although FCV may be more prevalent in some populations. Dual infections with these viruses may occur. Other organisms such as *C felis*, *Mycoplasma* spp, and reoviruses are believed to account for most of the remaining infections or further complicate FVR or FCV infection. Concurrent *Bartonella henselae* also may further complicate infection.

Natural transmission of these agents occurs via aerosol droplets and fomites, which can be carried to a susceptible cat by a handler. Convalescent cats may harbor virus for many months. Calicivirus is shed continually, while infectious FVR virus is released intermittently. Stress may precipitate a secondary course of illness. The incubation period is 2–6 days for FVR and FCV, and 5–10 days for pneumonitis.

41	42	43	44	45	46	47	48	49	50

Which drugs are beta-blockers used to treat arrhythmias, systemic hypertension, and hypertrophic cardiomyopathy (HCM)?

Dobutamine, Isoproteronol	HIDE
Propranolol, Atenolol	HIDE
Milrinone, Amrinone	HIDE
Diltiazem, Verapamil	HIDE
Enalapril, Benazapril	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

==Propranolol and atenolol== are [beta-blockers](#) used to treat arrhythmias, systemic hypertension, and HCM. They physiologic effect is to slow the heart rate (negative chronotrope) and decrease contraction strength (==negative inotrope).==

Examples of positive inotropes include:
[Beta adrenergic agonists](#) (dopamine, dobutamine, isoproterenol and epinephrine)
[Cardiac glycosides](#) (digoxin, digitoxin)
[Phosphodiesterase (PDE) inhibitors](#) like milrinone and amrinone.
[ACE inhibitors](#) like enalapril are vasodilators that help increase cardiac output.

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 740-2, 1173-6, and the Merck Veterinary Manual online edition.

41 ✓	42	43	44	45	46	47	48	49	50

Which choice has been associated in dogs and cats with cystic endometrial hyperplasia, pyometra, bone marrow suppression and potentially fatal aplastic anemia?

Mibolerone	HIDE
Finasteride	HIDE
Megestrol acetate	HIDE
Human chorionic gonadotropin	HIDE
Estradiol	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

==Estradiol. Estrogenic therapy may be teratogenic in pregnant animals== and has been associated in dogs and cats with cystic endometrial hyperplasia, pyometra, bone marrow suppression and potentially fatal aplastic anemia. Click here to see radiograph of pyometra.

According to the Food and Drug Administration (FDA) the use of ECP in animals is illegal. ECP has been used as an estrogenic hormone for reproductive therapy in food animals, but even extra-label, this is not allowed.

See also this Update on drugs prohibited from extralabel use in food animals, Davis, et al., JAVMA, Vol 235, No.5, Sep 1,2009

Mibolerone and megestrol acetate are both used to delay or suppress estrus in dogs

Mibolerone and megestrol acetate are both used to delay or suppress estrus in dogs and have many potential side effects. Megestrol has been associated with cystic endometrial hyperplasia and pyometra, but not blood dyscrasias.

Finasteride is a 5 alpha-reductase inhibitor that prevents activation of testosterone in male accessory sex glands. It is used to treat benign prostatic hyperplasia (BPH) in dogs. Expensive.

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 530-3, 570, 853-7 and the Merck Veterinary Manual online edition.

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41 ✓	42 ✗	43	44	45	46	47	48	49	50

What is the major site of drug metabolism in the body?

Spleen	HIDE
Kidney	HIDE
Gastrointestinal tract	HIDE
Brain	HIDE
Liver	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

The majority of metabolism occurs in the liver, but additional sites include the kidney and gastrointestinal tract, among others.

Drugs are metabolized by enzyme systems to inactive or detoxified forms. Some prodrugs are metabolized into active forms.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, p. 1012.

41 ✓	42 ✗	43 ✓	44	45	46	47	48	49	50

A 3-year-old male neutered German shepherd dog in the clinic is inadvertently given a 10-fold overdose of oxymorphone following a femoral fracture repair.

Which one of the following choices is the preferred treatment for an oxymorphone overdose?

Diamorphine	HIDE
Naloxone	HIDE
Atipamezole	HIDE
Yohimbine	HIDE
Flumazenil	HIDE

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Correct:

Naloxone is the most commonly used pure opioid ANTAGonist in veterinary medicine.

Naloxone is effective at all the opioid receptors (mu, kappa, and delta) but has a greater activity at the mu receptor. Nalmefene is similar but it is longer lasting.

At very low doses, side effects may be reversed while preserving the analgesic effects.

However, reversal must be performed with great care, as a sudden exacerbation of pain can result in adverse cardiovascular effects; even death is reported. A low dose is calculated and diluted with saline, then given very slowly intravenously.

Yohimbine, an alpha-2 antagonist, is used primarily to reverse the effects of xylazine in dogs.

Atipamezole, also an alpha-2 antagonist, reverses alpha-2 agonists such as medetomidine and dexmedetomidine.

Flumazenil reverses the effects of benzodiazepines.

Diamorphine is **heroin.**

Refs: Gaynor & Muir Handbook of Vet Pain Mgt 2nd ed. pp. 180-1, Greene's Vet Anes & Pain Mgt Secrets pp. 81, Riviere & Papich Vet Pharm & Therapeutics, 9th ed. pp. 325-7, the Merck Veterinary Manual online edition and Plumb's Veterinary Drug Handbook, 8th edition, *Atipamezole HCL, Flumazenil, Yohimbine HCl.*.

| 41 ✓ | 42 ✗ | 43 ✓ | 44 M ✓ | 45 | 46 | 47 | 48 | 49 | 50 |

Which one of the following NSAIDs is the least likely to cause gastrointestinal ulcers and renal disease in horses?

None; these all have a similar risk	HIDE
Flunixin meglumine	HIDE
Phenylbutazone	HIDE
Firocoxib	HIDE
Ketoprofen	HIDE

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Correct:

Firocoxib is a COX-2 selective nonsteroidal anti-inflammatory (NSAID) and therefore has lower ulcerogenic and renal risk than the other nonselective NSAIDs listed.

NSAIDs inhibit at least one step in the metabolism of arachidonic acid, usually by inhibiting cyclooxygenase (COX) production of prostaglandins.

COX-1 is present in almost all tissues and is involved in normal homeostatic physiology. COX-2 is activated by inflammation or trauma in tissues and its inhibition is the main desired effect of NSAIDs which leads to their anti-inflammatory, antipyretic, and analgesic actions.

Concurrently blocking COX-1 leads to the possible adverse effects of NSAIDs - ulcerating gastroenteritis (oral cavity, stomach, and right dorsal colon) with hypoalbuminemia and diarrhea, and renal papillary necrosis.

NEB Candidate Information - NE ✕ | Google Translate ✕ | Pharmacology | Zukureview ✕ | G what is lysine - Google Search ✕ | +

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What is the major site of drug excretion in the body?

Heart	HIDE
Kidney	HIDE
Spleen	HIDE
Liver	HIDE
Gastrointestinal tract	HIDE

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Overview | Mark this Question | Lab Values | Definitions | Report a Problem

Correct:

Drugs are primarily excreted by the ==kidneys.== Animals with kidney disease can have decreased drug excretion and therefore are at increased risk of toxicity or adverse reactions to drugs.

Dosages of some drugs are decreased in geriatric patients due to their decreased kidney function.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, p. 1015.

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41 ✓	42 ✗	43 ✓	44 M ✓	45 M ✗	46 ✓	47	48	49	50

Which one of the following choices does NOT produce energy when ingested?

Protein	HIDE
Sucrose	HIDE
Cellulose	HIDE
Carbohydrate	HIDE
Mineral	HIDE

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Overview   Mark this Question   Lab Values   Definitions

Correct:

<mark>Minerals</mark> are necessary for health, but are not sources of energy.

With the help of ruminal microorganisms, ruminants (cows, sheep, goats) can break cellulose down to into digestible energy.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th ed pp. 294-5, 341-2.
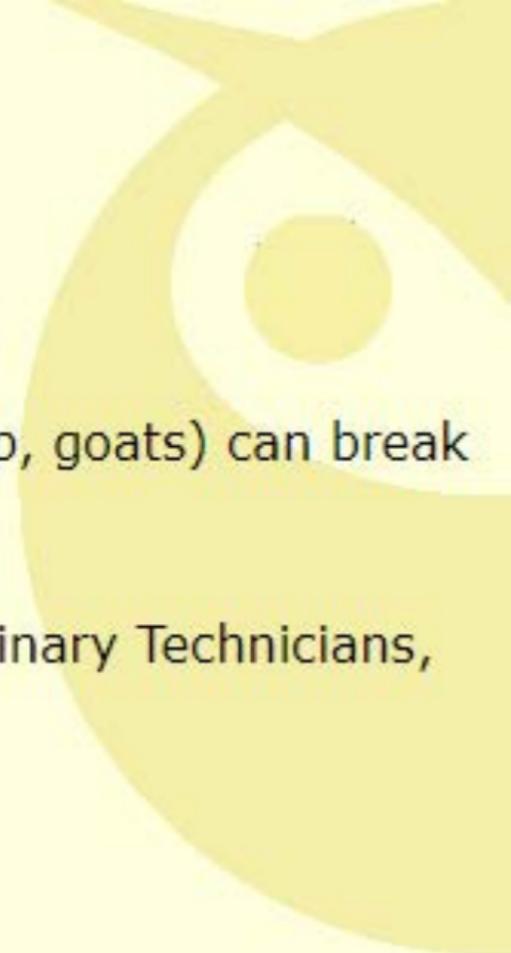
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| 41 ✓ | 42 ✗ | 43 ✓ | 44 M ✓ | 45 M ✗ | 46 ✓ | 47 ✓ | 48 | 49 | 50 |

What category of drug is diltiazem?

Beta blocker	HIDE
Phosphodiesterase (PDE) inhibitor	HIDE
Calcium channel blocker	HIDE
Angiotensin-converting enzyme (ACE) inhibitor	HIDE
Positive inotrope	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Diltiazem is a calcium channel blocker. Calcium channel blockers are antiarrhythmic and have negative inotropic effects (decrease force of cardiac muscle contraction).

They are used to treat atrial fibrillation and supraventricular tachycardias, as well as hypertrophic cardiomyopathy (HCM) and hypertension. Amlodipine (used more for hypertension) and verapamil are two other examples of calcium channel blockers.

ACE inhibitors like enalapril are vasodilators that help increase cardiac output.

Beta blockers like propranolol and atenolol are used to treat arrhythmias, systemic hypertension, and HCM.

Positive inotropes increase the cardiac muscular contraction strength by making more intracellular calcium available for muscle proteins.

Positive inotropes increase the cardiac muscular contraction strength by making more intracellular calcium available for muscle proteins.

Examples of positive inotropes include:
Phosphodiesterase (PDE) inhibitors (pimobendan, amrinone, milrinone)
Beta-adrenergic agonists (dopamine, dobutamine, isoproterenol and epinephrine)
Cardiac glycosides (digoxin, digitoxin)

Refs: Plumb's Vet Drug Handbook, 7th ed. pp. 70-2, 431-6, 453-5 and the Merck Veterinary Manual online edition.

| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Which of the following would make a veterinarian ==less likely to use== ==phenobarbital== as a ==first-line anticonvulsant in a dog with seizures==?

Recent cerebrospinal fluid aspirate	HIDE
Young dog	HIDE
Epilepsy	HIDE
Hepatopathy	HIDE
Renal disease	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct:

Phenobarbital is usually the first-line anticonvulsant administered to dogs. However, it can cause hepatotoxicity, so it may not be selected in animals with underlying liver disease (i.e., hepatopathy).

The second-most commonly used anticonvulsant in dogs is potassium bromide. It is NOT recommended for use in cats.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, p. 1027 and Plumb's Veterinary Drug Handbook, 7th edition.

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| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Where should a chart of standard drug dosages and resuscitation steps be kept in a clinic?

On exam room doors	HIDE
In the controlled substances cabinet	HIDE
In the surgical suite	HIDE
In the emergency crash cart	HIDE
On a wall near the treatment area	HIDE

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Overview   Mark this Question   Lab Values

Correct:

==On a wall near the treatment area==. A chart with drug dosages (and basic CPCR protocol) should be posted prominently on the wall where everyone can read it easily.

The crash cart contains most of the basic supplies needed to work up and treat emergency patients, especially when ==cardiopulmonary cerebral resuscitation== is needed.

An oxygen source and supplies (Ambu Bag, hoses, flowmeter, etc), an electrocardiogram, and a defibrillator should be close by.

Refs: McCurnin's Clin Textbk for Vet Techs, 8th ed. p. 915 and the Merck Veterinary Manual online edition.

Veterinary / Emergency Medicine and Critical Care / Emergency Medicine Introduction

Ready Area in Emergency Medicine

By **Andrew Linklater, DVM, DACVECC, Clinical Instructor, Lakeshore Veterinary Specialists, Glendale, Wisconsin**

A central area of the clinic should be designated as the "ready area," where resuscitation therapeutics and equipment are organized and available for immediate use. Front desk and triage staff should be aware of presenting conditions that require immediate evaluation by a veterinarian. All members of the veterinary team must be familiar with the ready area and location of all necessary emergency equipment and medications. Regular drills should be organized for emergency situations such as CPA with subsequent cardiopulmonary resuscitation efforts to ensure everyone knows his or her role and to improve techniques. An emergency treatment or "crash" cart should contain endotracheal tubes of various sizes, a laryngoscope, syringes of different sizes with 18- or 20-gauge needles attached, and drugs for cardiac resuscitation. Oxygen and a small and large bag-valve-mask apparatus or other ready access to oxygen (such as an anesthetic machine flushed free of anesthetic gas) should be immediately available, so positive-pressure ventilation can be started. Other necessary materials include hair clippers, surgical scrub, tape, intravenous and intraosseous catheters with flushing solutions, intravenous isotonic crystalloids, pressure infusion bags, synthetic colloids, bandage material, and trauma transport materials. Additional beneficial equipment includes a defibrillator, monitoring devices (ECG, SpO_2, $ETCO_2$, and indirect blood pressure), a suction unit with Yankauer and whistle tip suction attachments, and warming devices.

MERCK

| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Atropine has a variety of uses in veterinary medicine. Which one of the following choices lists common indications for atropine use?

Xylitol toxicosis, glaucoma, atrial fibrillation	HIDE
Organophosphate toxicity, bradycardia, sinoatrial arrest	HIDE
Urinary obstruction, biliary stasis, electrical alternans	HIDE
Right bundle branch block, ethylene glycol ingestion, ileus	HIDE
Ventricular tachyarrhythmias, muscle relaxation, appetite stimulant	HIDE

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Correct:

Atropine, an ==anticholinergic agent==, is commonly used for organophosphate toxicity, bradycardia, and sinoatrial arrest.

==Atropine is also used for the following purposes==:

-Preanesthetic to reduce respiratory secretions

-To differentiate vagally-induced bradycardia from other causes

-To treat other toxicities (e.g., blue-green algae, muscarinic mushrooms, carbamates)

CONTRAINDICATIONS for atropine use include:

CONTRAINDICATIONS for atropine use include:

-Tachyarrhythmias

-Narrow-angle glaucoma

-Ileus or GI obstruction

-Urinary obstruction

Refs: Plumb's Veterinary Drug Handbook, 8th edition, *Atropine Sulfate* and Merck Veterinary Manual online edition.

| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Collies have a nonfunctional P-glycoprotein pump on the cellular membrane.

This affects what aspect of pharmacokinetics?

Clearance	HIDE
It has no effect on pharmacokinetics	HIDE
Biotransformation	HIDE
Drug distribution	HIDE
Mechanism of action	HIDE

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Overview   Mark this Question   Lab Values   Definitions   Report a Problem

Correct: The Rough Collie is a long-coated breed of medium to large size dog that in its original form was a type of collie used and bred for herding in Scotland

Distribution describes how a drug moves to various parts and tissues of the body after absorption. The blood- brain barrier (BBB) is one of the most important physical barriers to drugs.

Collies have a genetic mutation in the P-glycoprotein pump on the BBB that renders it nonfunctional. This allows drugs like ivermectin to readily cross into the central nervous system and cause toxicity.

Mechanism of action is a parameter of pharmacodynamics.

Refs: Bassert and Thomas, McCurnin's Clinical Textbook for Veterinary Technicians, 8th edition, pp. 1011–4.

| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Which one of the following choices correctly describes the potential role of calcitonin in the treatment of a hypercalcemic cat?

Decreases bone resorption	HIDE
Increases renal reabsorption of calcium	HIDE
Decreases movement of phosphorus into soft tissues	HIDE
Increases movement of calcium from bone to plasma	HIDE
Increases renal reabsorption of phosphorus	HIDE

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[×] Resorption is the absorption into the circulatory system of cells or tissue examples are:Bone resorption and Tooth resorption

Correct: Decreases bone resorption

Calcitonin decreases bone resorption, which decreases the amount of calcium available to move from the bone to plasma.

Calcitonin also promotes renal excretion of calcium and phosphorus, and increases the incorporation of plasma phosphorus into the soft tissues.

combination

Click on these links for more information on Calcitonin and Endocrine control of calcium and phosphorus homeostasis by Dr. R. Bowen at Colorado State University.

Refs: The Merck Veterinary Manual online edition.

VIVO
Pathophysiology

Endocrine System > Thyroid and Parathyroid Glands

Endocrine Control of Calcium and Phosphate Homeostasis

It would be very difficult to name a physiologic process that does not depend, in one way or another, on calcium. It is critical to maintain blood calcium concentrations within a tight normal range. Deviations above or below the normal range frequently lead to serious disease.

- Hypocalcemia refers to low blood calcium concentration. Clinical signs of this disorder reflect increased neuromuscular excitability and include muscle spasms, tetany and cardiac dysfunction.

- Hypercalcemia indicates a concentration of blood calcium higher than normal. The normal concentration of calcium and phosphate in blood and extracellular fluid is near the saturation point; elevations can lead to diffuse precipitation of calcium phosphate in tissues, leading to widespread organ dysfunction and damage.

Preventing hypercalcemia and hypocalcemia is largely the result of robust endocrine control systems.
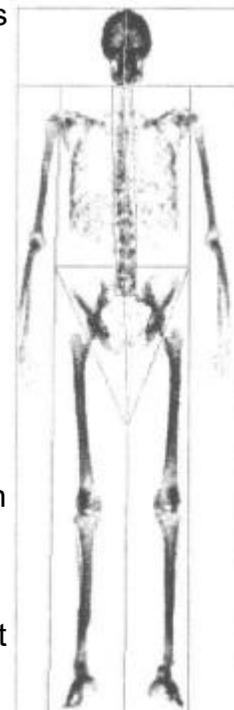
Body Distribution of Calcium and Phosphate

There are three major pools of calcium in the body:

- **Intracellular calcium:** A large majority of calcium within cells is sequestered in mitochondria and endoplasmic reticulum. Intracellular free calcium concentrations fluctuate greatly, from roughly 100 nM to greater than 1 uM, due to release from cellular stores or influx from extracellular fluid. These fluctuations are integral to calcium's role in intracellular signaling, enzyme activation and muscle contractions.

- **Calcium in blood and extracellular fluid:** Roughly half of the calcium in blood is bound to proteins. The concentration of ionized calcium in this compartment is normally almost invariant at approximately 1 mM, or 10,000 times the basal concentration of free calcium within cells. Also, the concentration of phosphorus in blood is essentially identical to that of calcium.

- **Bone calcium:** A vast majority of body calcium is in bone. Within bone, 99% of the calcium is tied up in the mineral phase, but the remaining 1% is in a pool that can rapidly exchange with extracellular calcium.

As with calcium, the majority of body phosphate (approximately 85%) is present in the mineral phase of bone. The remainder of body phosphate is present in a variety of inorganic and organic compounds distributed within both intracellular

and extracellular compartments. Normal blood concentrations of phosphate are very similar to calcium.

Fluxes of Calcium and Phosphate

Maintaining constant concentrations of calcium in blood requires frequent adjustments, which can be described as fluxes of calcium between blood and other body compartments. **Three organs participate in supplying calcium to blood and removing it from blood when necessary:**

- The **small intestine** is the site where dietary calcium is absorbed. Importantly, efficient absorption of calcium in the small intestine is dependent on expression of a calcium-binding protein in epithelial cells.

- **Bone** serves as a vast reservoir of calcium. Stimulating net resorption of bone mineral releases calcium and phosphate into blood, and suppressing this effect allows calcium to be deposited in bone.

- The **kidney** is critcally important in calcium homeostasis. Under normal blood calcium concentrations, almost all of the calcium that enters glomerular filtrate is reabsorbed from the tubular system back into blood, which preserves blood calcium levels. If tubular reabsorption of calcium decreases, calcium is lost by excretion into urine.
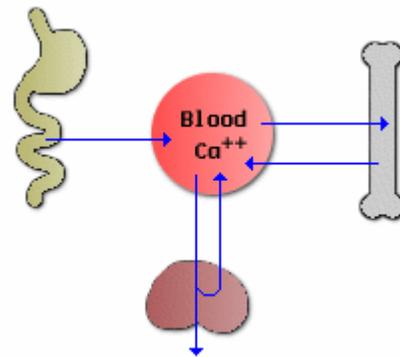
Hormonal Control Systems

Maintaining normal blood calcium and phosphorus concentrations is managed through the concerted action of three hormones that control fluxes of calcium in and out of blood and extracellular fluid:

Parathyroid hormone serves to increase blood concentrations of calcium. Mechanistically, parathyroid hormone preserves blood calcium by several major effects:

- Stimulates production of the biologically-active form of vitamin D within the kidney.

- Facilitates mobilization of calcium and phosphate from bone. To prevent detrimental increases in phosphate, parathyroid hormone also has a potent effect on the kidney to eliminate phosphate (phosphaturic effect).

- Maximizes tubular reabsorption of calcium within the kidney. This activity results in minimal losses of calcium in urine.

Vitamin D acts also to increase blood concentrations of calcium. It is generated through the activity of parathyroid hormone within the kidney. Far and away the most important effect of vitamin D is to facilitate absorption of calcium from the small intestine. In concert with parathyroid hormone, vitamin D also enhances fluxes of calcium out of bone.

Calcitonin is a hormone that functions to reduce blood calcium levels. It is secreted in response to hypercalcemia and has at least two effects:

- Suppression of renal tubular reabsorption of calcium. In other words, calcitonin enhances excretion of calcium into urine.

- Inhibition of bone resorption, which would minimize fluxes of calcium from bone into blood.

Although calcitonin has significant calcium-lowing effects in some species, it appears to have a minimal influence on blood calcium levels in humans.

A useful way of looking at how hormones affect tissues to preserve calcium homeostasis is to examine the effects of calcium deprivation and calcium loading. The following table summarizes body responses to conditions that would otherwise lead to serious imbalances in calcium and phosphate levels in blood.

	Calcium Deprivation	Calcium Loading
Parathyroid hormone	Secretion stimulated	Secretion inhibited
Vitamin D	Production stimulated by increased parathyroid hormone secretion	Synthesis suppressed due to low parathyroid hormone secretion
Calcitonin	Very low level secretion	Secretion stimulated by high blood calcium
Intestinal absorption of calcium	Enhanced due to activity of vitamin D on intestinal epithelial cells	Low basal uptake
Release of calcium and phosphate from bone	Stimulated by increased parathyroid hormone and vitamin D	Decreased due to low parathyroid hormone and vitamin D
Renal excretion	Decreased due to enhanced tubular reabsorption stimulated	Elevated due to decreased parathyroid hormone-

of calcium	by elevated parathyroid hormone and vitamin D; hypocalcemia also activates calcium sensors in loop of Henle to directly facilitate calcium reabsorption	stimulated reabsorption.
Renal excretion of phosphate	Strongly stimulated by parathyroid hormone; this phosphaturic activity prevents adverse effects of elevated phosphate from bone resorption	Decreased due to hypoparathyroidism
General Response	Typically see near normal serum concentrations of calcium and phosphate due to compensatory mechanisms. Long term deprivation leads to bone thining (osteopenia).	Low intestinal absorption and enhanced renal excretion guard against development of hypercalcemia.
Summary		
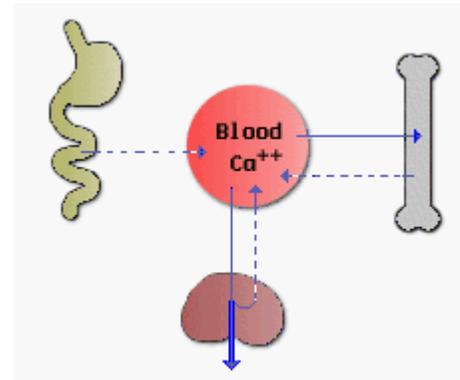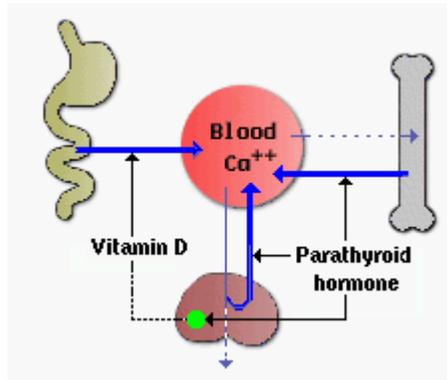
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Send comments to Richard.Bowen@colostate.edu

Calcitonin

Calcitonin is a hormone known to participate in calcium and phosphorus metabolism. In mammals, **the major source of calcitonin is from the parafollicular or C cells in the thyroid gland**, but it is also synthesized in a wide variety of other tissues, including the lung and intestinal tract. In birds, fish and amphibians, calcitonin is secreted from the ultimobrachial glands.

Calcitonin is a 32 amino acid peptide cleaved from a larger prohormone. It contains a single disulfide bond, which causes the amino terminus to assume the shape of a ring. Alternative splicing of the calcitonin pre-mRNA can yield a mRNA encoding calcitonin gene-related peptide; that peptide appears to function in the nervous and vascular systems. The calcitonin receptor has been cloned and shown to be a member of the seven-transmembrane, G protein-coupled receptor family.

Physiologic Effects of Calcitonin

A large and diverse set of effects has been attributed to calcitonin, but in many cases, these were seen in response to pharmacologic doses of the hormone, and their physiologic relevance is suspect. It seems clear however, that calcitonin plays a role in calcium and phosphorus metabolism. In particular, calcitonin has the ability to decrease blood calcium levels at least in part by effects on two well-studied target organs:

- *Bone*: Calcitonin suppresses resorption of bone by inhibiting the activity of osteoclasts, a cell type that "digests" bone matrix, releasing calcium and phosphorus into blood.

- *Kidney*: Calcium and phosphorus are prevented from being lost in urine by reabsorption in the kidney tubules. Calcitonin inhibits tubular reabsorption of these two ions, leading to increased rates of their loss in urine.

It seems clear that there are species differences in the importance of calcitonin as a factor affecting calcium homeostasis. In fish, rodents and some domestic animals, calcitonin appears to play a significant role in calcium homeostais. In humans, calcitonin has at best a minor role in regulating blood concentrations of calcium. One interesting piece of evidence to support this statement is that humans with chronically increased (medullary thyroid cancer) or decreased (surgical removal of the thyroid gland) levels of calcitonin in blood usually do not show alterations from normal in serum calcium concentration.

Addition information on calcitonin and calcium balance can be found in the section Endocrine Control of Calcium and Phosphate Homeostasis.

Control of Calcitonin Secretion

The most prominent factor controlling calcitonin secretion is the extracellular concentration of ionized calcium. Elevated blood calcium levels strongly stimulate calcitonin secretion, and secretion is suppressed when calcium concentration falls below normal. A number of other hormones have been shown to stimulate calcitonin release in certain situations, and nervous controls also have been demonstrated.

Disease States

A large number of diseases are associated with abnormally increased or decreased levels of calcitonin, but pathologic effects of abnormal calcitonin secretion per se are not generally recognized.

There are several therapeutic uses for calcitonin. It is used to treat hypercalcemia resulting from a number of causes, and has been a valuable therapy for Paget disease, which is a disorder in bone remodeling. Calcitonin also appears to be a valuable aid in the management of certain types of osteoporosis.

Advanced and Supplemental Topics

- [Endocrine Control of Calcium and Phosphate Homeostasis](#)

Send comments to
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Yohimbine is the reversal agent for which two drugs?

Ketamine, physostigmine	HIDE
Acepromazine maleate, ketamine	HIDE
Xylazine, amitraz (Mitaban®)	HIDE
Amitraz (Mitaban®), fomipazole	HIDE
Organophosphates, xylazine	HIDE

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Correct:

Yohimbine, atipamezole, or tolazoline are reversal agents for xylazine an alpha 2-adrenergic agonist with analgesic and sedative effects.

Remember 2 things about xylazine:
1. Cattle are EXTREMELY SENSITIVE to xylazine. Cow dose is about 10 times LESS than dogs or horses.
2. Used as an EMETIC in CATS, causes vomiting.

Amitraz is used to treat generalized demodicosis as a dip. The most common side effect to watch out for with amitraz is SEDATION, seen in 30% of patients within 12-36 hours after treatment.

Fomipazole (4-MP) is used to treat dogs with ethylene glycol toxicity.

When you hear organophosphate toxicity, think 3 things
1. Sedative for seizures (diazepam (Valium®), phenobarbital or pentobarbital)
2. Atropine
3. Pralidoxime chloride (Protopam®)

Refs: Cote, Clinical Veterinary Advisor-Dogs and Cats, 3rd ed., OPP Toxicosis, Plumb's Veterinary Drug Handbook, 8th ed. and Blackwell's 5-Minute Vet Consult Canine Feline, 4th ed. pp. 342-43 and the Merck Veterinary Manual online edition.

Mange in Dogs and Cats

By **Michael W. Dryden, DVM, PhD, DACVM, University Distinguished Professor of Veterinary Parasitology, College of Veterinary Medicine, Kansas State University**

Sarcoptic Mange (Canine Scabies):

Sarcoptes scabiei
Courtesy of Dr. Michael W. Dryden.

Sarcoptes scabiei var *canis* infestation is a highly contagious disease of dogs found worldwide. The mites are fairly host specific, but animals (including people) that come in contact with infested dogs can also be affected. Adult mites are 0.2–0.6 mm long and roughly circular in shape; their surface is covered with small triangular spines, and they have four pairs of short legs. Females are almost twice as large as males. The entire life cycle (17–21 days) is spent on the dog. Females burrow tunnels in the stratum corneum to lay eggs. Sarcoptic mange is readily transmitted between dogs by direct contact; transmission by indirect contact may also occur. Clinical signs may develop anytime from 10 days to 8 wk after contact with an infected animal. Asymptomatic carriers may exist. Intense pruritus is characteristic and probably due to hypersensitivity to mite products. Primary lesions consist of papulocrustous eruptions with thick, yellow crusts, excoriation, erythema, and alopecia.

Secondary bacterial and yeast infections may develop. Typically, lesions start on the ventral abdomen, chest, ears, elbows, and hocks and, if untreated, become generalized. Dogs with chronic, generalized disease develop seborrhea, severe thickening of the skin with fold formation and crust buildup, peripheral lymphadenopathy, and emaciation; dogs so affected may even die. "Scabies incognito" has been described in well-groomed dogs; these dogs, infested with sarcoptic mites, are pruritic, but demonstrating the mites on skin scrapings is difficult because the crusts and scales have been removed by regular bathing. Atypical, including localized, clinical forms that are probably linked to extensive use of insecticides or acaricides are being increasingly seen.

Sarcoptic mange, dog
Courtesy of Dr. Michael W. Dryden.

Diagnosis is based on the history of severe pruritus of sudden onset, possible exposure, and involvement of other animals, including people. Making a definitive diagnosis is sometimes difficult because of negative skin scrapings. Concentration and flotation of several scrapings may increase chances of finding the mites, eggs, or feces. Several extensive superficial scrapings should be done of the ears, elbows, and hocks; nonexcoriated areas should be chosen. A centrifugation fecal flotation using sugar solutions may reveal mites or eggs. A specific and sensitive commercially available ELISA to detect specific antibodies has been developed and may be useful. Because mites can be difficult to detect, if *Sarcoptes* is on the differential diagnosis list but no mites are found, a therapeutic trial is warranted.

Systemic treatments of scabies are based on administration of macrocyclic lactones, some of which are FDA approved for this purpose. Among them, selamectin is given as a spot-on formulation at 6 mg/kg. This drug appears to be safe, even in ivermectin-sensitive breeds. Another is the imidacloprid-moxidectin formulation, which may be used on dogs as young as 7 wk of age. In some countries, moxidectin is also registered for treatment of scabies. It is available as a spot-on formulation in combination with imidacloprid and should be given in two doses of 2.5 mg/kg, 4 wk apart; additionally, oral uptake should be prevented in breeds at risk of avermectin sensitivity. Other endectocides, such as milbemycin oxime and ivermectin, which are not registered for treatment of sarcoptic mange in dogs, have been reported to be effective depending on the dosage and route of administration. The recommended dosage for milbemycin oxime is 2 mg/kg, PO, weekly for 3–4 wk; potential

toxicity should be considered in dogs with avermectin sensitivity. Ivermectin (200 mcg/kg, PO or SC, 2–4 treatments 2 wk apart) is very effective and usually curative. Ivermectin at this dosage is contraindicated in avermectin-sensitive breeds. Additionally, the microfilaremic (*Dirofilaria immitis*) status of the dog should be evaluated before treatment with a macrocyclic lactone. For topical treatment, hair can be clipped, the crusts and dirt removed by soaking with an antiseborrheic shampoo, and an acaricidal dip applied. Lime sulfur is highly effective and safe for use in young animals; several dips 7 days apart are recommended. Amitraz is an effective scabicide, although it is not approved for this use. It should be applied as a 0.025% solution at 1- or 2-wk intervals for 2–6 wk. In addition, the owner must observe certain precautions to avoid self-contamination. Fipronil spray was reported to be effective but should be considered an aid in control rather than a primary therapy. Treatment can be topical or systemic, and should include all dogs in contact.

Notoedric Mange (Feline Scabies):

This rare, highly contagious disease of cats and kittens is caused by *Notoedres cati*, which can opportunistically infest other animals, including people. The mite and its life cycle are similar to the sarcoptic mite. Pruritus is severe. Crusts and alopecia are seen, particularly on the ears, head, and neck, and can become generalized. Mites can be found quite easily in skin scrapings. Treatment consists of both topical and systemic therapies. Nonapproved but effective and safe treatments include selamectin (6 mg/kg, spot-on) and moxidectin (1 mg/kg, spot-on, in the imidacloprid-moxidectin formulation). Ivermectin (200 mcg/kg, SC) has also been used. Another effective topical therapy is lime sulfur dips at 7-day intervals.

Otodectic Mange:

Otodectes cynotis mites are a common cause of otitis externa, especially in cats but also in dogs. Mites that belong to the family Psoroptidae are usually found in both the vertical and horizontal ear canals but are occasionally seen on the body. Clinical signs include head shaking, continual ear scratching, and ear droop. Pruritus is variable but may be severe. Dark brown cerumen accumulation in the ear and suppurative otitis externa with possible perforation of the tympanic membrane may be seen in severe cases. Affected and in-contact animals should receive appropriate parasiticide treatment in the ears. Systemic therapies have been approved and include topically applied selamectin and moxidectin. Direct applications to the external ear canal of cats using approved ivermectin and milbemycin formulations are also effective. As a general rule, ear cleansing with an appropriate ceruminolytic agent is indicated with any therapy.

Cheyletiellosis (Walking Dandruff):

Cheyletiella
Courtesy of Dr. Michael W. Dryden.

Cheyletiella blakei infests cats, *C yasguri* infests dogs, and *C parasitovorax* infests rabbits, although cross-infestations are possible. This disease is very contagious, especially in animal communities. Human infestation is frequent. Mite infestations are rare in flea-endemic areas, probably because of the regular use of insecticides. These mites have four pairs of legs and prominent hook-like mouthparts. They live on the surface of the epidermis, and their entire life cycle (3 wk) is spent on the host. Female mites can, however, survive for as long as 10 days off the host. Clinical disease is characterized by scaling, a dorsal distribution, and pruritus, which varies from none to severe. Cats can develop dorsal crusting or generalized miliary dermatitis. Asymptomatic carriers may exist. The mites and eggs may not be easy to find, especially in animals that are bathed often. Acetate tape preparations, superficial skin scrapings, and flea combing can be used to make the diagnosis.

Cheyletiellosis (walking dandruff), domestic rabbit
Courtesy of Dr. Louise Bauck.

Both topical and systemic acaricides are effective against cheyletiellosis, although no drugs are currently licensed for this indication. In addition to treatment of the affected animals, it is necessary to treat all in-contact animals. Topical drugs include lime sulfur, fipronil spot-on and spray, permethrin, and amitraz (the latter two are contraindicated in cats). Extra-label systemic drugs include selamectin spot-on, milbemycin oxime (PO), and ivermectin (SC). Care must be taken to avoid or minimize the risks of adverse reactions as described above (see Sarcoptic Mange (Canine Scabies)). The treatment period depends on the selected drug but must be long enough to eradicate the mites from both the animals and their environment, which can be difficult in animal communities (eg, breeding colonies, kennels). In practice, treatment lasts 6–8 wk and should continue for a few weeks beyond clinical cure until parasitologic cure is achieved.

Canine Demodicosis:

Demodex canis

Canine demodicosis occurs when large numbers of *Demodex canis* mites inhabit hair follicles and sebaceous glands. In small numbers, these mites are part of the normal flora of canine skin and usually cause no clinical disease. The mites are transmitted from dam to puppies during nursing within the first 72 hr after birth. The mites spend their entire life cycle on the host, and the disease is not considered to be contagious. The pathogenesis of demodicosis is complex and not completely understood; evidence of hereditary predisposition for generalized disease is strong. Immunosuppression, natural or iatrogenic, can precipitate the disease in some cases. Secondary bacterial deep folliculitis, furunculosis, or cellulitis may occur, leading to a guarded prognosis.

Juvenile-onset generalized demodicosis, dog

Three forms of demodicosis are seen in dogs: localized demodectic mange, juvenile-onset generalized demodicosis, and adult-onset generalized demodicosis. Localized demodicosis is seen in dogs usually <1 yr old, and most of these cases resolve spontaneously. Lesions often consist of one to five well-demarcated small areas of alopecia, erythema, and scaling. Lesions are usually confined to areas around the lips, periorbital area, and forelimbs but may be found in other locations. Pruritus is usually absent or mild. A small percentage of these cases, especially the diffuse localized forms, progress to a more severe generalized form. Juvenile-onset generalized demodicosis is the result of an inherited immunologic defect with functional abnormality associated with the cell-mediated immune system. It is a severe disease of young dogs with generalized lesions (erythema, papules, alopecia, oily seborrhea, edema, hyperpigmentation, and crusts) that are usually aggravated by secondary bacterial infections (pyodemodicosis). Accompanying pododermatitis is common. Dogs can have systemic illness with generalized lymphadenopathy, lethargy, and fever when deep pyoderma, furunculosis, or cellulitis is seen. Diagnosis is not difficult; deep skin scrapings or hair plucking typically reveal mites, eggs, and larval forms in high numbers. The third form is adult-onset generalized demodicosis and clinically appears similar to juvenile-onset generalized demodicosis but is seen in adult dogs. It is typically associated with or triggered by some neoplastic process or debilitating disease that may be producing immunosuppression, such as malignant lymphosarcoma, malignant melanoma, hyperadrenocorticism, hypothyroidism, diabetes mellitus, etc. However, in many cases an underlying immunosuppressive condition may not be found.

Localized demodicosis can generally be left untreated. The prognosis for this form is usually good, and spontaneous recovery is frequent. In contrast, treatment is required in cases of generalized demodicosis, for which prognosis is guarded. Hair clipping and body cleansing, especially with benzoyl peroxide shampoo used for its follicular flushing activity, may be required. Whole-body amitraz dips (0.025%) applied every 2 wk remains the only approved treatment in the USA for generalized demodicosis. Higher concentrations (0.05%) and shorter treatment intervals (1 wk) may be more efficient.

A number of other protocols are commonly used for refractory generalized demodicosis. Among macrocyclic lactones, milbemycin oxime (0.5–1 mg/kg/day, PO), moxidectin, and ivermectin have all demonstrated varying degrees of effectiveness. Moxidectin is available as a spot-on formulation in combination with a flea product (imidacloprid) and should be given at 2.5 mg/kg at 1–4 wk intervals. More frequent applications are associated with higher degrees of success. Other reportedly successful but unapproved systemic treatments include moxidectin (400 mcg/kg/day, PO) and ivermectin (300–600 mcg/kg/day, PO). For the latter, different therapeutic protocols have been proposed with a gradually increased dosage and thorough monitoring of treated animals to detect any potentially toxic effect. Ivermectin is contraindicated in Collies and Collie crosses. However, idiosyncratic toxicity may be seen in any breed. Testing for mutation in the MDR1 allele (ABCB1) may be required before initiating therapy. Local and systemic corticosteroids are contraindicated in any animal diagnosed with demodicosis. Secondary bacterial infections must be treated aggressively with an appropriate antibiotic. Antiparasitic therapy must be continued not only until clinical signs abate but also until at least two consecutive negative skin scrapings are obtained at 1-mo intervals. Although some dogs respond rapidly, others may need several months of treatment. Recurrence within the first year of treatment is not uncommon. As the sole prophylactic measure, dogs developing juvenile-onset generalized demodicosis should not be used for breeding.

Feline Demodicosis:

Feline demodicosis is an uncommon to rare skin disease caused by at least two species of demodectic mites. *Demodex cati* is thought to be a normal inhabitant of feline skin. It is a follicular mite, similar to but narrower than the canine mite, that can cause either localized or generalized demodicosis. One other species of *Demodex* (named *D gatoi*) is shorter, with a broad abdomen, and is found only in the stratum corneum. It causes a contagious, transmissible, superficial demodicosis that is frequently pruritic and can be generalized. In follicular localized demodicosis, there are one or several areas of focal alopecia most commonly on the head and neck. In generalized disease, alopecia, crusting, and potential secondary pyoderma of the whole body are seen. The generalized form is often associated with an underlying immunosuppressive or metabolic disease such as feline leukemia virus infection, feline immunodeficiency virus infection, diabetes mellitus, or neoplasia. In some cases, ceruminous otitis externa is the only clinical sign.

Diagnosis is made by superficial (*D gatoi*) and deep (*D cati*) skin scrapings, although mite numbers are often small, especially with *D gatoi*. Medical evaluation is indicated in cats with generalized disease. Dermatophyte cultures are essential, because dermatophytosis and demodicosis can be concomitant conditions. Prognosis of generalized demodicosis is unpredictable because of its potential relationship with systemic disease. Some cases spontaneously resolve. Weekly lime sulfur dips (2%) are safe and usually effective; amitraz (0.0125%–0.025%) has been used but is not approved for use in cats and can cause anorexia, depression, and diarrhea. The use of antiparasitic macrocyclic lactones has been reported but their efficacy is unclear.

Trombiculosis:

Chigger mite
Courtesy of Dr. Michael W. Dryden.

Trombiculosis is a common, seasonal, noncontagious acariasis caused by the parasitic larval stage of free-living mites of the family Trombiculidae (chiggers). It can affect domestic carnivores, other domestic or wild mammals, birds, reptiles, and people. Two common species found in cats and dogs, *Neotrombicula autumnalis* and *Eutrombicula alfreddugesi*, are reported in Europe and in America, respectively. Adults (harvest mites) and nymphs look like small spiders and live on rotting detritus. In temperate areas from summer to fall, dogs and cats can acquire the larvae as parasites when lying on the ground or walking in suitable habitat. In warmer regions, infestation occurs throughout the year. The larvae (0.25 mm long) attach to the host, feed for a few days, and leave when engorged. At that time, they are easily identified as ovoid, 0.7 mm long, orange to red, immobile dots, usually found clustering on the head, ears, feet, or ventrum. Pathogenicity is through traumatic and proteolytic activities. Hypersensitivity reactions are suspected in some animals, because pruritus may vary from none to severe. Lesions include erythema, papules, excoriations, hair loss, and crusts. When present, intense pruritus can persist for hours to several days even after the larvae have left the animal.

Diagnosis is based on history and clinical signs. The infestation is a seasonal threat to free-ranging dogs and cats. Differential diagnoses include other pruritic dermatoses. Diagnosis is confirmed by careful examination of the affected areas. Microscopic examination of samples obtained from skin scrapings may help to identify the larvae, which have an oval-shaped body densely covered with setae, six long legs, and curved pedipalps terminating in claws.

Management is difficult. The most useful approach, if feasible, consists of keeping pets away from areas known to harbor large numbers of mites to prevent reinfestation during periods of risk. The application of pyrethroids (dogs only) with repellent-like activity to prevent infestation has yielded variable results. Fipronil and permethrin (dogs only) can be used, both for prevention and treatment of infested animals. Symptomatic treatment may be required in cases of severe pruritus.

Straelensiosis:

Canine straelensiosis is a rare, noncontagious, sporadic, but potentially emerging parasitic dermatitis caused by the temporary encystment in the epidermis of the parasitic larval stage of *Straelensia cynotis*. This mite belongs to a family close to the family Trombiculidae. To date, the life cycle is largely unknown, and the disease has been reported only in France, Portugal, Spain, and Italy. Transmission occurs mainly in rural and small-sized hunting dogs, probably through contact with contaminated soil, litter, and other terrestrial habitat of foxes. No contagion has been reported to congeners and people. *S cynotis* has distinct differences from other trombidioid mites, especially in clinical presentation, histopathologic features, and response to treatment.

Straelensiosis is sudden in onset and may be accompanied by systemic signs such as anorexia and prostration. Lesions are painful, variably pruritic, and either generalized or multifocal, most often affecting the dorsal regions of the head and trunk. The characteristic erythematous papules and nodules resemble small craters. Scaling, pustules, and crusts can be seen.

Differential diagnoses include bacterial folliculitis, sarcoptic mange, and gunshot. Microscopic examination of samples obtained from deep skin scrapings may help identify the larvae (0.7 mm long, 0.45 mm wide), each in a thick-walled cyst. The larvae, which resemble *Neotrombicula*, are more easily visualized by histopathology.

The prognosis is favorable; a self-cure generally occurs after several months if reinfestation is prevented. However, management of clinical signs is difficult. Amitraz may be somewhat effective.

Lynxacariasis:

Feline lynxacariasis is a quite common but to date geographically restricted (Australia, Brazil, Hawaii, Florida, North Carolina, Texas) parasitic dermatitis caused by the fur mite *Lynxacarus radovskyi*, which belongs to the family Listrophoridae. The life cycle remains poorly described, and this species has not been reported from hosts other than cats. Infestation typically occurs by direct contact, but fomites may be important for transmission. Clinical signs include a salt-and-pepper appearance of the hair coat, variable pruritus, and alopecia. Diagnosis is based on visualization of mites (0.5 mm long) using a magnifying glass or on isolation of any parasitic stage in skin scrapings or acetate tape preparations. Treatment with acaricidal sprays, weekly lime sulfur dips, and ivermectin (300 mcg/kg, SC) are effective. The only case of contagion to people that has been reported involved a transient rash in an owner with a heavily infested cat.

Tyler K-L

Lab Animal Research: Rats are Awesome

This semester I have a class dedicated to only lab animals and lab animal health and manipulations. Honestly, going into this class I thought that I would...

More Student Stories

Merck and the Merck Veterinary Manual

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| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Which one of the following choices is a common side effect of oclacitinib (Apoquel®), a common therapy for allergic dermatitis?

Nephrotoxicity	HIDE
Vomiting	HIDE
Panting	HIDE
Systemic hypertension	HIDE
Pulmonary fibrosis	HIDE

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Correct:

Common side effects of oclacitinib (Apoquel®) include gastrointestinal upset (vomiting, inappetance, diarrhea), lethargy, and polydipsia.

Oclacitinib, a janus kinase inhibitor, is frequently used to control pruritus in dogs with allergic/atopic dermatitis.

Severe side effects include increased susceptibility to infections, neoplasia and skin disorders.

Refs: Plumb's Veterinary Drug Handbook, 8th edition, *Oclacitinib*, and Merck Veterinary Manual online edition

| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

What is the best method to induce parturition in a late-pregnant cow?

Gonadotropin-releasing hormone	HIDE
Estradiol cypionate	HIDE
Diethylstilbesterol	HIDE
Dexamethasone	HIDE
Human chorionic gonadotropin	HIDE

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Overview   Mark this   Lab   Definitions   Report

Correct:

Dexamethasone will induce parturition in late-term cows. Typically use 20-30 mg dexamethasone, IM, given within 2 wk of normal term.

Gonadotrophic releasing hormone (GnRH) initiates the release of luteinizing hormone from the anterior pituitary and Human chorionic gonadotropin (HCG) is luteotrophic- neither drug is indicated to stimulate parturition.

Diethylstilbesterol (DES) is banned for use in food producing animals and should never be used.

Estrogenic therapy may be teratogenic in pregnant animals and has been associated in dogs and cats with cystic endometrial hyperplasia, pyometra, bone marrow suppression and potentially fatal aplastic anemia.

According to the Food and Drug Administration (FDA) the use of ECP in animals is **illegal**. ECP has been used as an estrogenic hormone for reproductive therapy in food animals, but even extra-label, this is not allowed.

Here is a statement from the FDA regrding estradiol cypionate (ECP) and food-producing animals:
"The Animal Medicinal Drug Use Clarification Act (AMDUCA) amended the Federal Food, Drug, and Cosmetic Act to allow licensed veterinarians to prescribe extra-label uses of approved animal drugs and human drugs in animals. However, under AMDUCA extra-label use is limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat. The extra-label use of ECP for reproductive purposes does **not** qualify under these provisions."

Refs: Pasquini's Guide to Bov Clin, 4th ed. p.105, Smith, Lg An Int Med, 3rd ed. p.

zukureview

SAVE & EXIT
Score: 43 / 60 (72%)

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| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

Which one of the following choices is the mechanism of action of diazepam?

Enhances GABA receptor binding, inhibits neural activity in brain	HIDE
Agonist at alpha-2 receptors to decrease release of norepinephrine	HIDE
Activates kappa receptors in cerebellum and spinal cord	HIDE
Inhibits N-methyl-D-aspartate receptors in spinal cord	HIDE
Antagonizes the effects of dopamine in basal ganglia	HIDE

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Overview   Mark this   Lab   Definitions   Report

Binding of a benzodiazepine (BZ) to the gamma-amino butyric acid (GABA) receptor enhances the binding of the inhibitory neurotransmitter GABA. A chloride channel opens, the cell membrane becomes hyperpolarized, and neuronal activity is inhibited.

Sedation, muscle relaxation, and anti-seizure effects are seen with BZs. Diazepam and midazolam are the BZs used most often in veterinary medicine. Zolazepam is combined with tiletamine in the general anesthetic Telazol®.

BZs are often used with opioids as premedication prior to general anesthesia in small ruminants, young foals, and older or compromised small animals (SA). Agitation can be seen when given as premedication to young healthy SA patients, especially cats.

Xylazine, medetomidine, romifidine, and detomidine are alpha-2 agonists.

Acepromazine is a dopamine antagonist in the brain. Ketamine is a N-methyl-D-aspartate (NMDA) receptor antagonist. Butorphanol activates opioid kappa receptors.

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| 51 ✗ | 52 ✓ | 53 ✓ | 54 ✗ | 55 ✗ | 56 ✓ | 57 ✓ | 58 ✓ | 59 ✗ | 60 ✗ |

In which of the following large animal species is xylazine not very effective as a sedative?

Bovine	HIDE
Equine	HIDE
Camelid	HIDE
Swine	HIDE
Caprine	HIDE

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This is the last question. Click Save and Exit after you finish it.

FINISH

Correct:

Swine respond poorly to xylazine (an alpha-2 agonist); even with high doses and the addition of ketamine, pigs are still responsive and may vocalize.

The addition of a benzodiazepine such as midazolam and a narcotic such as butorphanol greatly improves the sedation seen with xylazine in pigs. Xylazine can also be combined with telazol to produce profound sedation or general anesthesia in pigs.

Better sedation is seen with more potent alpha-2 agents such as medetomidine. The addition of an opioid and/or midazolam is still recommended, as better quality sedation is seen, lower doses can be given, and side effects are minimized.

Refs: Tranquilli, Thurmon, and Grimm's Lumb & Jones Veterinary Anesthesia, 4th ed. p. 52. Muir, Hubbell, Bednarski, and Skarda's Handbook of Veterinary Anesthesia, 4th