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For AVEPA Members & Beyond

After the WSAVA Congress, I was off again to attend the Southern European Veterinary Conference (SEVC) in Barcelona and to join the celebration of the 50th anniversary of the Spanish small animal veterinary association (AVEPA). AVEPA members constitute one of the largest groups to receive the Global Edition of Clinician’s Brief, and we registered many more subscribers. This edition contains much of interest to them as well as all global readers.

First is our specially commissioned Consultant on Call on canine distemper, which provides a review of this devastating disease that is unfortunately still too common in parts of the world. Then, Dr. Elke Rudloff presents some basic approaches to dyspneic patients in Top Five: the take-home is that tranquilization and oxygen supplementation come first, not chest radiographs.

You will also appreciate our dual Diagnostic Trees for diabetes in dogs and cats, as well as a solid review of cystine urolithiasis in an Ask the Expert feature. We also offer two how-to articles on enteral feeding and another two on testing for and treating hyperadrenocorticism, a challenge for international practitioners who do not have tests and treatments readily available. In an accompanying sidebar, Dr. Ellen van Nierop of Ecuador explains how she manages affected patients. We will continue to be sensitive to issues such as this and strive to provide information of use to all global readers.

Colin F. Burrows, BVetMed, PhD, Hon FRCVS, DACVIM
WSAVA President
Editor, Global Edition

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Clarification
In “Top 5 Pain Medications in Clinical Practice” by Dr. Julia Tomlinson (September 2014 issue, page 23), the discussion of NSAID use in cats should have read as:

The only NSAID licensed for oral use in cats in the United States is robenacoxib (Onsior, us.onsior.com), which is FDA approved for 6-day use q24h in oral form; an IV injection can precede this.

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WSAVA Calls for Quarantine, Not Euthanasia, for Dogs Exposed to Ebola

The WSAVA has called for the testing and quarantine, not automatic euthanasia, of dogs exposed to the Ebola virus in countries not endemic for the disease. It has spoken out following the euthanasia of a pet dog belonging to an infected woman in Spain on the government’s orders and against her wishes.

The infection of a nurse in Spain with Ebola virus after caring for an infected priest has caused international concern; people who have come into contact with her were placed in quarantine. The Madrid regional government also obtained a court order to euthanize her dog, claiming that "available scientific information" could not rule out "a risk of contagion." Quarantine was not considered as an alternative and the dog has been now been destroyed.

Dr. Shane Ryan, Chair of the WSAVA Animal Wellness and Welfare Committee, says this sets a dangerous precedent: "While it is possible that dogs may harbor the virus, particularly in endemic areas where they may have access to infected animal carcasses, domestic pets that are potentially exposed in developed countries represent a very different scenario. A precedent for automatic euthanasia is both unnecessary and a significant breach of animal welfare.

"The dog in question was not tested for the virus and it is our view that available technology should allow for testing and quarantine as the first-line response."

Professor Michael Day, Chairman of the WSAVA One Health Committee, added: "Zoonotic diseases, particularly those transmitted through pets, are concerning to the pet-owning public, but there have been no scientific reports indicating that Ebola virus has been isolated from or directly transmitted by dogs. One investigation has shown that dogs may develop antibody to Ebola virus consistent with exposure, but dogs do not develop any symptoms of the disease.

"As the virus spreads into more developed regions, we are likely to see increasing concern and media interest as to the role of dogs in the transmission of disease and, as a profession, we must respond to pressure to euthanize pets as the exposure levels increase and fear escalates."

Full scientific evidence to support WSAVA views is available at wsava.org.

See Ebola Virus & Dogs: Where Do We Stand? by Dr. J. Scott Weese at cliniciansbrief.com/ebola-virus-dogs-where-do-we-stand
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Global Outreach: A Pathway to a Goal

Shane Ryan, BVSc (Hons), MVS, CVA, GradDipAnimChiro, MChiroSc, MRCVS
Executive Board Member
Honorary Treasurer, WSAVA

Both WSAVA and the NAVC use the word *community* in their taglines. At WSAVA, we pride ourselves on being and representing a Global Veterinary Community. But what does this really mean, and how can this community spirit manifest itself?

Communities have shared values, shared ideals. They work together toward a common goal. WSAVA’s stated goal—*to advance the health and welfare of companion animals worldwide through an educated, committed, and collaborative global community of veterinary peers*—is a noble aim. How can we make this happen?

**Bridging Differences**

The veterinary profession is not homogeneous. There are obvious differences in veterinary care throughout the world, with different paces of development in veterinary education and standards of practice. One relatively modest yet direct method of forging community ties and helping improve standards is through volunteer outreach. Two outreach programs were included at the recent WSAVA Congress in South Africa. One of these—at the Community Lead Animal Welfare (CLAW) project in Johannesburg—was sponsored by WSAVA’s Animal Wellness & Welfare Committee (AWWC). CLAW is supported by the International Fund for Animal Welfare (IFAW).

**The Volunteer Spirit**

The AWWC volunteer veterinarians came from Canada, Malaysia, the Netherlands, Norway, and the Philippines, truly a multinational veterinary effort. They assisted with spay and neuter surgeries, outpatient clinics, vaccination programs, and, of course, community outreach. AWWC also sponsored the attendance of local CLAW veterinary staff at the congress, who were then WSAVA’s guests at the animal welfare lecture stream.

Organizing such an outreach program presented a variety of challenges: complications with visas and veterinary licensing of volunteers to allow them to work legally, different standards of veterinary volunteers and practice, issues with safety perceptions, among others. Nevertheless, the community spirit shown by both volunteers and CLAW staff helped overcome these obstacles, and new professional relationships and friendships were forged.

WSAVA and AWWC are now planning outreach programs for the WSAVA 2015 Congress in Bangkok, Thailand. Possible outreach opportunities include those both in Thailand and further afield. For example, the Philippines has been identified. Negotiations are underway to get volunteers to these projects as part of the congress experience.

**A Call to Action**

And so, an invitation: Be an active participant in the global veterinary community; volunteer in 2015. We would love to have you on board. You can help drive the community spirit that advances the health and welfare of companion animals.
Free veterinary clinics were offered to community residents by volunteers during the WSAVA outreach program outside Johannesburg, South Africa.
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Perianal pruritus (PP) is common in dogs with anal sac disease (ASD) and manifests as scooting, licking, or chewing at the anal area. In dogs with allergic skin disease, the perianal skin is commonly affected; however, the prevalence of PP as a manifestation of allergy without concurrent ASD is unknown. In this prospective study, dogs \( n = 250 \) with skin disease were evaluated. Exclusion criteria included history of ASD, anal sacs that required regular emptying, perineal hernia, GI disorders within the week before consultation, and a variety of empiric therapies.

A total of 31 dermatologic diagnoses were identified, and those most commonly associated with PP included canine atopic dermatitis (CAD), adverse food reaction (AFR), and concurrent CAD and AFR. The presence of PP was significantly higher in dogs with CAD and AFR than for other diseases. The most common clinical signs were perianal alopecia, erythema, excoriations, lichenification, and hyperpigmentation. The most common behaviors were licking, chewing, or scooting. PP was not associated with anal sac impaction.

Global Commentary
This study confirmed what have been anecdotal reports that PP is mostly associated with allergy, especially CAD. CAD commonly affects the front feet and ear pinnae, while the ear margins and dorsolumbar skin are normally spared. The perianal site is not included as a predisposed area for CAD but, based on this study, perhaps it should be. It is not uncommon for my practice’s dermatology department to see PP patients that have their anal glands removed without any improvement in clinical signs. Most of these dogs have allergy. Anal gland involvement should be assessed in all cases of PP with palpation of the gland and cytology of the exudate, but glands should not be removed if these findings are normal without first investigating a possible allergic cause of the clinical signs.—Sue Paterson, MA, VetMB, DVD, DipECVD, MRCVS

Source

Soft tissue surgery

Soft tissue surgery may cause mild, moderate or severe postoperative pain. Preventive and multimodal analgesic techniques should be employed and local anaesthetic techniques included whenever possible. The balance between pre-, intra- and postoperative analgesia will depend on the severity of the preoperative condition and the location and magnitude of surgical trauma. Where postoperative pain is not successfully controlled with NSAIDs, alternative or additional analgesics or analgesic techniques should be employed. Major soft tissue surgery may lead to chronic pain which may have a neuropathic component. To date no veterinary studies have been performed assessing the benefit of adding gabapentin to the perioperative anaesthetic and analgesic protocol in surgical situations where there is significant nerve damage. However, based on its use in human medicine there may be potential value for use in the prevention of neuropathic pain.

Note: The choice of opioid, alpha, adrenoceptor agonists or NSAID used will vary based on availability and contraindications. Loco-regional anaesthetic techniques such as intra-articular, incisional and specific nerve blocks, wound infusion catheters or combinations thereof before and/or after surgery are highly recommended in all cases. Such techniques become mandatory when opioids and other controlled analgesic drugs are not available.

Minor soft tissue surgery

Pre- and intraoperative: Combination of an opioid, NSAID ± alpha, adrenoceptor agonist ± ketamine (cats). Local anaesthetic techniques. Postoperative analgesia: NSAID (unless administered preoperatively) ± opioid and/or non-drug therapies.

Protocol without controlled drugs:

Same as above but without the opioid.

Protocol with limited availability of analgesic drugs:

Pre- and intraoperative: Combination of alpha, adrenoceptor agonists, tramadol, a NSAID and local anaesthetic technique. Immediate and later postoperative (24 h): NSAID (unless administered preoperatively), paracetamol (acetaminophen) (not in cats) or dipyrone, and non-drug therapies.

Major soft tissue surgery

Preoperative: Same as for minor soft tissue surgery. Intraoperative: Boluses or infusions of opioids ± alpha, adrenoceptor agonists ± ketamine ± lidocaine. These drugs may not be required if an effective local anaesthetic block has been performed. Immediate and later postoperative (24 hours): NSAID (unless administered preoperatively), continuous infusions or boluses of drugs used intraoperatively as needed ± other adjunctive drugs and non-drug therapies such as cold therapy and acupuncture.

Example of a protocol for a dog undergoing a perineal hernia repair

- Preoperative: NSAID (24 h dose; ideally one approved in cats), morphine 0.5 mg/kg IM, and acepromazine 0.02 mg/kg IM.
- Induction of anaesthesia: ketamine 5 mg/kg and diazepam 0.25 mg/kg IV, or to effect.
- Maintenance of anaesthesia: Inhalation anaesthesia with lumbosacral epidural administration of 0.5% bupivacaine (1 mL/5 kg before surgery).
- Immediate postoperative (24 h): Morphine 0.3 mg/kg IM (every 4–6 h depending on evaluation, or as needed), non-drug techniques such as cold therapy.
- Later postoperative days: NSAID (same drug as preoperative, starting 24 h after preoperative dose), q24 h and buprenorphine 0.01 mg/kg IM, q8 h up to 3 days postoperatively.

Example of a protocol for a cat undergoing a surgical removal of injection site sarcoma

- Preoperative: NSAID (24 h dose; ideally one approved in cats), morphine 0.2 mg/kg IM, ketamine 5 mg/kg and midazolam 0.25 mg/kg IM.
- Induction of anaesthesia: Propofol to effect IV.
- Maintenance of anaesthesia: Inhalation anaesthesia with constant rate infusions of fentanyl 10 μg/kg/h following a loading dose of 2 μg/kg IV and ketamine 0.6 mg/kg/h. Infiltration anaesthesia with local anaesthetics.
- Immediate postoperative (24 h): Constant rate infusions of fentanyl 1–3 μg/kg/h and ketamine 0.12 mg/kg/h. Cold therapy ± acupuncture.
- Wound therapy catheter with administration of bupivacaine 0.5% (up to 2 mg/kg).
- Later postoperative days: NSAID (same drug as preoperative, starting 24 h after preoperative dose) and buprenorphine 0.02 mg/kg IM, q6–8 h up to 3 days postoperatively.

Protocol without controlled drugs:

See above, without the opioid. Injectable tramadol may be administered in the perioperative period. The use of local anaesthetic techniques, particularly regional blocks, lidocaine infusion intra- and postoperative, non-drug therapies combined with NSAIDs becomes critical when opioids are not available.

Protocol with limited availability of analgesic drugs:

See above without opioids. A combination of low dose alpha, adrenoceptor agonist, NSAID (unless administered preoperatively), gabapentin, paracetamol (acetaminophen) (not in cats) or dipyrone, amantadine, non-drug therapies, further regional blocks or continuous wound block (wound catheters).

Later postoperative days: NSAID as required non-drug therapies, further regional blocks or continuous wound block (wound catheters).

If pain cannot be controlled or ameliorated with available techniques and the prognosis is poor, consider euthanasia.
CRAIG DATZ, DVM, MS, DABVP, DACVN, is adjunct associate professor at University of Missouri. He is also the Nutrition and Scientific Affairs Manager of Royal Canin USA. Dr. Datz has spoken at a number of CE conferences, including the NAVC Conference, and is a consultant for the Veterinary Information Network (VIN) in parasitology, immunology, and infectious disease. ASK THE EXPERT PAGE 24 & PROCEDURES PRO PAGE 27

ALEX GALLAGHER, DVM, MS, DACVIM, is clinical assistant professor of small animal medicine at University of Florida. His clinical interests include interventional procedures, endocrinology, and gastroenterology, topics on which he has been published and has spoken nationally and internationally. He earned his DVM from University of Florida and completed his residency and master's degree at Virginia Polytechnic Institute and State University. ASK THE EXPERT PAGE 45 & CONSULTANT ON CALL PAGE 19

GREGORY F. GRAUER, DVM, MS, DACVIM, is professor and Jarvis chair of medicine in the department of clinical sciences at Kansas State University. He has also served as professor and section chief of small animal medicine at Colorado State University and faculty member at University of Wisconsin–Madison, where he completed his internship and residency and earned his MS. His area of interest, research, and teaching is the small animal urinary system. Dr. Grauer earned his DVM from Iowa State University. ASK THE EXPERT PAGE 59

MELISSA A. KENNEDY, DVM, PhD, DACVIM, is associate professor in the Department of Biomedical and Diagnostic Sciences at University of Tennessee. Her interests include feline coronavirus, infectious disease diagnostics, and diseases of wildlife. She earned her DVM in 1983 at University of Tennessee and her PhD in comparative & experimental medicine there in 1991. Dr. Kennedy completed her residency in microbiology in 1992. CONSULTANT ON CALL PAGE 19

ELKE RUDLOFF, DVM, DACVECC, is a clinical instructor at Lakeshore Veterinary Specialists in Glendale, Wisconsin. Her special interests include fluid resuscitation and trauma management, topics on which she has published in peer-reviewed journals and book chapters. She is past-president of the Veterinary Emergency and Critical Care Society and the 2008 recipient of the Ira Zaslow Award for distinguished service in the field of veterinary emergency and critical care. Dr. Rudloff is a frequent speaker at the NAVC Conference. Dr. Rudloff is a 1991 graduate of Purdue University. She completed her residency training at the Animal Emergency Center and achieved board certification in the American College of Veterinary Emergency and Critical Care in 1995. TOP 5 PAGE 54

THOMAS SCHERMERHORN, VMD, DACVIM, has been assistant professor at Kansas State University since 2001. His clinic focuses on cellular and molecular endocrinology, especially the study of diabetes mellitus and related metabolic disorders in dogs and cats. Dr. Schermerhorn’s clinical interests include all aspects of canine and feline endocrinology. He has a special interest in the epidemiology, pathology, and therapeutic management of feline diabetes. A graduate of University of Pennsylvania, Dr. Schermerhorn completed a medical internship at South Shore Veterinary Associates and a residency in Small Animal Internal Medicine at Cornell University. He received research training as a graduate fellow in the Department of Molecular Medicine at Cornell University. Dr. Schermerhorn was awarded Board Certification in Internal Medicine in 1997. DIAGNOSTIC TREE PAGES 14 & 16

SOMPORN TECHANGAMSUWAN, DVM, MSc, PhD, is assistant professor in the department of pathology at Chulalongkorn University, Thailand. Her interests include pathology and molecular diagnosis of viral-associated infectious diseases in companion and exotic animals. Dr. Techangamsuwon earned her DVM from Chulalongkorn University; her MSc in clinical pathology from Mahidol University, Thailand; and her PhD in neuroscience from University of Veterinary Medicine Hannover, Germany. CONSULTANT ON CALL PAGE 19

ALLISONWARA, DVM, is a second-year small animal clinical nutrition resident at the University of Missouri College of Veterinary Medicine. Dr. Wara’s research interests include feline diabetes, clinical nutrition, and obesity in companion animals. After earning her BS from University of Guelph, Dr. Wara earned her DVM at Atlantic Veterinary College at University of Prince Edward Island. ASK THE EXPERT PAGE 24 & PROCEDURES PRO PAGE 27

This month’s issue proudly features the following speakers from recent NAVC Conferences: Craig Datz, Alex Gallagher, Gregory F. Grauer, Melissa A. Kennedy, & Elke Rudloff
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Lack of Diabetic Control in Cats

Suspicion for poorly controlled diabetes

- Persistent hyperglycemia/hypoglycemia for all/part of the day
- Mild hyperglycemia may only be evident on laboratory evaluation
- Clinical signs related to magnitude of hyperglycemia:
  - Polydipsia
  - Polyuria (may produce incontinence)
  - Weight loss
  - Dehydration
- Chronic/intermittent hypoglycemia

Direct (ie, fructosamine) and indirect (ie, glucosuria) evaluation of glycemia

- Poor glycemic control
- Acceptable glycemic control

Evaluate compliance
- Insulin protocol (type, dose, administration, storage)
- Ancillary therapy (eg, diet)

- Non-compliance
- Compliance

Client education
- Educate about principles and goals of treating diabetes
- Review insulin handling (storage), preparation, administration

Re-evaluate after 7–10 days

Assess environment and lifestyle
- Changes to home environment?
- Changes to daily routine?

- Recent changes
- No changes

Mitigate negative environmental factors
- Adjust insulin dose as indicated
- Adjust ancillary diabetic therapy as indicated
- Evaluate response after 7–10 days
Evaluate for concurrent disorders
• Physical examination
• Minimum database (CBC, chemistry panel, urinalysis, urine culture)
• Additional testing to confirm diagnosis

Consequences
Chronic poor control of diabetes may increase risk for:
• Hypoglycemia
• Ketoacidosis
• Hyperosmolarity
• Neuropathy

Disorders that cause insulin resistance
• Acromegaly: Excess growth hormone production caused by pituitary neoplasia can cause severe insulin resistance.
• Obesity
• Bacterial infection: Includes severe urinary, skin, oral infection
• Iatrogenic: Exposure to exogenous glucocorticoid (most common) or progesterone compounds may produce insulin resistance. Glucocorticoids absorbed after application of topical ocular or otic medications/owner hormone creams may contribute to insulin resistance.
• Pancreatitis: Severe inflammation may produce insulin resistance; direct damage to pancreatic islet cells may result in loss of functional beta cells and decreased insulin production.
• Hyperadrenocorticism: Uncommon, but can produce severe insulin resistance.

Disorders that mimic uncontrolled diabetes
• Renal disease: Causes polyuria/polydipsia; early kidney disease may be difficult to recognize with poorly controlled diabetes.
• Hyperthyroidism: Loss of body condition with healthy appetite, polyuria/polydipsia; possible but poorly documented cause for insulin resistance.
• Neoplasia: Loss of body condition (cachexia/chronic illness) may occur in diabetic cats with neoplasia.
• Lower urinary tract disorders: Pollakiuria associated with lower urinary tract disorders (urolithiasis, UTI) may be mistakenly reported as polyuria by owners.
• Hypercalcemia: Causes polyuria/polydipsia; look for loss of body condition, inappetence.
Lack of Diabetic Control in Dogs

**Suspicion for poorly controlled diabetes**

- Persistent hyperglycemia for all/part of the day
- Mild hyperglycemia may only be evident on laboratory evaluation
- Clinical signs related to magnitude of hyperglycemia:
  - Polydipsia
  - Polyuria (may produce incontinence)
  - Weight loss
  - Dehydration

**Direct (ie, fructosamine) and indirect (ie, glucosuria) evaluation of glycemia**

- Poor glycemic control
- Acceptable glycemic control

**Evaluate compliance**
- Insulin protocol (type, dose, administration, storage)
- Ancillary therapy (eg, diet)

- Non-compliance
- Compliance

**Client education**
- Educate about principles and goals of treating diabetes
- Review insulin handling (storage), preparation, administration

- Re-evaluate after 7–10 days

**Assess environment and lifestyle**
- Changes to home environment?
- Changes to daily routine?

- Recent changes

- Mitigate negative environmental factors
  - Adjust insulin dose as indicated
  - Adjust ancillary diabetic therapy as indicated
  - Evaluate response after 7–10 days
Evaluate for concurrent disorders
- Physical examination
- Minimum database (CBC, chemistry panel, urinalysis, urine culture)
- Additional testing to confirm diagnosis

**Consequences**
Chronic poor control of diabetes may increase risk for:
- Hypoglycemia
- Cataracts
- Ketoacidosis
- Neuropathy
- Hyperosmolarity

Disorders that cause insulin resistance
- Common:
  - Hyperadrenocorticism
  - Obesity
  - Bacterial infection (severe urinary, skin, oral infections)
  - Pancreatitis
- Less common:
  - Hypothyroidism
  - Gestation: Gestational diabetes is partly mediated by progesterone.
  - Iatrogenic: Exposure to exogenous glucocorticoid (most common) or progesterone compounds may produce insulin resistance. Glucocorticoids absorbed after application of topical ocular or otic medications/owner hormone creams may contribute to insulin resistance.

Disorders that mimic uncontrolled diabetes
- Consider:
  - Hypercalcemia: Causes polyuria/polydipsia; look for loss of body condition, inappetence.
  - Renal disease: Causes polyuria/polydipsia; early kidney disease may be difficult to recognize with poorly controlled diabetes.
  - Liver disease: Many liver disorders are associated with polyuria and may cause hypoglycemia.
  - Insulinoma: Hypoglycemia secondary to insulin production by an endocrine tumor; rare in diabetic dogs.
  - Neoplasia: Loss of body condition ( cachexia/chronic illness) may occur in diabetic dogs with neoplasia. Lymphoid and other neoplasias that produce parathyroid hormone-related peptide (PTH-rP) may also produce hypercalcemia. Large tumors (hepatic neoplasms) may produce hypoglycemia.
  - Lower urinary tract disorders: Pollakiuria associated with disorders (urolithiasis, UTI, urinary incontinence) may be reported as polyuria. An increase in urine volume from loss of diabetes control can manifest as overflow incontinence.
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Canine Distemper Virus

Somporn Techangamsuwan, DVM, MSc, PhD
Chulalongkorn University
Melissa A. Kennedy, DVM, PhD, DACVM
University of Tennessee

Profile

Definition
- Canine distemper virus (CDV) is a morbillivirus in the Paramyxoviridae family.
  - The causal viruses of rinderpest and measles are also included in this family.
- CDV is an enveloped virus.
  - CDV is relatively easy to inactivate and requires only the removal of the lipid outer membrane.
  - Any disinfectant with detergent activity effectively inactivates this virus.
- CDV, an RNA virus, has a significant mutation rate that is much greater than that of DNA viruses.
- Domestic dogs are considered the reservoir species.
- CDV also affects multiple wildlife species (eg, raccoons, skunks, foxes, ferrets) and can infect and cause disease in large felids (eg, lions).
- Antigenic drift and strain diversity have been increasingly associated with outbreaks in wild species, domestic dogs, and exotic animals in zoos and parks.
  - New strains can emerge, so monitoring is necessary to ensure current vaccines are fully protective against predominant circulating strains.

Systems
- The infection is associated with all lymphatic tissue.

CDV = canine distemper virus
Consultant on Call

Geographic Distribution
- The H-gene of CDV exhibits the highest variability within the genome.
- Based on H-gene alignment, CDV is classified into 11 lineages: Asia-1, Asia-2, Asia-3, Asia-4, Europe, European wildlife, vaccine (America-1), America-2, South America, South Africa, and Arctic-like.

Signalment
- The disease has been reported in dogs, bears, raccoons, ferrets, civets, red pandas, elephants, and large or exotic cats.
- There is no breed or sex predilection.
- Animals <6 months are particularly vulnerable.

Pathogenesis
- The main route of infection is via aerosol droplet secretions from the oral or nasal cavities of infected animals.
  - Can also spread by direct contact.
- The virus initially replicates in the epithelia and lymphoid tissue of the upper respiratory tract.
- Depending on the level of immunity, CDV may spread via the bloodstream in an infected host, replicating in mononuclear WBCs.
  - The virus may then target epithelia of the respiratory system as well as the CNS.
  - In cases where CNS invasion occurs, neurons will become infected.
- The degree of viremia and the extent of viral spread to other tissue are moderated by the level of specific humoral immunity in the host during the viremic period.

Signs
- Signs most often involve the respiratory tract.
  - GI signs may also occur.
- Affected dogs are listless and have a decreased appetite.
  - In milder cases, signs may be similar to other agents of canine infectious respiratory disease complex.
  - Subclinical infection with shedding may also occur, depending on the level of host immunity.
- Systemic signs are most common in unvaccinated dogs (eg, puppies) as maternal immunity wanes.
- Conjunctivitis, nasal discharge, cough, and fever are classic signs.
- Respiratory infection may involve the lower respiratory tract with possible primary viral pneumonia.
- Secondary bacterial infection may occur.
- Vomiting and diarrhea may be present.
- Neurologic signs may be concurrent with epithelial signs (ie, respiratory disease, conjunctivitis, vomiting, diarrhea) with encephalitis caused by direct viral replication.
  - Alternately, neurologic disease may occur several weeks after resolution of epithelial invasion.
  - A significant amount of pathology results from virus immune response, as well as the virus itself.
  - Seizures and myoclonus are two of the more common signs.
  - The latter may affect limbs or manifest as chewing motion of the jaw.
- Ocular disease may also occur.
  - Lesions include anterior uveitis, optic neuritis, and retinal detachment.
- Infection during pregnancy may lead to abortion or stillbirth.

Geographic Distribution
- The H-gene of CDV exhibits the highest variability within the genome.
- Based on H-gene alignment, CDV is classified into 11 lineages: Asia-1, Asia-2, Asia-3, Asia-4, Europe, European wildlife, vaccine (America-1), America-2, South America, South Africa, and Arctic-like.

Signalment
- The disease has been reported in dogs, bears, raccoons, ferrets, civets, red pandas, elephants, and large or exotic cats.
- There is no breed or sex predilection.
- Animals <6 months are particularly vulnerable.

Pathogenesis
- The main route of infection is via aerosol droplet secretions from the oral or nasal cavities of infected animals.
  - Can also spread by direct contact.
- The virus initially replicates in the epithelia and lymphoid tissue of the upper respiratory tract.
- Depending on the level of immunity, CDV may spread via the bloodstream in an infected host, replicating in mononuclear WBCs.
  - The virus may then target epithelia of the respiratory system as well as the CNS.
  - In cases where CNS invasion occurs, neurons will become infected.
- The degree of viremia and the extent of viral spread to other tissue are moderated by the level of specific humoral immunity in the host during the viremic period.

Signs
- Signs most often involve the respiratory tract.
  - GI signs may also occur.
- Affected dogs are listless and have a decreased appetite.
  - In milder cases, signs may be similar to other agents of canine infectious respiratory disease complex.
  - Subclinical infection with shedding may also occur, depending on the level of host immunity.
- Systemic signs are most common in unvaccinated dogs (eg, puppies) as maternal immunity wanes.
- Conjunctivitis, nasal discharge, cough, and fever are classic signs.
- Respiratory infection may involve the lower respiratory tract with possible primary viral pneumonia.
- Secondary bacterial infection may occur.
- Vomiting and diarrhea may be present.
- Neurologic signs may be concurrent with epithelial signs (ie, respiratory disease, conjunctivitis, vomiting, diarrhea) with encephalitis caused by direct viral replication.
  - Alternately, neurologic disease may occur several weeks after resolution of epithelial invasion.
  - A significant amount of pathology results from virus immune response, as well as the virus itself.
  - Seizures and myoclonus are two of the more common signs.
  - The latter may affect limbs or manifest as chewing motion of the jaw.
- Ocular disease may also occur.
  - Lesions include anterior uveitis, optic neuritis, and retinal detachment.
- Infection during pregnancy may lead to abortion or stillbirth.

Pitfalls
- CDV should not be ruled out simply because there is no history of contact with other dogs.
  - Wildlife (eg, raccoons, foxes) can be an important source of CDV.
- Although current vaccines appear to be protective against most circulating strains, vaccine breaks may occur.
- PCR can detect virus from the vaccine for a few weeks postvaccination.
  - It is important to know if the dog has recently been vaccinated when testing samples for CDV.
  - The testing laboratory can help discern whether a positive result is from natural infection or vaccine.
- Canine distemper virus, including the canine distemper vaccinal virus, kills ferrets. It is critical never to use the canine vaccine in this species.
  - Use vaccines licensed for use in ferrets only.

CDV = canine distemper virus, CSF = cerebrospinal fluid, PCR = polymerase chain reaction
Puppies infected before permanent dentition may have enamel hypoplasia.

Digital hyperkeratosis may be noted.

**Diagnosis**

**Definitive Diagnosis**

- Diagnosis is established via virus identification in a clinical sample through use of reverse-transcriptase PCR of whole blood, a swab of conjunctiva or tissue, CSF, or urine.
- Urine is a good choice for PCR testing in patients with CDV encephalitis after resolution of epithelial signs.
- CDV may be detected in urine for a longer period than other sample types.¹
- CDV detection in urine and CSF was equivalent in one study of neurologic cases.¹
- Postmortem evaluation and microscopic findings confirm infection.
- The specific lesion of CDV is eosinophilic intranuclear/intracytoplasmic inclusion bodies in glial cells, neurons, epithelial respiratory cells, and cells of the GI and urogenital tracts (Figure 1).
- Virus isolation is the gold standard for diagnosis and is useful in low levels of viral infection through observation of typical syncytial cell formation (Figure 2).
- Immunocytology can be used to enhance the visibility of inclusion bodies by fluorescein-conjugated CDV antibodies.
- Fluorescent color confirms distemper infection, but the lack of color does not rule it out.

Distemper is sometimes confused with other systemic infections, including leptospirosis, canine infectious hepatitis, rabies, canine infectious respiratory disease complex, or Rocky Mountain spotted fever.

![](image1.png)

Eosinophilic intranuclear inclusion bodies in glial cells in the cerebrum of a dog infected with CDV.

![](image2.png)

Typical cytopathic effect of CDV isolation shows numerous small and large syncytium cell formations.
Differential Diagnosis
- Distemper is sometimes confused with other systemic infections (eg, leptospirosis, canine infectious hepatitis, rabies, canine infectious respiratory disease complex, Rocky Mountain spotted fever).

Laboratory Findings
- Clinical findings may include lymphopenia.
- Inclusions in WBCs and RBCs may be noted, especially in early infection.
- Analysis of a CSF specimen in dogs with neurologic disease shows increased protein and WBCs—primarily lymphocytes.
- Serologic studies can be helpful in unvaccinated dogs, particularly if IgM is detected.

Diagnosis by immunohistochemistry using specific antibodies against CDV shows positive infected transitional epithelial cells (brown color).

Postmortem Findings
- Thymic atrophy is a consistent finding in infected puppies.
- Hyperkeratosis of the nose and footpads is often found in dogs with neurologic manifestations.
- Bronchopneumonia, enteritis, and skin pustules may also be present, depending on the degree of secondary bacterial infection.
- In cases of acute to peracute death, respiratory abnormalities may be found exclusively.
- Histologically, CDV causes necrosis of lymphatic tissue; interstitial pneumonia with cytoplasmic and intranuclear inclusion bodies in respiratory, urinary, and GI epithelium; and neurologic complications.

In dogs with unknown history or in vaccinated animals, the usefulness of serology is dubious.
- Measuring CDV-specific IgM can be useful if the vaccination history is known.
- If the dog has not been vaccinated in the past 1–2 months, IgM should be negative unless exposed to infection with a field strain.
- Detection of antibodies in CSF is significant if the blood–brain barrier is intact.
- This does not occur unless CNS invasion is present.
- Immunohistochemistry using specific antibodies against CDV is helpful when typical lesions are not evident (Figure 3).

Treatment
Inpatient or Outpatient
- Treatment depends on severity of clinical signs.
- If mild respiratory distress occurs, animals may be treated as outpatients with supportive care (ie, nebulization, antibiotics for secondary infections, mucolytics, cough suppressants).
- If signs are more severe, dogs may require hospitalization and should be housed in isolation.
- If neurologic disturbances are present (eg, tetraplegia, semicoma, seizure), euthanasia should be considered.
**In General**

**Relative Cost**
- Diagnostics: $–$$
- Treatment and follow-up care: $$–$$$-

**Prognosis**
- Prognosis is guarded.

**Cost Key**
- $ = up to $100
- $$ = $101–$250
- $$$ = $251–$500
- $$$$ = $501–$1000
- $$$$$ = more than $1000

**Prevention**
- Control is accomplished through vaccination.
  - Current vaccines include strains of the American lineage (Onderste-poort or Lederle strains).
  - After recovery from natural infection or following booster vaccination, immunity can persist for years.
- Vaccination for CDV can begin as early as 6–8 weeks of age, with boosters every 2–4 weeks until at least 16 weeks of age. For naïve puppies or adults vaccinated after maternal immunity has waned (approximately 16 weeks of age) a single live or recombinant vaccine should be sufficient to induce protection.
- In older vaccinated dogs, an annual or triennial distemper booster is recommended, depending on the risk for infection.
- Client education about purchasing puppies from crowded pet markets is important.
- CDV is susceptible to ultraviolet light, heat, drying, and all routinely used disinfectants.
- No vaccine is 100% effective, but regular vaccination can help protect animals.

**Follow-Up**

**Patient Monitoring**
- Infected dogs with systemic signs (eg, vomiting, diarrhea) should undergo extensive daily monitoring.
- Disinfection of the environment (eg, shelter, house, kennel) is recommended.
  - CDV is extremely susceptible to common disinfectants.

**Medications**

**Drugs & Fluids**
- Treatment is supportive only.
- Antiviral medications are not routinely used.
  - No single treatment is specific or uniformly successful.
- Secondary bacterial infection frequently results in bronchopneumonia, which requires broad-spectrum antibiotic therapy and expectorants or nebulization.
- Parenteral therapy is required when GI signs or dehydration is present.
  - Fluids such as lactated Ringer’s solution may be supplemented with vitamin B and/or C to replace lost vitamins and to stimulate the appetite.
- Water, food, and oral drugs should be discontinued if vomiting and diarrhea are present.
  - Parenteral antiemetics may be required.
- In dogs with status epilepticus, diazepam should be administered IV or PR, followed by phenobarbital for maintenance prevention.

**After recovery from natural infection or following booster vaccination, immunity can persist for years.**
There are several veterinary critical care diets that can be fed directly through large feeding tubes or after diluting with small amounts of water.
How Much & How Often?
The first step is to calculate the patient’s daily resting energy requirement (RER) at current body weight (BW; see RER Calculation, next page). If the patient is obese (>20% above ideal BW), then RER may be calculated at ideal or target weight. Multiples of RER (illness factors) are no longer recommended because of the risk for complications from overfeeding.

The second step is to determine how many times per day the patient will be tube-fed (eg, 4–6 feedings). The RER (kcal/d) is divided by the number of feedings for the kcal/feeding. The final step is to divide the kcal/feeding by the kcal/mL of the diet for the number of mL/feeding (see Example Feeding Plan).

Overfeeding or rapid reintroduction of enteral nutrition may lead to vomiting, diarrhea, and/or discomfort. In rare cases, this can lead to refeeding syndrome, which can result in sudden hypokalemia, hypophosphatemia, and hypomagnesemia. For patients with prolonged history of anorexia (eg, starvation, hepatic lipidosis) that are at risk for refeeding syndrome, a longer, slower ramp-up may be needed. On day 1, 25% to 33% of the daily RER can be given. On day 2, this amount can be increased to 50% to 67% RER; on day 3, 75% to 100% RER; and on day 4 and beyond, 100% RER until the patient resumes voluntary food intake. Most animals with E- and G-tubes do well with 3 to 6 feedings per day. Feeding once or twice per day is often not tolerated because of volume overload.

Preparing Canned Diets for Tube Feeding
After an appropriate diet is selected for the patient’s needs, it must be diluted and mixed sufficiently to form a slurry or liquefied diet (see Enteral Nutrition: Step-by-Step, page 27).

Example Feeding Plan
An older dog with chronic kidney disease is anorectic and losing weight. The current BW is 7 kg. A 14-French esophagostomy tube is placed to provide nutritional support:

- Calculate RER at current BW: 70 × (7)^0.75 = 301 kcal/d.
- Determine starting amount for feeding and rate of increase. If there are no complications, this dog may receive 100 kcal on day 1, 200 kcal on day 2, 300 kcal on day 3, continuing at 300 kcal/d long term or until voluntary intake resumes.
- Determine number of times per day the dog will be fed. Aim for 3–6 feedings per day as needed.
- Calculate kcal/feeding. For example, if feeding 5× per day, day 1 = 100 kcal/5 = 20 kcal; day 2 = 200 kcal/5 = 40 kcal, etc.
- Choose an appropriate diet. For chronic kidney disease, a canned renal diet is indicated. The selected example diet weighs 370 g and has 458 kcal/can.
- Using a blender, add measured amounts of water until the slurry is liquefied and flows easily through a 14-French tube. In this case, 200 mL of water blended with 1 can of diet results in an appropriate consistency.
- Calculate energy density (kcal/mL) of the slurry. Assume 1 g of diet is equivalent to 1 mL. Add the weight of the diet in grams per can to the amount of water (in mL) needed to make a slurry: 370 g + 200 mL = 570 mL. Divide the kcal/can by the final volume of the slurry: 458 kcal/570 mL = 0.8 kcal/mL.
- Divide the kcal/feeding by the kcal/mL of the slurry to calculate mL to administer at each feeding. On day 1, this dog will receive 20 kcal/0.8 = 25 mL/feeding. On day 2, 40 kcal/0.8 = 50 mL/feeding, etc.
- Monitor the dog for changes in BW and complications, such as discomfort and vomiting. Once the dog is receiving its full calculated RER, if the owner wants to try 4 feedings per day, the calculation will be 300 kcal/4 = 75 kcal, 75/0.8 = 94 mL/feeding. This larger volume may or may not be tolerated by the patient, so careful monitoring is necessary.
To determine the kcal/mL of the slurry, the product weight in grams (g/can) and the kcal/can of the diet must first be determined. This information may be printed on the product label, but the company, feeding guide, or website may need to be consulted. The next step is to determine how much water will be added to ensure an adequate consistency of the slurry. The number of grams of diet and number of mL of water are then added together (or the final volume of the slurry is determined in mL). Finally, the kcal/can can be divided by the total mL to determine the kcal/mL.

### RER Calculation

Equation to determine resting energy requirement:

\[ 70 \times BW_{kg}^{0.75} = \text{kcal/d} \]

For example:

10-kg dog: \( 70 \times (10)^{0.75} = 70 \times 5.6 = 394 \text{ kcal/d} \)

If there is no exponent key on a handheld calculator (\(y^x\)), the square root key (\(\sqrt{}\)) can be used. Enter BW and multiply by itself twice \((BW \times BW \times BW)\), then press square root key twice \((\sqrt{}, \sqrt{})\). Multiply the result by 70.

For example:

10-kg dog: \(10 \times 10 \times 10 = 1000\)

\[ \sqrt{\sqrt{1000}} = 31.6, 5.6 \]

\[ \times 70 = 394 \text{ kcal/d} \]

The first step in designing a feeding plan is to calculate the patient’s daily resting energy requirement (RER) at current body weight.

### Conclusion

Tube feeding is an effective method of providing nutrition to sick and injured patients that are unable to voluntarily consume sufficient amounts or types of food. It is important to calculate the amount to feed per day using the RER equation, and it is equally important to determine the kcal/mL of the slurry administered so that appropriate feeding instructions can be written and followed. ■ cb

See Aids & Resources, back page, for references & suggested reading.
The first step in designing a feeding plan that incorporates esophagostomy and gastrostomy tubes is to calculate the patient’s daily resting energy requirement at current body weight (see RER Calculation). The second step is to determine how many times per day the patient will be tube-fed. After an appropriate diet is selected, it must be diluted and mixed sufficiently to form a slurry or liquefied diet.

What You Will Need
- Good quality blender
- Canned diet of choice
- Strainer
- Appropriate-sized feeding tube
- Catheter-tip syringe
- Bowl
- Spatula
- Storage container

Step-by-Step Feeding Slurries

Step 1
Place the desired amount of diet in a blender. Add enough water to form the appropriate consistency needed for tube administration. Blend on high speed for 2–3 minutes.
Step 2
Pour the reconstituted slurry through a strainer and discard remaining chunks.

Step 3
Aspirate a portion of the slurry into a catheter-tip syringe.

Step 4
Run the sample through a feeding tube of the same diameter and type as the one placed in the patient to ensure adequate flow. Monitor for any evidence of clogging. If clogging occurs, add more water to the slurry to dilute further.

Step 5
Pour the final product into a clean container. Keep refrigerated until use. Discard after 48 hours.

See Aids & Resources, back page, for references & suggested reading.
Special Feature
Chordae Tendineae Rupture in a Dog
Amara Estrada, DVM, DACVIM (Cardiology)
cliniciansbrief.com/chordae-tendineae-rupture-dog

Special Feature
A New Threat for “Counter Surfers”: GI Foreign Body in a Dog
Kirk Miller, DVM, DABVP
cliniciansbrief.com/new-threat-counter-surfers-gi-foreign-body-dog

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cliniciansbrief.com/dermatology-quiz

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An 8-year-old spayed Shih Tzu was presented with a 1-week history of ulcerative keratitis in the right eye. Diabetes mellitus was diagnosed 3 months earlier and was reasonably well controlled. A referring veterinarian prescribed liquid paraffin ointment and fusidic acid drops, but the eye worsened. Ophthalmologic examination revealed a large paracentral melting corneal ulcer extending to 50% of the corneal depth. Chemosis, reflex uveitis with mitosis, and blepharospasm were present. Corneal scrape revealed degenerate neutrophils with a mixed bacterial population. Schirmer tear test revealed low tear production in the left eye; it was not measured in the right eye.

Initial treatment included bandage contact lens placement and topical ophthalmic drops (ie, autologous serum, chloramphenicol, ofloxacin) OD q2h; atropine sulfate drops OD q12h on day 1, then q24h; liquid paraffin OU q12h; cyclosporine 0.2% OS q12h; oral oxytetracycline and carprofen; and Elizabethan collar placement. The right eye responded to treatment, but the deep corneal stromal defect remained. A corneal conjunctival transplantation graft was performed; the dog was discharged on the same medication regimen, with atropine reduced to q48h and cyclosporine given OU q12h. The graft was stable and fully vascularized 7 days postoperatively. On day 28, the eye was visual, corneal scarring and pigmentation was moderate, and tear production was normal bilaterally. Aggressive multimodal treatment aimed at inciting causes, paired with timely surgical intervention, was critical in saving the eye.

Commentary
This case illustrated the potential difficulties a diabetic patient can have with corneal wound healing. Corneal innervation may be impaired and corneal sensitivity decreased, which may delay healing when a corneal ulcer develops. This is worse in brachycephalic animals that have decreased corneal sensitivity. In addition, diabetic patients may not exhibit the same degree of discomfort with a corneal injury than nondiabetic patients, leading to delayed presentation and more advanced disease at diagnosis. Also, keratoconjunctivitis sicca (common in diabetics and brachycephalic breeds) should be a consideration whenever a diabetic (or brachycephalic) patient presents with a corneal problem. Impaired corneal sensitivity, keratoconjunctivitis sicca, and a propensity for infection can lead to a corneal ulcer and can have disastrous consequences.

Initial microbiological cytology culture and sensitivity results would not have informed the choices of drugs used empirically; however, these tests are still warranted and should be considered. If an ulcer fails to stabilize or the clinical response with initial medical therapy is not as expected, different antimicrobial medications are needed. Laboratory results, if available from the initial evaluation, can allow for directed therapy, and this is especially important for patients prone to infections.—Caryn E. Plummer, DVM, DACVO

■ Source

Copper: Not Enough or Too Much
The Labrador retriever has a genetic predisposition to copper-associated hepatitis (CAH). Affected dogs accumulate copper in the liver to levels that (untreated) can cause liver cirrhosis. The most common treatment is chelation therapy with the metal chelator d-penicillamine, which promotes copper excretion in urine and can be used for long-term treatment. Many dogs, however, develop adverse effects (eg, anorexia, vomiting, copper and zinc deficiency).

This study aimed to determine if nutritional management could be used as an alternative treatment for CAH. Labrador retrievers (n = 16) previously treated successfully with d-penicillamine were put on a low-copper (1.3 ± 0.3 mg/1000 kcal) and high-zinc (64.3 ± 5.9 mg/1000 kcal) diet. Copper levels and histological samples were evaluated via liver biopsy every 6 months, as were alkaline phosphatase, alanine transaminase, and serum albumin levels. Twelve dogs maintained hepatic copper concentration below 800 mg/kg dry weight liver on the diet; 4 dogs required retreatment with d-penicillamine. A low-copper and high-zinc diet can be an effective therapy for CAH, but long-term monitoring protocols must be in place as the reaccumulation rate of copper in individual dogs varies. Study supported by Royal Canin

Commentary
CAH has become a more widely recognized primary and secondary disease. Nutritional versus medical management aside, the biggest take-home from this study is that we should repeat biopsies in dogs with CAH to monitor their therapy. A large amount of individual variation to therapy was documented—and this was just within one breed. Owners and veterinarians are often reluctant to collect a biopsy a second, let alone a third, time, but we do our patients no service by committing to a chronic course of therapy without follow-up.—Jessica Markovich, DVM, DACVIM (SAIM)

■ Source
This study examined the efficacy of oral docetaxel in combination with cyclosporine for treatment of canine epithelial cancer. Docetaxel, a human anticancer drug with a wide spectrum of activity, is usually given IV. In dogs, the IV route carries a high anaphylaxis risk, but the drug has limited oral bioavailability, unless given after a PO cyclosporine dose. Dogs (n = 51) with confirmed epithelial neoplasia were given 5 mg/kg PO cyclosporine followed (5–15 minutes later) with 1.625 mg/kg docetaxel. Both drugs were administered through a stomach tube. Treatments were planned for 2-week intervals. Forty-eight of the dogs were evaluated for treatment response (2 dogs died during treatment, 1 dog was withdrawn at owner request). An overall response rate of 16.7% was seen: 8 dogs showed a partial response (≥50% reduction in tumor volume), 24 dogs had stable disease (<50% or <25% increase in tumor volume), and 16 dogs showed progressive disease (≥25% increase in tumor volume or identification of new lesions). Oral squamous cell carcinoma (SCC) had the highest response rate; 50% of oral SCC dogs had partial responses. Transitional cell carcinoma appeared to be nonresponsive. GI toxicity was the most common adverse effect and could be managed effectively with dose reduction, treatment delay, oral medications, or hospitalization. Because of the possible risk for significant drug–drug interactions (blamed for one of the fatalities), vigilant monitoring is imperative.

Commentary
Prompted by human data, this study’s authors evaluated a docetaxel–cyclosporine combination in dogs with carcinomas; it mostly failed to show marked efficacy against the tumors evaluated. Partial responses in SCC are encouraging, as this disease is typically extremely chemoresistant. Taxanes are an underutilized family of chemotherapy drugs in veterinary patients, mostly because of their toxicity (particularly hypersensitivity caused by the cremophor excipient). In humans, taxanes have a broad spectrum of activity. Recently, a cremophor-free formulation of paclitaxel was conditionally approved for treatment of SCC and mammary tumors in dogs. Further studies are to be published in the coming years to clarify the role of taxanes in veterinary medicine.—Cecilia Robat, DVM, DACVIM (Oncology)

Source

Cardiomyopathy in Hedgehogs
Cardiomyopathy has been reported postmortem in hedgehogs, but there have been no published reports of its treatment. This report detailed the diagnosis and treatment of congestive heart failure (CHF) secondary to dilated cardiomyopathy (DCM) in a 1-year-old African pygmy hedgehog (Atelerix albiventris) that presented in severe respiratory distress after 1 week of nighttime coughing and decreased appetite. The hedgehog weighed 175 g and was cyanotic, dyspneic, tachypneic, and laterally recumbent with a thin body score and harsh lung sounds.

The patient was stabilized in a heated oxygen cage before intramuscular sedation with butorphanol and midazolam for radiographs, which showed generalized cardiomegaly and severe pulmonary edema. Echocardiogram revealed markedly decreased systolic function, an increased left-ventricular internal dimension, and an enlarged left atrium consistent with DCM. Treatment was initiated with furosemide 5 mg/kg IM q6h and enalapril 1 mg/kg PO q24h. The patient showed vast clinical improvement over 12 hours, with radiographic resolution of edema at 24 hours. L-carnitine (50 mg/kg) and pimobendan (0.3 mg/kg) were added, both PO q12h. Furosemide was decreased to q8h. Although the patient appeared clinically normal 10 days later with echocardiographic improvement in cardiac contractility, it was found dead at home 1 month after presentation and was not presented for necropsy. Because of the high incidence of cardiomyopathy in hedgehogs, practitioners are encouraged to establish baseline cardiac data when patients are young.

Commentary
Heart disease is not limited to domestic animals. A 2011 informal review of records from an exotic animal practitioner identified heart disease in at least 20% of all avian patients; this statistic should be considered when evaluating any other species. However, cardiac tissue has similar structure, properties, and response to therapy across species, thus strengthening the principle of One Medicine. Not only should heart disease be considered in exotic patients with suggestive presentations, but the attending veterinarian should be confident about successful management.—Adolf Maas, DVM, DABVP (Reptile & Amphibian)

Source
Tracking Bacterial Pathogens

Routine monitoring of bacterial sensitivity trends are key to the long-term efficacy of antimicrobials. This study evaluated antibiotic susceptibility profiles of common canine and feline bacterial pathogens to 9 frequently used antibiotics over 8 years. A total of 1857 bacterial strains from otitis, respiratory, urinary, and dermatologic infections in dogs and cats across Europe from 2002–2009 were sampled. Organisms tested were Pasteurella multocida, Bordetella bronchiseptica, Pseudomonas aeruginosa, Staphylococcus intermedius and S pseudintermedius, S aureus, Escherichia coli, and Proteus mirabilis. Bacterial susceptibility testing was performed on all strains for the following antibiotics: amoxicillin–clavulanic acid, ampicillin, penicillin, clindamycin, doxycycline, enrofloxacin, marbofloxacin, trimethoprim, and trimethoprim–sulfamethoxazole. The minimum inhibitory concentration (MIC) of marbofloxacin was also evaluated for all pathogens.

Results showed patterns of antimicrobial susceptibility that were consistent with previous reports. Marbofloxacin susceptibility was high across isolates and over time, with the exception of some strains of B bronchiseptica. Susceptibility to marbofloxacin was superior to that of enrofloxacin for some dermal isolates of P aeruginosa (88.37% vs 4.65%). Marbofloxacin may be better at eluding acquired fluoroquinolone resistance mechanisms because it is less lipophilic than enrofloxacin. Increased MIC values for marbofloxacin with respect to isolated strains of P multocida and S (pseudo)intermedius were noted. Judicious antibiotic use and pretreatment susceptibility testing are critical in slowing development of antimicrobial resistance. Study supported by Vétoquinol.

Commentary

Of particular interest in this study was a detailed evaluation of antibiotic resistance development toward marbofloxacin, a fluoroquinolone introduced in Europe in 1995 and FDA-approved for use in dogs and cats in the U.S. in 1999 and 2001, respectively. A low percentage of marbofloxacin resistant strains of E coli and P aeruginosa were identified, which emphasized the importance of continued antimicrobial stewardship. Nevertheless, no overall increase in marbofloxacin resistance was noted between 2002–2009 or when compared to an earlier European epidemiosurveillance study (1994–2001). Enrofloxacin, another commonly used fluoroquinolone, was fairly ineffective against P aeruginosa. Bacterial antibiotic resistance is thought to depend on acquisition of an efflux pump system that is more effective at eliminating lipophilic antibiotics like enrofloxacin.—Glenn Allen Olah, DVM, PhD, DABVP (Feline)

Source


FOCUS

Tissue microarray (TMA) is a technique in which dozens of tumor samples, embedded in paraffin blocks, can be prepared and evaluated on the same slide. It allows specimens from a large patient cohort to be analyzed simultaneously under the same immunohistochemical conditions. TMA has been used for high-throughput histopathologic evaluation of human tumor specimens but has yet to be widely adopted in veterinary medicine. This study applied TMA technology to veterinary science using canine insulinoma (INS) as a model. Core tissue biopsy samples from 32 primary canine INSs and 13 INS metastases were arranged and embedded in paraffin blocks. Normal canine tissue served as controls. TMAs were sectioned and immunohistochemistry performed for insulin, chromogranin A, growth hormone receptor, Ki67, and other markers. TMAs were then evaluated and scored by 3 veterinary pathologists. Findings were compared against the same tissue samples prepared as individual sections. Results showed excellent agreement across histopathologic parameters and good agreement across immunohistochemical parameters. Statistical analysis was performed to determine any relationships between histopathologic and immunohistochemical findings and clinical outcomes for dogs with INS. The presence of nuclear atypia was a useful prognostic indicator of disease-free interval. Tumor size, TMA stage, presence of necrosis, and Ki67 index were predictive of disease-free interval and survival time. TMA technology is a useful methodology for studying canine INS.

Source

Jealous as a Dog

Jealousy in humans is a complex emotion. It has been hypothesized that there may be a core or primordial form of jealousy that developed to secure resources and as a survival mechanism for species with siblings. Infants as young as 6 months have shown behaviors suggestive of jealousy when their mothers interacted with a life-like doll. In this study, 36 dogs and their owners participated in a study modeled from the infant studies. Interactions with owners and dogs were videotaped and scored. Owners ignored their dogs and interacted with 3 objects: a stuffed dog the owners treated as another dog, a novel object (carved pumpkin), or a children’s book with pop-up pages and music. Dogs exhibited significantly more jealous behaviors (snappy, getting between owner and object, pushing or touching the object) when owners interacted with the stuffed dogs. The majority of dogs (86%) sniffed the anal region of the toy dog during and after the experiment. No one behavior was indicative of jealousy, but when all were considered, the authors concluded there was a strong case that domestic dogs have a form of jealousy.

■ Commentary
Most veterinarians or veterinary team members, when asked if dogs can show jealousy, would likely answer yes. This is, of course, a subjective observation. It is interesting to see behavioral scientists identify and investigate pet dogs separate from medically-oriented behavioral studies (eg, pain). Because behavioral advice is often sought from the veterinary team, this study is useful to provide a novel, up-to-date perspective on one aspect of canine behavior. It is also valuable in illustrating the detail with which behavioral scientists investigate their subjects. —Elizabeth Layne, DVM

Source

Surgical Treatment for Patellar Luxation

Patellar luxation is a common developmental orthopedic condition of small-breed dogs. Medial luxation predominates and has been associated with patella alta in some cases. Lateral luxation occurs infrequently and is more common in larger breed dogs; bidirectional patellar luxation is rare. Surgical strategies include a combination of soft-tissue reconstruction, deepening of the femoral trochlear groove, and lateral transposition of the tibial crest.

This case series documents surgical treatment of bidirectional patellar luxation in 7 Pomeranians. The proximal–distal position of the patella was no different than that of a cohort of Pomeranians with normal stifle joints using the relationship of patellar tendon length to patellar bone length. Surgical treatment included a femoral trochleoplasty that extended proximally into the femoral metaphyseal cortical bone and soft tissue capsular modification. The tibial tuberosity was not transposed. The patella remained stable in 6 of 7 dogs at 48 weeks after surgery, with mild progression of stifle osteoarthrosis in all dogs.

■ Commentary
Treatment of patellar luxation has remained unchanged in the past several decades. The major goal is intuitive; realignment of the quadriceps axis and containment of the patella to allow for functional efficacy of stifle extension and weight bearing. Bidirectional luxation is particularly interesting, as the mechanism of luxation to allow this laxity is unclear. Furthermore, treatment is challenging, as many traditional strategies cannot be used to contain the patella from luxating medially and laterally. Although patella alta was not supported in these dogs, an extensive proximal femoral wedge recession trochleoplasty was successful for patella containment in the majority of cases. This strategy may be considered in dogs with medial patellar luxation in which the patella luxates proximal to the femoral trochlear groove.—Jason Bleedorn, DVM, DACVS

Source
Extended proximal trochleoplasty for the correction of bidirectional patellar luxation in seven Pomeranian dogs. Wangdee C, Hazewinkel HAW, Temwichitr J, Theyse FH. J SMALL ANIM PRACT DOI: 10.1111/jsap.12248

November 2014 • Clinician’s Brief 33
A Guiding Analyte: Variation of Analytes in Cats

Subject-based reference intervals allow clinical test results to be evaluated in terms of the magnitude of deviation from the patient’s previous baseline—the reference change value (RCV)—and may be more accurate than the generally used population-based reference intervals. This is especially true for analytes with higher biological variation.

This study sought to determine the biological variation of standard biochemistry analytes in cats. Blood was collected from 14 healthy cats weekly for 6 weeks. Twenty standard serum chemistry analytes were measured. The index of individuality (ie, the ratio of individual biological variation to group biological variation) was calculated for each analyte. ALP, ALT, cholesterol, creatinine, and globulin had the highest individuality, while sodium had the lowest; the remaining analytes were intermediate. The authors concluded that in cats, population-based reference intervals are appropriate only for use with sodium. For the other analytes, subject-based measures would be more appropriate. Serial sampling, subject-based reference values, and RCVs are recommended for evaluating feline plasma chemistry values.

**Commentary**
Chemistry analytes are usually interpreted by comparing values against population-based normal reference ranges or against previously determined values from the same cat. Depending on the ratio between these sources, the validity of analyte interpretation can be assessed. The authors showed that population-based ranges were inappropriate for 5 chemistry analytes for cats. The remaining analytes, excluding sodium, had intermediate ratios, suggesting that veterinarians should be cautious when evaluating almost all analytes against population-based ranges. Eventually, stratifying population-based and individual-based ranges with respect to age, gender, neuter status, and breed will be useful; most cats in this study were spayed females.—Glenn Allen Olah, DVM, PhD, DABVP (Feline)

**Source**

Doxorubicin: Finding the Right Dose

Doxorubicin (DOX) is a widely used chemotherapy drug with a narrow therapeutic window. Large interpatient variability exists in the development and degree of myelosuppression following equivalent dosages. Pharmacokinetic (PK) studies, which describe the relationship between drug dose and exposure, have been used to predict clinical effects, but they are laborious and expensive. Pharmacodynamic (PD) studies involve the relationship between exposure and efficacy or toxicity. Traditionally, chemotherapeutic drugs are dosed based on body surface area (BSA) to normalize the maximum tolerated dose. BSA may correlate better than weight with physiologic processes influencing drug activity; however, BSA dosing causes increased toxicity in smaller dogs, may not account for breed differences, and does not account for the effect of disease states on drug disposition. Size-independent factors such as absorption from the administration site, distribution and storage in tissue, enzymatic and nonenzymatic metabolism, and excretion are likely to have a greater effect than body size.

This study described the development and validation of a limited-sampling strategy in which blood samples were obtained from 27 dogs 3 times within 1 hour following DOX treatment to accurately predict drug exposure. This strategy will be used for further studies to evaluate the relationship of exposure to toxicity, possibly enabling refinement of dosing variables and the use of therapeutic drug monitoring to ensure optimized dosing.

**Commentary**
This is a good first step toward answering the question of optimal dosing of chemotherapy in dogs. The calculation based on BSA is imperfect, and, clinically, this is translated as huge variations in toxicity of a drug used at the predetermined dosage. Indeed, small dogs tend to be relatively overdosed using the BSA formula; however, we also see large dogs occasionally experiencing high-grade toxicities and small dogs having no adverse effects. Basing a drug calculation on PK parameters may be more accurate, and the method used here appears less cumbersome. Further studies are necessary to determine the accuracy and applicability of this strategy for optimal dosing.—Cecilia Robat, DVM, DACVIM (Oncology)

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Dealing with Dog Breath

The malodor from periodontal disease and halitosis is caused by accumulation of a microbial biofilm that results in inflammation. Twenty dogs were enrolled in a blinded, crossover clinical trial to evaluate a topical gel to control malodor. All dogs received a dental examination and cleaning; after, the clients applied either the active ingredient in gel form or a placebo q12h for 4 weeks. The dental cleaning was repeated at the end of this time, and dogs received the alternate treatment for another 4-week period. Halitosis was scored on a scale of 0 (nonexistent) to 10 (putrid); 3 clinicians scored each dog at 0, 4, and 8 weeks. Clients scored the dogs weekly. When the active ingredient gel was used, veterinarians and clients reported a decrease in oral odor.

Commentary
This study addressed the scourge of halitosis, citing that 40% of dogs aged 1–4 years have periodontal disease. This problem only increases with age because of the decreased ability of saliva to counteract free radicals. Volatile sulfur compounds from the general milieu of oral decay result in malodor. An antimicrobial antioxidant might mitigate this problem. In this study, a significant 4-week postinitiation improvement in scores was noted from initial treatment. The authors hypothesized that the success of this treatment is governed by control of oral flora and reactive oxygen species. Much human research is currently focused on addressing the problem of bacterial and biofilm products on oral odor. Regardless of whether this study provides hope for decreasing canine oral malodor, the importance of treating the root cause of the problem—periodontal disease—cannot be overstressed.—Ewan Wolff, DVM, PhD

Source

Fibrinolysis: The Difference Between Dogs & Humans

Hyperfibrinolysis is a risk factor for bleeding; compared with humans, dogs have accelerated fibrinolysis. Antifibrinolytic drugs have been used in veterinary medicine to reduce postoperative hemorrhage in greyhound dogs, a breed at greater risk for postoperative bleeding complications. In humans, tranexamic acid (TEA) and ε-amino caproic acid (EACA) are used to inhibit fibrinolysis. This study sought to determine the minimum plasma concentrations of TEA and EACA needed to completely inhibit fibrinolysis in canine blood after induction of in vitro hyperfibrinolysis. The concentration of EACA and TEA needed to inhibit fibrinolysis was 511.7 µg/mL and 144.7 µg/mL, respectively. This study confirmed that dogs were hyperfibrinolytic compared with humans, who require EACA and TEA concentrations of 122 µg/mL and 14.7 µg/mL, respectively, for complete inhibition of fibrinolysis.

Commentary
The use of antifibrinolytic agents (TEA and EACA) has increased in veterinary patients for the treatment of observed or anticipated postoperative hemorrhage. Although evidence has supported that these drugs may reduce postoperative complications in dogs, ideal therapeutic blood concentrations and doses have not been established. This study demonstrated that higher concentrations of TEA or EACA were necessary to inhibit in vitro fibrinolysis in canine plasma compared with human plasma. This opens the door for further pharmacokinetic studies, which will bring veterinarians closer to establishing canine antifibrinolytic treatment protocols. Once dose ranges have been established, veterinarians will be better suited to assess therapeutic efficacy. Although antifibrinolytic treatment already shows promise in reducing postoperative hemorrhage in greyhounds, additional benefits (and possibly additional complications) may be observed when higher doses are used.—Julie Walker, DVM, DACVECC

Source
The Case: A Dental Accident, Potential Blindness

Dental procedures, specifically those involving the caudal maxillary teeth, are associated with risk of damage to the globe and periorbital structures. Brachycephalic breeds are at an increased risk. In dogs, the floor of the orbit contains only soft tissue and not bone, making it susceptible to penetration during a dental procedure.

This case study followed a 5-year-old Tibetan terrier treated medically after a suspected globe penetration during dental extraction. Four days after the procedure, which involved removal of the upper left and right molar teeth, the dog presented with a 24-hour history of blepharospasm and periorbital swelling of the left eye. The eye was mildly exophthalmic and had an elevated nictitans membrane and positive dazzle reflex; menace and papillary light reflexes were negative. Other findings included hyperemic and chemotic conjunctiva, pancorneal edema, miotic pupil, and aqueous flare in the anterior chamber.

Ultrasound examination was consistent with a penetrating wound in the globe, most likely from a root elevator during the dental procedure.

Treatment included oral prednisolone, marbofloxacin, and tramadol, as well as a topical treatment applied to the left eye with prednisolone acetate 1%, atropine sulfate 1%, and brinzolamide. Significant improvement was seen in the first week. Oral and topical steroids were gradually decreased over 10 weeks and marbofloxacin stopped after 3 weeks. Ten months after the dental procedure, the left globe was visual and the ocular exam almost completely normal. The long-term use of steroids likely significantly contributed to the positive outcome by reducing the severe inflammation caused by globe penetration.

Commentary
This case illustrated the care necessary when performing dental extractions, particularly in brachycephalic breeds, and the potential for even a severely affected globe to respond favorably to medical treatment. Penetrating globe trauma, particularly involving the sclera, usually requires surgery either to repair or remove the globe. Surgery may preserve a cosmetic globe but not visual function; however, in this case, medical therapy with topical and oral antibiotics and corticosteroids achieved both. It is possible that carprofen may have resulted in a similar outcome, but in conjunction with an oral antibiotic (with a spectrum appropriate for oral flora), oral prednisolone allowed long-term therapy with a tapering dosage to ensure no recurrence of inflammation and discomfort.—Alison Clode, DVM, DACVO

Blood Transfusion Restriction in Ferrets

Blood transfusions have been used in ferrets to treat multiple causes of anemia. Using fresh donor blood within 4 hours poses little clinical risk, even without cross-matching of blood groups; however, blood banking is not routine for ferrets. This study aimed to determine the stability of ferret blood stored at 4°C in an anticoagulant citrate–phosphate–dextrose solution with adenine (CPDA).

Blood samples were taken from 2 male donors once a month for 5 months and stored for 4 weeks in polyethylene terephthalate (PET) blood tubes at a ratio of 6 mL blood:1 mL CPDA. Glucose, pH, lactate, potassium, and sodium were measured in samples at days 0, 7, 14, 21, and 28. Hematocrit measurement and microscopic blood smear examinations were also performed.

Evidence of RBC deterioration was observed more rapidly in the ferret samples than in that previously described for canine or human samples, with significant biochemical and morphological changes by day 7 and hemolysis evident by day 21. Although further studies are needed, these results indicate that ferret blood stored in CPDA should not be transfused after 7 days.

Commentary
Veterinary blood transfusions are not new science, but bank programs are currently limited to dogs, cats, and other domestic animals. Successful transfusions have been reported in many exotic species (eg, ferrets, tortoises, rodents, birds). However, little is known about storing blood from nontraditional species; with advancements in exotic animal medicine, this research is immediately usable in practice. With continued research, routine transfusions should be an option in virtually any species.—Adolf Maas, DVM, DABVP (Reptile & Amphibian)

Source
A 5-year-old neutered cat developed neurologic signs subsequent to rapid resolution of azotemia after treatment for urinary obstruction, suggesting a process similar to dialysis disequilibrium syndrome (DDS). At hospital admission, the cat was stabilized, a urinary catheter was placed to relieve obstruction, and IV fluid therapy was initiated to help reverse significant hyperkalemia and azotemia. Several hours later, the patient had a grand mal seizure, subsequently developing respiratory arrest requiring endotracheal intubation. After a bolus of hypertonic saline, his neurological status improved and he began breathing on his own. Following a second neurological episode, a CRI of hypertonic saline was started; eventually, the cat became more responsive and had no further seizures.

DDS has been reported in human and veterinary patients undergoing dialysis for renal disease and was initially associated with rapid decrease in blood urea nitrogen concentrations. This is the first known report of DDS-like signs secondary to treatment for urethral obstruction. Currently, 2 theories exist to explain the pathogenesis of DDS; both assume an initial hyperosmolar state and development of a gradient between the blood and cerebral tissue. When a rapid reduction in peripheral osmolality occurs via dialysis, there is a shift of fluid intracellularly, causing neuronal swelling, increased intracranial pressure, and the resulting clinical signs. Treatment is typically achieved through the administration of an osmotic agent.

**Commentary**

Dialysis and continuous renal replacement therapy (CRRT) are becoming more readily available, and awareness is increasing. The blocked cat in this report (although he was not dialyzed) will be familiar to many, although his complication—DDS—likely will not. I have seen many blocked cats but never treated one that developed postobstructive seizures or dialysis disequilibrium. This case is useful to bridge the gap between the familiar (blocked cat) and the unfamiliar (dialysis and CRRT). This study is helpful to increase sentience of this rare complication of a common disease and raise awareness about a possible complication of a promising treatment modality.—Tony Johnson, DVM, DACVECC

**Source**

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Source

Tooth Extraction: Lingering Roots, Lingering Pathology

Medical records of patients referred to a dental specialty center for reasons other than incomplete dental extraction were reviewed for specific reference to complete extractions of the maxillary fourth premolars (108 and 208) and the mandibular first molars (309 and 409). Seventy-four dogs and 42 cats were included; extraction sites were radiographed to identify root fragments and associated pathology. An additional 25 dogs and 25 cats that had extractions with preoperative and postoperative radiography were included as a control group.

Sixty-one dogs (82.4%) had retained tooth roots, with pathology identified in 39 of these cases (54.9%). Retained tooth roots were found in 39 cats (92.8%), with associated pathology in 27 (69.2%). Periapical pathology included severe osseous ankylosis, sclerosis, and alveolar bone loss. No patients with radiographically documented complete extractions showed evidence of pathology. Radiographically evident periapical pathology indicates infection of the root fragment leading to either granuloma or abscess formation, making complete root extraction necessary. However, crown amputation and intentional root retention may be preferable for cases of feline type II resorption.

This study occurred in a state that allows licensed veterinary technicians to perform extractions, and the authors speculated that the majority of the extractions studied may have been thus performed. The study’s results highlighted the importance of dental training and postoperative dental radiography.

■ Commentary
Dental radiography is a popular subject and, in addition to the ability to accurately evaluate radiographs, is recognized as a valuable diagnostic tool. This study demonstrated a tremendous discrepancy between believing a tooth has been completely extracted and actually completely extracting a tooth. The underwhelming emphasis on veterinary dental education and lax practice laws that permit individuals without advanced training to perform extractions contribute to a high prevalence of root fragments following extraction, and a high prevalence of those fragments demonstrating evidence of pathology. Accurate identification and diagnosis are important steps toward ensuring every patient has a functional, comfortable bite.—Christopher Snyder, DVM, DAVDC

Source
Reconsidering *Ancylostoma ceylanicum*

Recent epidemiologic surveys have determined that *Ancylostoma ceylanicum* is the second most common hookworm species infecting humans in Asia. *A. ceylanicum* was originally found in humans in such low numbers as not to cause clinical concern. However, where *A. ceylanicum* is endemic in dogs and cats, its prevalence in humans is rising.

Experimental infection of human volunteers with *A. ceylanicum* produced skin lesions in those infected cutaneously and abdominal symptoms (eg, GI discomfort, flatulence, diarrhea) in all who developed a patent infection. Natural infection is also under investigation; in some human patients, a single visualized and positively identified *A. ceylanicum* worm was implicated as the cause of symptoms (eg, abdominal pain, nausea, poor appetite). As with other zoonoses and public health concerns, it is important to take a One Health approach to controlling *A. ceylanicum* by combining chemotherapeutic interventions with improved sanitation. This is particularly important in communities where the parasite is endemic and humans live in close contact with dog and cat reservoirs (eg, Southeast Asia, Northern Australia, South Africa).

**Commentary**

Although *A. ceylanicum* is not endemic in North America, veterinarians should know important aspects of this parasite. Because of recent molecular diagnostic advances, we now know *A. ceylanicum* is the second most common hookworm infecting humans in Asia. Human infections have been reported in almost all regions where *A. ceylanicum* is known to infect dogs and cats. While anthelmintic therapy in humans has been endorsed, and likely controls morbidity, it most likely does not impact reinfection rates. Parasite populations vary from region to region; however, using proper treatment and preventive strategies for community dogs and cats has a positive impact on *Ancylostoma* spp infections in humans. —Chris Adolph, DVM, MS

**Source**

AVMA Annual Convention ■ July 25–July 29, 2014

The AVMA represents more than 85,000 veterinarians across the United States with the goal of advancing the art and science of veterinary medicine. The AVMA Annual Convention offers interactive laboratories, symposia, and other CE opportunities.

Bad Dog or Bad Vet? Managing the Aggressive Patient During the Veterinary Visit
Aggression is a dog’s typical response to the threat posed by a veterinarian during an examination. Forceful handling and restraint are often necessary to maintain the safety of doctor and patient. Behavioral patterns noted with the stress response include escape (flight), aggression (fight), hypervigilance or tonic immobility (freeze or fright), and/or displacement (fidget). It is beneficial for the owner and the doctor to recognize specific behaviors that indicate early signs of increasing stress and arousal (eg, lip licking, yawning, paw lifting, flattened ears, dilated pupils, piloerection). Should any of these signs be noted, the team should adjust the approach to make the situation less threatening to the dog. Owners should be encouraged to participate in operant and classical conditioning with their dog at home, such as repeatedly touching sensitive areas on the dog’s body. Anxiolytics or tranquilizers may be helpful if administered at home before the veterinary visit; a home trial using the medication should be performed to assess the dog’s response. These drugs may not be as effective if administered after the dog has entered panic mode.—Siracusa C

The Use of Ketamine in Clinical Practice: Anesthesia or Analgesia?
Chronic or repetitive noxious stimuli translate into electrical impulses that are transmitted to the dorsal horn of the spinal cord. Excessive release of excitatory neurotransmitters (eg, glutamate) stimulates N-methyl-D-aspartate (NMDA) receptors. Current evidence shows that long-term changes in the CNS after injury to peripheral tissue and nerves are dependent on NMDA receptor activation. NMDA antagonists (eg, ketamine) contribute to multimodal analgesia if used in conjunction with other analgesics; doses of ketamine associated with NMDA antagonism are subanesthetic and lower than those required for induction of anesthesia. Used as part of a multimodal analgesic plan in dogs, ketamine has been shown to improve feeding behavior after surgery and has been associated with analgesia of longer duration. In cats, ketamine may decrease inhalant anesthetic requirements and provide analgesia to cats that respond poorly to opioids.
—Steagall PVM

Your Pet Has a Murmur
Cardiac murmurs are a common finding on routine and illness examinations in dogs and cats. They are usually associated with turbulent or high-velocity blood flow in the heart or great vessels caused by valvular incompetence or stenosis, or the presence of a shunt. Murmurs are classified in several ways, including timing in the cardiac cycle, intensity or loudness, point of maximal intensity, degree of radiation, and pitch and quality. In feline patients, innocent murmurs are common; benign dynamic right ventricular outflow tract stenosis is the most important. Murmurs that disappear as the heart rate slows are more likely to be innocent. Patients with a history suggestive of primary heart disease, a continuous or diastolic murmur, cardiomegaly on radiographs, or additional examination findings consistent with cardiac disease (eg, gallop sound or arrhythmia) should warrant a more thorough investigation, such as echocardiography. In dogs, murmurs softer than grade IV/VI auscultated for the first time in patients <4
diagnosis; for instance, developmental orthopedic disease and physeal fractures occur in growing dogs, while degenerative joint disease, fractures, and luxations are common in adults. Large-breed dogs have higher incidence of elbow and hip dysplasia, OCD, hypertrophic osteodystrophy, and panosteitis, while patellar luxation and Legg–Calvé–Perthes disease are commonly seen in smaller breeds. Vehicular trauma affects more intact male dogs. Osteosarcoma is seen more frequently in older large or giant breeds. A thorough history and observation of the patient at rest and in motion should precede a meticulous physical examination, at which time muscle atrophy, weight shifts during evaluation, abnormal reflexes, lack of anal tone, crepitus, range of motion, effusion, pain, and instability should be noted to pinpoint the affected limb. Radiographs should be used to confirm the working diagnosis. Sedation improves positioning and decreases exposure. Collimation is recommended, as is comparison of opposite limbs. If the diagnosis is still unclear, symptomatic treatment is acceptable in an adult dog. Delaying diagnosis in a puppy is not advised. Referral may be necessary. More specialized tests may be needed once the site of the lameness has been identified.—Marcellin-Little DJ

## Treatment of the “Common Mass”: Mast Cell Tumors & Soft Tissue Sarcomas

Canine cutaneous and subcutaneous masses can range widely from benign to different grades/types of malignant behavior; the two most commonly seen are mast cell tumors (MCTs) and soft tissue sarcomas (STS).

MCTs are more common; their cells exfoliate easily, so a fine-needle aspiration (FNA) is a useful first diagnostic step. Once diagnosis is made, FNA of the draining lymph node follows, with inclusion of an abdominal ultrasound when necessary to evaluate intraabdominal lymph nodes, liver, or spleen. Thoracic radiographs are an important preoperative consideration, especially in older patients. Surgical removal is the most important first step and must extend beyond the palpable mass in an attempt to include all abnormal tissue, with second surgeries necessary if resection proves incomplete. Histopathologically identified prognostic factors help the clinician decide on further therapy since both types of tumors can be locally invasive and have metastatic potential. Neither chemotherapy nor radiation is recommended as primary treatment for gross disease.

—Ross SJ
Chemotherapy is recommended as adjunct therapy for higher grade MCTs and STS, as well as MCT cases with existing metastatic disease. Radiation therapy may be pursued with incomplete resection of MCTs and in conjunction with surgery in the case of STS. Prognosis for STS is generally good to excellent. For MCT, prognosis varies depending on several factors, including histologic grade and particular cellular characteristics (eg, mitotic index).—Culp WTN

Update on Compounding for the Veterinary Patient

Compounded drugs are approved drugs manipulated in various ways to differ from a labeled product; for example, by dilution, mixing to allow delivery by a different route, conversion to a different form, combining one or more drugs, adding a nonapproved drug component (eg, flavor), or creation of a product from a bulk drug. Compounded drugs should be used only when a veterinarian perceives a legitimate medical use that justifies all risks. The FDA Center for Veterinary Medicine provides regulatory surveillance and enforcement for drug compounding in veterinary medicine. This agency acts under the authority of the Animal Medicinal Drug Use Clarification Act of 1994, which legitimizes compounding under certain criteria, including good pharmacy and compounding practices, adherence to relevant scientific literature, and applicable state/provincial laws. Difficult-to-compound products include sterile, extended-release, and transdermal products.

Products suited to compounding include drugs with a wide therapeutic index, drugs with good clinical data pertaining to target species and conditions, and drugs that can be therapeutically monitored. Commonly compounded veterinary drugs include prednisolone oral liquid, metronidazole suspension, potassium bromide, and methimazole oral liquid. Compounded drugs must possess purity, potency, and stability. Other requirements for legitimate compounding practices include: a valid veterinarian–patient–client relationship, compounding performed by a veterinarian or pharmacist, rational therapy originating from a veterinarian, presence of informed consent, and adequate labeling and records.—Johnson R

The New Pathogens of CIRDC: Way More Than Bordetella

This session outlined environmental and infectious factors contributing to canine infectious respiratory disease complex (CIRDC). Environmental factors in shelters include close physical proximity, poor air handling, sanitation difficulties, continued exposure to new animals and pathogens, and stress.

Bordetella bronchiseptica accounts for up to 25% of CIRDC cases, but other infectious causes are numerous. Other bacterial pathogens include Mycoplasma and Streptococcus equi subsp zooepidemicus. Many Mycoplasma spp are commensal organisms, but their exact role in CIRDC is unclear; culture is seldom performed unless requested. These species often evade immune responses, likely cause chronic low-grade infection, and are susceptible to doxycycline or azithromycin. S zooepidemicus can cause severe acute to peracute infection, can be highly contagious, and is sometimes fatal. It is characterized by suppurative and necrotizing pneumonia; human infection is possible. Viral pathogens include canine adenovirus and parainfluenza, which are highly contagious but less prevalent because of vaccination. Canine respiratory coronavirus causes self-limiting tracheobronchitis often worsened by coinfection; diagnosis is determined by PCR. Canine distemper, much less widespread because of vaccination, may result in GI and respiratory signs. Canine influenza has a short incubation period, and exposure may be widespread. Diagnostic testing can be difficult because of timing and vaccination status. In suspected kennel outbreaks of CIRDC, at least 10%–30% of the affected population should be tested; PCR panels are helpful. Antibiotics are indicated for pneumonia but not necessarily for tracheobronchitis. Treatment of CIRDC is mostly supportive, and frequently disease is self-limiting.—Cohn LA

Parasitology Update: New Parasites, New Problems

The protozoan Trypanosoma cruzi is a zoonotic parasite that affects humans and dogs. It is transmitted through the feces of blood-feeding triatomine bugs (kissing bugs). Dogs may also become infected through ingestion of an infected bug through transfusion or transplacentally. Infection can cause Chagas disease; in dogs, this can lead to cardiac electrical conduction disorders, chronic progressive myocardial disease, or fatal myocarditis. In the U.S., Chagas disease is more prevalent in the south and southwest.

Leishmania spp, another protozoan parasite, causes visceral or cutaneous disease in dogs and cats. Biting sand flies are the vector; transmission occurs through blood feeding on dogs, cats, some wild mammals, and humans. An outbreak occurred more than 10 years ago in U.S. foxhounds; continued transmission among this breed is not fully understood.

Encephalitozoon cuniculi is a microsporidian parasite that most commonly affects rabbits and rodents, but it may also infect dogs. Infected dogs can transmit the spores in their urine and feces. Infection occurs through spore ingestion. The parasites localize in vascular endothelial cells and renal tubular epithelium and glomeruli. The disease produces an encephalitis–nephritis syndrome.

Heterobilharzia americana is a trematode parasite closely related
to the human parasite *Schistosoma mansoni*. It is found in many wild mammalian hosts in the mid-Atlantic and southern U.S. Diagnosis in dogs is difficult and is often only done postmortem. The parasite invades the mesenteric blood vessels of the abdominal cavity and can cause chronic granulomatous inflammation and fibrosis.—Snowden K

**Solving the Problems of the Diabetic Cushingoid**

Hyperadrenocorticism (HAC) diagnosis can be difficult in diabetic patients, as clinical signs and biochemical abnormalities often overlap. Insulin resistance from nonadrenal illness should be ruled out first. The author performs ACTH stimulation testing for initial HAC screening in relatively well-controlled diabetic dogs. False-positive results can occur in chronically stressed or unregulated diabetics. The low-dose dexamethasone suppression test has good sensitivity but is subject to false-positive results. The author often runs both tests, but only in well-regulated diabetics exhibiting classic HAC clinical signs. Treating concurrent diabetes mellitus (DM) and HAC is challenging. Excess cortisol increases hepatic gluconeogenesis, inhibits beta cell function, and causes insulin resistance. As HAC is controlled, these effects vary unpredictably.

Careful diabetic monitoring is essential during treatment induction and maintenance phases to avoid life-threatening hypoglycemia. Some clinicians empirically reduce the patient’s insulin dose by ≥25% before initiating treatment. This author maintains the current dose but monitors urine glucose twice daily and performs serial blood glucose curves; insulin dosage is adjusted accordingly. Once control of both diseases is attained, patients are monitored with ACTH stimulation testing and diabetic evaluation after 1 and 3 months, then every 4–6 months. These patients frequently develop concurrent illnesses (eg, pancreatitis, urinary tract infection), which can affect regulation. Cats with HAC frequently have concurrent DM. As with dogs, screening for HAC should be done on stable patients with good glycemic control. Monitoring during HAC treatment is especially important; 6/9 cats in one study required an average insulin dose reduction of 36% within 2 months of starting trilostane therapy.—Bugbee AC

**A New Option for Healthy Fat**

Dechra has announced the availability of Eicosa 3FF SnipCaps Omega-3 Fatty Acid Capsules as part of their existing fatty acid product line. The new capsules are available in 2 strengths. The small SnipCaps are suitable for dogs under 60 lbs and cats; whereas the large SnipCaps are suitable for dogs weighing more than 30 lbs. Each strength capsule comes in 60 and 120 count bottles and delivers ~180mg EPA per 10 lbs and 120 mg DHA per 10 lbs. For more information, visit dechra-us.com.—Press release 8/2014

**Loyalty Has Its Rewards**

The specialists of Vetlocity announced the launch of their new company, offering a unique automated loyalty program. The Vetlocity platform makes promotion, practice management system integration, sign-up, and administration fast and easy-to-manage and offers analytics capabilities; the company’s proactive services facilitate the validation, qualification, and processing steps required for smooth program execution. Find out more at vetlocity.com.—Press release 10/2014

**Connect with an App**

IDEXX Laboratories announced the availability of the IDEXX VetConnect PLUS mobile app for Android devices. The VetConnect PLUS mobile app was introduced to iPhone users earlier this year. The new Android app further supports the company’s Strengthen the Bonds initiative, which is designed to help veterinarians deliver exceptional care to pets while sustaining a healthy practice. See the complete story at IDEXX.com.—Press release 9/2014

**Flea Relief for Homeless Pets**

Veterinary Products Laboratories, makers of Ovitrol X-Tend Flea & Tick Spot On products for dogs and cats, has donated flea and tick treatments ($15,000 value) to 5 animal shelter organizations located in flea prevalent regions for a total donation of $75,000. The donation will help protect 120 pets from fleas and ticks for an entire year. Read more about Ovitrol X-Tend Flea & Tick Spot On at ovitrolxtend.com.—Press release 10/2014
Hip Dysplasia in a Red Fox
Current research at the Illinois State Museum in Springfield includes a report Suspected Hip Dysplasia in a Red Fox. The report describes the hip joints of a 20th century red fox (Vulpes vulpes) curated at the Research and Collections Center. Features that researchers noted are similar to hip dysplasia in domestic dogs. Potential consequences of hip dysplasia could include impaired movement and hunting ability, thus reducing ability to compete for food. These findings suggest a need for research to understand potentially important ecological implications. Discover more at museum.state.il.us.—Press release 10/2014

Therapy Dog Wins First Nationwide Books & Barks Contest
Pets Best Insurance Services announced a therapy dog from Newtown, Connecticut, has been selected as the winner of the agency’s first Books & Barks contest. Kona, a therapy dog that regularly visits the students of Reed Intermediate School, won the nationwide contest, which was created to recognize and bring awareness to the inspirational work of therapy dogs in classrooms and libraries across the nation. Pets Best awarded $1000 to Reed Intermediate School and $500 to a pet therapy organization selected by Kona’s owner and handler. Learn more about the contest at petsbest.com.—Press release 10/2014

Good News for Goldens
The Golden Retriever Lifetime Study is seeking 3000 participant for a long-term study to better prevent, diagnose, and treat cancer and other canine diseases. All 48 contiguous states are represented. Join the 2000 golden retrievers already enrolled (including Watson, shown here) and help Morris Animal Foundation reach 3000 strong in the largest and longest veterinary study ever conducted. Learn more at CanineLifetimeHealth.org.—Press release 10/2014

Another Dose for Management of Bacterial Diseases
Norbrook Laboratories announced the introduction of new Enroflox (enrofloxacin) Injection for Dogs 2.27%. Enroflox Injection is a fluoroquinolone designed for the management of bacterial diseases, with broad-spectrum activity against both gram-negative and gram-positive bacteria, including those causing dermal, urinary, and respiratory tract infections. Enroflox Injection will be available in 20 mL and 100 mL vials. Each mL of injectable solution contains 22.7 mg of enrofloxacin and is available for dogs only. For more information, visit norbrookinc.com.—Press release 10/2014

Back on the Market
Zoetis announced that Terramycin (oxytetracycline hydrochloride) Ophthalmic Ointment with Polymyxin B Sulfate is once again available to veterinarians nationwide. Terramycin is indicated for the treatment of superficial ocular infection and bacterial inflammatory conditions in dogs and cats. A topical antibiotic, not a steroid, Terramycin offers broad-spectrum effectiveness against both gram-positive and gram-negative organism, including Pseudomonas aeruginosa. Read more about Terramycin at zoetisus.com/products/cats/terramycin-opthalmic-ointment.aspx.—Press release 10/2014

Plans for New Cancer Center Underway
Colorado cancer researchers and medical doctors announced they are launching a $200,000 feasibility study as a key step to building the nation’s first carbon-ion radiotherapy research and treatment facility in Aurora, where researchers and colleagues hope to investigate and provide human and animal patients leading-edge radiation therapy effective against the deadliest cancers and currently only available in Europe and Japan. The project’s collaborators include cancer experts at University of Colorado and Colorado State University. They have signed a memorandum of understanding to pursue the project with University of Colorado Health’s Poudre Valley Hospital in Fort Collins and with carbon-ion radiotherapy pioneers at the National Institute of Radiological Sciences (NIRS) in Japan, the first nation to build a facility of this kind. Learn more about this project at news.colostate.edu.—Press release 9/2014

Send Information
For Practice Hotline to editor@cliniciansbrief.com
Demystifying Tests for Hyperadrenocorticism

Alex Gallagher, DVM, MS, DACVIM (Small Animal)
University of Florida

You have asked…
How do I test a dog for hyperadrenocorticism?

The expert says…

Hyperadrenocorticism (HAC) is a common differential diagnosis in dogs with polyuria/polydipsia (PU/PD), chronic skin issues (eg, alopecia, recurrent pyoderma), increased alkaline phosphatase (ALP) activity, weight gain, or hepatomegaly (Figure 1). Veterinarians must often decide when to test for HAC and which test to use.

When to Test for Hyperadrenocorticism
When evaluating the utility of a diagnostic test, test sensitivity and specificity must be considered. In addition, positive predictive value (PPV), which indicates the likelihood that an individual with a positive test result truly has the disease, should be considered. PPV is influenced by disease prevalence in the population being tested. For instance, if every dog that enters the clinic (a population with low HAC prevalence) is tested for HAC, the likelihood that a positive test result represents a true positive would be low (ie, a low PPV); however, if only dogs that have PU/PD, increased ALP activity, a stress leukogram, and alopecia (a population with a higher HAC prevalence) are tested, a positive test result is more likely accurate (ie, a high PPV).

To maximize the usefulness of HAC tests, only dogs for which there is a clinical suspicion of disease based on history, physical examination, and routine laboratory findings (Tables 1 and 2, next page) should be tested. A diagnosis of HAC should never be made on the basis of adrenal function testing or imaging alone. Ideally, dogs should not be tested when other significant, concurrent diseases are present, as this increases the risk for false-positive results. However, finding

MORE

ALP = alkaline phosphatase, eACTH = endogenous ACTH, HAC = hyperadrenocorticism, PD = polydipsia, PPV = positive predictive value, PU = polyuria
an unexpected adrenal mass on imaging for a different presentation should prompt testing for HAC.

Which Test Is Best?
None of the currently available tests for HAC have 100% diagnostic accuracy (Table 3). Tests can be separated into screening and differentiating tests. Screening tests are used to support the clinical diagnosis of HAC and, rather than positive or negative, can be thought of as consistent with or not consistent with an HAC diagnosis. If a high suspicion for HAC exists but an initial screening test is negative, a different screening test should be performed.

Commonly used screening tests include the urine cortisol:creatinine ratio (UCCR), low-dose dexamethasone suppression test (LDDST), and the ACTH stimulation test. Differentiating tests are used to help differentiate pituitary-dependent (PDH) from adrenal-dependent hyperadrenocorticism (ADH) and should only be performed after a diagnosis of HAC is established. Differentiating tests include LDDST, high-dose dexamethasone suppression test (HDDST), endogenous ACTH (eACTH) measurement, and abdominal ultrasound.

The initial screening test should be partly chosen based on the circumstances of the case. In dogs with a known adrenal tumor, the LDDST should be the initial screening test because of its higher sensitivity in ADH compared with the ACTH stimulation test. Dogs with suspected iatrogenic HAC should be screened with the ACTH stimulation test, as it is the only test that can diagnose this condition. If testing must be done with concurrent disease present, the LDDST may be best, as a negative test likely excludes the presence of HAC. A positive LDDST requires further testing to confirm the diagnosis. If there is a low likelihood of HAC result, then the UCCR can be used as an easy, inexpensive screening test. When choosing between the LDDST and the ACTH stimulation test, the author does not recommend one test over the other except for cases as previously noted. Rather, it is more important to understand the sensitivity and specificity of the tests (Table 3) and interpret the results in light of the clinical findings.

Urine cortisol:creatinine ratio
The UCCR is a simple and inexpensive screening test best performed on a urine sample from a patient’s first urination of the day collected at home by the owner. The sample should not be collected within 2 days of a stressful event (eg, a clinic visit).

To maximize the usefulness of HAC tests, only dogs for which there is a clinical suspicion of disease based on history, physical examination, and routine laboratory findings should be tested.

<table>
<thead>
<tr>
<th>Common</th>
<th>Less common</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>PU/PD</td>
<td>Lethargy</td>
<td>Thromboembolism</td>
</tr>
<tr>
<td>Polyphagia</td>
<td>Thin skin</td>
<td>Cruciate ligament rupture</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>Comedones</td>
<td></td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>Hyperpigmentation</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>Poorly controlled diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td>Panting</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1 Clinical Findings in Canine Hyperadrenocorticism

<table>
<thead>
<tr>
<th>Chemistry</th>
<th>CBC</th>
<th>Urinalysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased ALP, ALT</td>
<td>Mature neutrophilia</td>
<td>Low urine specific gravity</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Lymphopenia</td>
<td>Proteinuria</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Eosinopenia</td>
<td>Possible pyuria/bacteriuria</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>Thrombocytosis</td>
<td></td>
</tr>
</tbody>
</table>

ADH = adrenal-dependent hyperadrenocorticism, ALP = alkaline phosphatase, eACTH = endogenous ACTH, HAC = hyperadrenocorticism, HDDST = high-dose dexamethasone suppression test, LDDST = low-dose dexamethasone suppression test, PD = polydipsia, PDH = pituitary-dependent hyperadrenocorticism, PU = polyuria, UCCR = urine cortisol:creatinine ratio
The sensitivity of this test is good (90%–100%) with a normal ratio making HAC unlikely. However, the specificity of the UCCR is poor (20%–40%), particularly in dogs with concurrent diseases.1-3 Hence, the UCCR is best used as a screening test in dogs for which the clinical suspicion of HAC is low; positive results should be investigated further with other screening tests.

Low-dose dexamethasone suppression test

The LDDST can be used as a screening and a differentiating test. In the recent ACVIM Consensus Statement, the LDDST was recommended as the initial screening test in dogs suspected to have HAC because of its better sensitivity compared with the ACTH stimulation test.4

The LDDST is performed by collecting blood for a baseline cortisol concentration, administering 0.01–0.015 mg/kg of dexamethasone IV, and collecting additional blood samples at 4 and 8 hours post-injection (see How to Perform an LDDST). As a screening test, only the 8-hour cortisol concentration is initially evaluated. If the 8-hour postdexamethasone cortisol level is <1.4 µg/dL, appropriate suppression has occurred and the test is not consistent with HAC. However, it has been recommended that this cut-off value be reevaluated because of changes in assays and populations used in early studies.4 A cut-off of 1.0 µg/dL has been suggested. Using a cut-off of 1.4 µg/dL, the LDDST has a good sensitivity (85%–100%), but the specificity is only fair (44%–73%).3, 5-8 An inverse pattern on the LDDST has been described where the 8-hour cortisol shows suppression but the 4-hour cortisol does not.9 While this pattern is suspicious for HAC, further testing is recommended for definitive diagnosis.

If there is no suppression of cortisol at 8 hours, then the test is consistent with HAC and the LDDST results are further used as a differentiating test. The baseline and 4-hour cortisol levels are evaluated; if the 4-hour cortisol is <1.4 µg/dL or is <50% of the baseline cortisol, the LDDST is consistent with a diagnosis of PDH. Additionally, suppression of the 8-hour cortisol to <50% of baseline has also been reported to be consistent with PDH, but the author prefers to verify this with an alternate differentiating test such as abdominal ultrasound. If none of these criteria is met, then either PDH or ADH may be present and further testing is needed.

ACTH stimulation test

The ACTH stimulation test is the only test that can diagnosis iatrogenic HAC. The test is performed using a synthetic ACTH (eg, cosyntropin, tetracosactrin) administered at a dose of 5 µg/kg IV. Cortrosyn can also be administered IM at the same dose. After reconstitution, unused product can be separated into aliquots in plastic syringes and frozen for up to 6 months (see How to Perform an ACTH Stimulation Test, next page). Compounded ACTH gels are not recommended because of variability in quality and timing of maximum stimulation of the adrenals. Blood samples are collected before and 1 hour after administration of ACTH for cortisol determination. Post-ACTH cortisol concentrations above the laboratory reference range are consistent with HAC. Cortisol concentrations that are only marginally increased should be interpreted with caution, especially in patients with minimal signs of HAC or with concurrent diseases. Dogs with iatrogenic HAC typically have a normal–low normal baseline cortisol with no-to-minimal

The low-dose dexamethasone suppression test (LDDST) can be used as a screening and a differentiating test.

### Table 3

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>UCCR</td>
<td>90–100</td>
<td>20–40</td>
<td>Good screening test when HAC unlikely</td>
</tr>
<tr>
<td>LDDS</td>
<td>85–100</td>
<td>44–73</td>
<td>Good initial test because of high sensitivity; best initial test for ADH; can also be a differentiating test</td>
</tr>
<tr>
<td>ACTH Stimulation</td>
<td>60–85</td>
<td>60–90</td>
<td>Only test that identifies iatrogenic HAC</td>
</tr>
</tbody>
</table>

*The Table 3 is a Comparative Aspects of Screening Tests for Canine Hyperadrenocorticism.*

### How to Perform an LDDST

- Collect blood for a baseline plasma cortisol concentration
- Administer 0.01–0.015 mg/kg of dexamethasone IV
- Collect additional blood samples at 4 and 8 hours

The low-dose dexamethasone suppression test (LDDST) can be used as a screening and a differentiating test.
increase post-ACTH despite having findings consistent with HAC. Test sensitivity ranges from 60% to 85% with poorer sensitivity in dogs with ADH compared to PDH. For this reason, LDDST is recommended as the initial screening test in any dog in which an adrenal mass is already known or suspected to be present. Specificity ranges from 60% to 90%, as nonadrenal illness can result in false-positive results.3,6, 10-12

High-dose dexamethasone suppression test
The HDDST is performed similarly to the LDDST with samples collected for cortisol measurement at baseline and then 4 and 8 hours after dexamethasone injection, but the dose of dexamethasone is 0.1 mg/kg IV. This test should only be performed once a diagnosis of HAC is established. Suppression occurs when either the 4- or the 8-hour cortisol is <1.4 µg/dL or <50% of the baseline. Suppression is consistent with PDH. A lack of suppression does not exclude PDH and, in fact, there is still almost an equal likelihood of PDH or ADH.

Endogenous ACTH measurement
Measurement of eACTH may be used to differentiate ADH and PDH. In ADH, eACTH concentration is typically low or unmeasurable. In PDH, eACTH may be high or normal because of the pulsatile release of ACTH. Sample handling is critical for accurate measurement. Plasma samples should be collected, frozen immediately, and shipped overnight to a laboratory on ice/dry ice so they remain frozen during transit. Poor sample handling can result in degradation of eACTH and artificially decreased measurements. For this reason, the author does not recommend routine use of eACTH measurement as a differentiating test.  

How to Perform an ACTH Stimulation Test
- Use a synthetic ACTH (eg, cosyntropin, tetracosactrin)
- Reconstitute the product*
- Administer a dose of 5 µg/kg IV. Cortrosyn can also be administered IM.
- Compounded ACTH gels are not recommended because of variability in quality and timing of maximum stimulation of the adrenals.
- Collect blood samples before and 1 hour after administration of ACTH for plasma cortisol determination

* Unused product can be separated into aliquots in plastic syringes and kept frozen for up to 6 months.

See Aids & Resources, back page, for references & suggested reading.

ADH = adrenal-dependent hyperadrenocorticism, eACTH = endogenous ACTH, HDDST = high-dose dexamethasone suppression test, LDDST = low-dose dexamethasone suppression test
Hyperadrenocorticism in Dogs

Alex Gallagher, DVM, MS, DACVIM (Small Animal)
University of Florida

Profile

Definition

- Hyperadrenocorticism (HAC) is caused by excess circulating cortisol or other steroid hormones.

Signalment

- Endogenous HAC occurs in middle-aged to older dogs.
  - Although the reported age range is 6 months to 20 years, almost all dogs with HAC are over 6 years of age.
- Poodles, dachshunds, boxers, and various terrier breeds may have a greater risk of pituitary-dependent hyperadrenocorticism (PDH).
- PDH occurs more frequently in smaller dogs, with 75% of dogs with PDH weighing <20 kg.
- There is no sex predilection for PDH.
  - Female dogs may have increased risk for adrenal-dependent hyperadrenocorticism (ADH).

Causes

- Endogenous HAC is caused by an ACTH-secreting pituitary tumor (~85% of dogs) or a benign or malignant adrenal tumor (~15% of dogs).
- Endogenous HAC may rarely be caused by ectopic ACTH secretion from a nonpituitary tumor or food-dependent hypercortisolism.
- Iatrogenic HAC is caused by administration of exogenous glucocorticoids of any form.

History

- Polyuria (PU) and polydipsia (PD) are the most common complaints (~90% of HAC dogs).
- Owners may note polyphagia, weight gain, and panting (50%–90% of dogs).
- Alopecia is common (~60%–75% of affected dogs).
- Lethargy may be noted and associated with muscle weakness, inability to rise.
- In dogs with a pituitary macroadenoma, owners may note behavioral changes (eg, disorientation, pacing, anorexia).

Physical Examination

- A distended or pendulous abdomen (pot-bellied appearance) is commonly noted (Figure 1).
  - Causes include abdominal muscular weakness, hepatomegaly, redistribution of fat, and urinary bladder distension.
- Dermatologic findings include alopecia, thinning of the skin, pyoderma, comedones, hyperpigmentation, and, less commonly, calcinosis cutis (Figure 2, next page).
- Muscle wasting may be present; pseudomyotonia is an uncommon finding, resulting in a stiff rear limb gait with a straight-legged appearance.
- Stupor or mental dullness may be noted in dogs with pituitary macroadenomas.

Diagnosis

Definitive Diagnosis

- HAC diagnosis depends on consistent clinical signs and laboratory findings, exclusion of exogenous administration of glucocorticoids, and testing of adrenal function.
- Adrenal function tests for HAC can be separated into screening and differentiating tests.

Screening Tests

- Screening tests are used to confirm HAC; results can be considered as consistent with or not consistent with diagnosis.
  - If results are not consistent with HAC, but clinical suspicion is high, a different screening test should be pursued or testing.

ACTH = adrenocorticotropic hormone, HAC = hyperadrenocorticism, PD = polydipsia, PDH = pituitary-dependent hyperadrenocorticism, PU = polyuria
Dermatologic manifestations that contribute to HAC suspicion: Close up view of the alopecia of the distal limb and foot (A). Typical dorsal trunk alopecia in a dog with PDH (B). Skin lesions on the cervical region are consistent with calcinosis cutis (C). Alopecia and thinning hair on the caudal aspects of the rear legs and the tail in a dog with PDH. The dog also has moderate muscle atrophy (D). Comedones on the ventral abdomen (E).

Consultant on Call

They should only be used once diagnosis has been established based on screening tests.
- Endogenous ACTH measurement should be low in dogs with ADH and high in dogs with PDH.
- Because of the pulsatile release of ACTH, dogs with PDH may have ACTH concentrations within range.
- ACTH degrades rapidly by plasma proteases. Appropriate sample handling is necessary for accurate results.
- LDDS test is unique in that it can serve as a screening and differentiating test if the 8-hour cortisol is higher than laboratory reference.
- If the 4-hour cortisol is <50% of basal cortisol, the test is consistent with PDH.

Differentiating Tests
- Differentiating tests are used to determine if HAC is caused by PDH or ADH.

Baseline cortisol, dexamethasone (0.01–0.015 mg/kg) is administered IV and additional blood samples obtained at 4 and 8 hours for cortisol measurement.
- This test may be the screening test of choice in dogs with endogenous HAC; the author prefers this test for all dogs with suspected ADH.
- ACTH stimulation test has a reported sensitivity and specificity of 60%–85% and 60%–90%, respectively.
- This is the only test that can differentiate endogenous and iatrogenic HAC.

Repeated in 3–6 months if initial clinical signs are mild.
- Testing should be postponed if significant concurrent illness is present.
- Urine cortisol:creatinine ratio has good sensitivity (90%–100%) but poor specificity (20%–40%).
- This can be used for screening when clinical suspicion is low but HAC is considered in the differential.
- A first-morning urine sample collected 2–3 days or more after clinic visit or other stressful event is recommended.
- Low-dose dexamethasone suppression (LDDS) test has reported sensitivity and specificity of 85%–100% and 44%–73%, respectively.
- After obtaining blood for a
If the 8-hour cortisol is <50% of basal cortisol but greater than the laboratory cut-off for normal suppression, the test may also be consistent with PDH.

Lack of suppression could be caused by PDH or ADH.  
High-dose dexamethasone suppression test is used if there is no suppression on the LDDS test.

If the cortisol at 4 or 8 hours is <50% of the basal cortisol, suppression has occurred and the test is consistent with PDH.

Approximately 25% of dogs with PDH will not suppress on either the low-dose or high-dose test and most dogs with ADH do not suppress.

The author prefers using abdominal ultrasound rather than the high-dose test for differentiating PDH from ADH.

Laboratory Findings

CBC: Common findings include a stress leukogram.

Thrombocytosis and, less commonly, mild erythrocytosis may be noted.

Serum chemistry panel: Increased alkaline phosphatase activity is seen in most (~85%–90%) but not all dogs with HAC.

Alanine aminotransferase activity may be mildly increased.

Other findings include hyperlipidemia, fasting hyperglycemia, decreased blood urea nitrogen, and hypophosphatemia.

Urinalysis: Urine specific gravity is commonly <1.020, but urine concentration can be variable.

Proteinuria is common.

Urinary tract infections are present in 40%–50% of dogs with HAC at initial diagnosis.

Pyuria, stranguria, and hematuria may not be present because of antiinflammatory effects of cortisol.

Urine culture should be performed.

In the absence of other evidence to treat (eg, pyelonephritis), these dogs should be monitored by urinalysis and clinical signs to determine if evidence of true infection occurs once HAC is controlled.

Imaging

Thoracic radiographs: Mineralization of the trachea or bronchi is commonly present.

Radiographs should be evaluated for evidence of metastasis in dogs with ADH.

Pulmonary thromboembolism, although uncommon in dogs with HAC, may be seen.

Abdominal radiographs: Hepatomegaly is seen in 80%–90% of dogs.

Approximately 50% of dogs with ADH will have adrenal glandular mineralization.

Calcium oxalate calculi may be found, and the author prefers abdominal radiographs to screen for uroliths, as ultrasound may miss stones in the ureters or urethra.

The author prefers abdominal ultrasound to help differentiate PDH and ADH.

With PDH, adrenal glands are typically symmetrical and may be normal size or enlarged.

With ADH, there is commonly enlargement and loss of shape of 1 adrenal gland with atrophy of the contralateral gland.

In some cases, the contralateral gland size will be normal.

Ultrasound can be used to evaluate for vascular invasion or evidence of metastasis.

The pituitary can be imaged with CT and MRI for evidence of a tumor.

MRI is more sensitive than CT.

Tumors >1 cm are more readily seen on CT.

Both modalities can be used to assess adrenal tumors and evidence of vascular invasion or metastasis.

The author typically recommends CT or MRI of the pituitary only when other tests are unable to differentiate PDH from ADH or if neurological signs of a macroadenoma are present.

If hypophysectomy or radiation is being considered, advanced imaging should be performed.

Treatment

Treatment for HAC should only be considered once a diagnosis has been established.

The author does not recommend trial therapy to confirm diagnosis.

The clinician should determine if treatment is indicated at diagnosis.

Dogs that are nonclinical or only have mild signs (eg, increased ALP, hepatomegaly, mild alopecia) likely do not need treatment but can be monitored for progression of signs.

Dogs with significant PU/PD, dermatological manifestations, or recurrent infections should be treated.

Hypertension or proteinuria may warrant treatment of HAC, though anecdotally require specific treatment in addition to HAC treatment.

Medical

Medical management is most commonly used for PDH but can be used for ADH if adrenalectomy is not an option.
post-ACTH cortisol is >8 µg/dL, the dose is increased by 25%–50% and the dog rechecked in 2–4 weeks.

- Mitotane
  - Adrenocortolytic agent predominantly targeting the zonas fasciculata and reticularis
  - Treatment includes 2 phases: induction and maintenance.
    - Induction: Initial dose is 30–50 mg/kg PO per day, usually split q12h.
      - Dosage continues until the owner notes a decrease in signs (eg, slower to eat, decreased PU/PD) or a maximum of 7–10 days.
      - ACTH stimulation testing is repeated to assess therapy with the goal of a post-ACTH cortisol concentration being within the baseline cortisol reference range (ie, 1–5 µg/dL).
    - Maintenance: Total daily induction dose is used as the total weekly maintenance dose, typically split over 3–4 days per week.
      - Monitoring should include assessment of signs and ACTH stimulation testing 4 weeks after starting maintenance therapy, then as needed if dose adjustments are made or signs return.

- Trilostane and mitotane are used most commonly; both have similar efficacy in PDH and ADH treatment.
  - Trilostane
    - Competitive inhibitor of 3-β-hydroxysteroid dehydrogenase
    - Reaches peak concentrations 2 hours after administration with return to baseline at 10–18 hours.
    - Administration with food enhances absorption
  - The manufacturer recommends a starting dose of 3–6 mg/kg PO q24h.
    - More recent studies have suggested better and faster control of signs with q12h administration, likely because of the duration of action being <13 hours in most dogs.
    - The author currently uses a starting dose of 1–2 mg/kg PO q12h.
    - Monitoring should include assessment of signs and ACTH stimulation testing 3–6 hours postadministration.
  - Time of testing should remain consistent; initial rechecks are 10–14 days and 30 days after start of therapy.
    - This ensures the initial dose is not causing hypoadrenocorticism.
    - If signs of HAC are not present or if financial constraints exist, the author omits this recheck.
    - At 30-day recheck, signs and an ACTH stimulation test should be evaluated.
    - If signs (PU/PD, polyphagia) are improved and the post-ACTH cortisol is between 3–8 µg/dL, the current dose is maintained and the dog is rechecked in 3 months.
    - If signs persist and the dose versus reinduction).

- In large dogs, the author prefers mitotane because the long-term cost is usually less expensive.
- Owners may prefer the less frequent dosing of mitotane.

Surgical

- Adrenalectomy
  - First choice for ADH
  - Early studies indicated high peri- and postoperative mortality rates, but these have greatly improved.
    - In one study, vena caval invasion, particularly when extensive, was a significant risk factor for postoperative mortality.17

- Hypophysectomy
  - Can be used for treatment of PDH.
  - Most treatments have been performed in Europe but now are being offered in some U.S. facilities.
  - Appears to be an effective treatment with good long-term survival; dogs with pituitary tumors >10 mm have a shorter reported survival.18
  - Hypophysectomy may result in permanent or prolonged diabetes insipidus or secondary hypothyroidism caused by loss of ADH or thyroid-stimulating hormone production, respectively.

Client Education

- Treatment and monitoring of PDH can be expensive, especially in large-breed dogs.
- Once HAC is controlled, signs such as polyphagia and PU/PD usually resolve within 7–10 days.
- Dermatologic changes may take months to resolve.
- Liver enzymes may take longer to resolve and may never fully normalize.
Alternative Therapy

- Ketoconazole inhibits the synthesis of glucocorticoids and androgens and has been used for PDH or ADH treatment but has a much lower efficacy.
- l-deprenyl inhibits monoamine oxidase type B, resulting in increased dopamine concentrations in the pituitary and inhibiting secretion of ACTH from the pars intermedia. Has poor efficacy and therefore is not recommended.
- Radiation therapy has been used in dogs with PDH and appears to improve neurologic signs associated with macroadenomas; it may not improve clinical signs of HAC.

In General

Relative Cost

- Medical therapy for PDH or ADH: $$$–$$$$
- Surgical therapy for PDH or ADH: $$$$$
- Radiation therapy for PDH: $$$$$$

Cost Key

$ = up to $100
$$ = $101–$250
$$$ = $251–$500
$$$$ = $501–$1000
$$$$$ = more than $1000

Prognosis

- Prognosis for dogs with PDH treated medically is good with a reported median survival rate of 2 years based on a 1991 study. 19
  - A more recent study found a survival rate of 900 days for dogs treated with twice daily trilostane versus 720 days for dogs treated with mitotane. 20
  - In the author’s experience, it is uncommon for dogs to die or be euthanized directly related to the consequences of HAC except for those with macroadenomas or in which PU/PD cannot be controlled.
  - Dogs with neurologic signs from a macroadenoma have a poorer prognosis but may do well with radiation therapy and medical treatment. 21

- Prognosis for dogs with ADH is good to excellent with complete excision of adrenal tumors without metastasis.
  - Medical therapy for ADH has a fair to good prognosis with a median survival of 14–15 months recently reported. 22

Hyperadrenocorticism: A Latin American Perspective

While there is knowledge of hyperadrenocorticism (HAC) in Latin America, diagnosing and treating it are difficult. Not all laboratories are able to run even the urine test in most of the region. In many countries, synthetic ACTH is not available, so the ACTH stimulation test cannot be employed. We do use the dexamethasone stimulation test both for screening and for differentiating pituitary- from adrenal-dependent HAC.

Once the diagnosis of HAC is confirmed, treatment is a key challenge: both mitotane and trilostane have not yet entered our markets. We normally depend on ketoconazole, which we know is not ideal, but is better than nothing. The necessity of long-term use presents the problem of significant adverse effects.

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See Aids & Resources, back page, for references & suggested reading.
Differentiating primary cardiac from primary pulmonary disease in small animals with respiratory distress can be daunting. To hurriedly force a patient starving for air into a position to take diagnostic radiographs is a misguided and life-threatening maneuver; instead, immediate therapeutic intervention and a thoughtful diagnostic approach are more effective. The initial approach in treating severe respiratory signs is to provide oxygen supplementation and sedation (eg, butorphanol, 0.4 mg/kg IV or IM; midazolam, 0.2 mg/kg IV or IM) to reduce anxiety associated with dyspnea. IV catheter placement, tracheal intubation, assisted ventilation with 100% oxygen, and suctioning of the airway may be necessary before diagnostic evaluation (even in a patient with congestive heart failure [CHF]).

**Examination**

Perfusion parameters can be altered with both primary cardiac and pulmonary diseases. Mucous membrane color can range from pink to pale pink to cyanotic, regardless of the degree of distress. In most instances, patients with primary cardiac disease have normal to subnormal body temperature, whereas patients with pulmonary disease have normal to increased body temperature.

A key to localizing the origin of a respiratory problem is to identify the breathing pattern (*Table 1*). When auscultating the thorax, it is best to listen to all lung fields before focusing on heart sounds. In this order, louder heart sounds do not desensitize the examiner from hearing finer changes associated with lung disease. Generalized reduced lung sounds may suggest pleural
space occupation with fluid or air. Focal reduction in lung sounds may identify a lobe that is not aerating (eg, torsion). Moist crackles can develop with pulmonary edema from cardiogenic and noncardiogenic causes, as well as with interstitial inflammation. If the crackles are focal, lobar pulmonary disease (eg, aspiration pneumonia, contusion, neoplasia) is more likely. If diffuse moist lung sounds are accompanied by a heart murmur and/or a cardiac dysrhythmia, then pulmonary edema secondary to CHF should be strongly considered. Heart murmurs in cats can be very focal or intermittent, and patience is required when auscultating the heart. Jugular venous distension may also support a primary cardiac problem.

**Patient history**

There is an increased suspicion for primary cardiac disease if there is historical evidence of heart disease, a known heart murmur, exercise intolerance, and/or coughing without activity. A cough may also be supportive of lower airway disease (eg, tracheobronchial inflammation) as well as heartworm disease. Recent history of anesthesia, vomiting, or regurgitation may prompt a directed examination for aspiration pneumonia. History of trauma or exposure to an anticoagulant drug or toxin may initiate investigation for intrathoracic hemorrhage. Anticoagulant intoxication can cause a variety of cardiopulmonary problems, including pulmonary interstitial hemorrhage, hemothorax.
mediastinal hemorrhage, and pericardial effusion—all of which can manifest with respiratory signs. Evidence of rib fractures or other external injuries may accompany pulmonary contusion or hemothorax resulting from trauma. A history of a cough in the dog and cat may prompt evaluation for lower airway disease. A recent prolonged seizure event, brain injury, systemic inflammatory response syndrome, or choking or electrocution may hasten the development of noncardiogenic pulmonary edema.

### Ultrasonography

In the acute care setting, thoracic-focused assessment sonography for trauma (TFAST) can be used during immediate evaluation of the patient with respiratory distress—with minimal handling or positioning—to identify the presence of pneumothorax, pleural effusion, pericardial effusion, atrial enlargement, a hypodynamic heart, and diffuse or infiltrative pulmonary changes (Table 2). Although it requires experience and training, ultrasonographic evaluation of the thorax can be completed rapidly and with the same, or increased, degree of sensitivity and specificity as thoracic radiography when identifying pleural space disease and cardiac dysfunction. A comprehensive echocardiogram is necessary in all cases of suspected cardiac disease to confirm or rule out the presence and type of underlying myocardial disease and guide definitive treatment.

### Thoracic radiography

A number of changes can be identified on thoracic radiographs to help distinguish primary cardiac from primary pulmonary disease; however, radiography should not supercede immediate intervention and stabilization. Information from a comprehensive physical examination and history should be sufficient to initiate reasonable treatment for immediate stabilization before seeking thoracic radiographs. Any pleural space air or fluid should be evacuated before obtaining thoracic radiographs; this not only stabilizes the patient for radiographic positioning but also permits adequate insufflation of the lungs and improves diagnostic quality of lung evaluation. If the patient is intubated and receiving assisted ventilation with oxygen support, then radiographs should be taken during the administration of a gentle inspiratory breath not exceeding 20 cm H2O.

Primary cardiac disease that leads to CHF-related pulmonary edema commonly causes diffuse (perihilar in the dog) or variable (in the cat) interstitial and alveolar patterns. The vertebral heart score (VHS) is an objective method for evaluating the size of the cardiac silhouette (see [Steps to Measure VHS](#), page 58). Certain cutoff values are used to determine whether acute respiratory distress is primarily pulmonary or cardiac in origin and to guide initial therapy for stabilization and planning for mediastinal hemorrhage, and pericardial effusion—all of which can manifest with respiratory signs. Evidence of rib fractures or other external injuries may accompany pulmonary contusion or hemothorax resulting from trauma. A history of a cough in the dog and cat may prompt evaluation for lower airway disease. A recent prolonged seizure event, brain injury, systemic inflammatory response syndrome, or choking or electrocution may hasten the development of noncardiogenic pulmonary edema.

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Right lateral thoracic radiograph of a cat that was presented with labored and rapid breathing synchronous with increased effort on inhalation. The patient had increased breath sounds in all fields and a 3/6 focal systolic heart murmur of the parasternal region. Rectal temperature was 97°F. Butorphanol and furosemide were administered and the patient was allowed to rest with supplemental oxygen before radiography. The radiograph showed a VHS of 9 and pulmonary venous and arterial distension consistent with left-sided heart failure (arrows). Unclassified cardiomyopathy was confirmed with echocardiography.

Right lateral thoracic radiograph of a dog with progressive breathing difficulty and red eyes. Breathing was synchronous with increased effort on exhalation. Expiratory wheezes were heard in all lung fields, and a 1/6 focal systolic heart murmur of the left region was present. Rectal temperature was 100°F. The patient received butorphanol, inhalation therapy with an aerosolized steroid, and rest with supplemental oxygen before radiography. The radiograph showed a VHS of 7, overinflation of the lungs, and peribronchial markings, changes consistent with acute allergic bronchitis. The patient was given injectable corticosteroids and was eupneic within 6 hours.
Steps to Measure VHS

1. Measure the long axis (LA) of the heart from top of the left atrium to the tip of the apex of the ventricle (blue arrow).

2. Measure the short axis (SA) of the heart at the widest part of the left and right heart chambers at the level of the coronary groove (red arrow).

3. Transpose the LA and SA dimensions onto the vertebral column and record the corresponding number of vertebrae (V), starting at the cranial edge of T4 moving caudally.

4. Take the sum of the SA and LA vertebral measurements to find the VHS.

5. In this patient, the VHS = 9.5.

Closing thoughts

Mixed cardiac and pulmonary disease can exist in small animals with respiratory distress. For example, a dog may be presented with a history of mitral valve insufficiency but have clinical and radiographic evidence of aspiration pneumonia following a dental prophylaxis; or, a cat may present with a heart murmur and evidence of lower airway disease based on breathing pattern and thoracic radiographs (Figure 4).

If a primary cardiac problem cannot be ruled out based on history and examination, or there are conflicting signs as to whether respiratory distress is primarily cardiac or pulmonary in origin, a dose of a diuretic (eg, furosemide at 2 mg/kg IV or IM) can be given pending diagnostic imaging. There should be little harm in administering a single dose in a patient that is not significantly dehydrated, and it could be of benefit if there is CHF.

Laboratory testing

A plasma N-terminal pro-B-type natriuretic peptide concentration (NT-proBNP) >1400 pmol/L in the dog and >270 pmol/L in the cat with respiratory difficulty, regardless of the presence of a heart murmur, is more likely to be found with primary cardiac problems than with primary respiratory problems. A blood sample should not be collected until the patient can tolerate restraint. Ultimately, this screening measure takes time to obtain results and does not replace the need for echocardiography to confirm primary cardiac disease.
Cystine Urolithiasis

Gregory F. Grauer, DVM, MS, DACVIM  
Kansas State University

You have asked…  
How do I manage cystine urolithiasis?

The expert says…

Cystine is a nonessential sulfur-containing amino acid made up of 2 cysteine molecules joined by a disulfide bond (Figure 1, next page). Cysteine is found in most high-protein foods, including pork, poultry, eggs, and dairy products, as well as oats and wheat germ. Cystine is absorbed by the small intestine, freely filtered by the glomerulus, and then reabsorbed by an active process in the proximal convoluted tubule. Decreased tubular reabsorption of cystine results in cystinuria. Cystinuria (>75–125 mg cystine/g creatinine) is a predisposing and required factor for—but not the sole cause of—cystine urolith formation; not all dogs with cystinuria form cystine uroliths or even have cystine crystals in their urine; the exact mechanism of cystine urolith formation is unknown. Cystine is most soluble in alkaline solutions, hence cystine uroliths usually form in acidic urine. Cystinuria can be detected with a cyanide–nitroprusside test (available at the University of Pennsylvania), but ampicillin and sulfur-containing drugs in the urine may cause false-positive results.

Cystine crystals are flat, colorless, and hexagonal. The sides of the hexagon may or may not be of equal lengths, and the crystals tend to aggregate in urine sediment, resulting in a layered appearance (Figure 2, next page). Cystine uroliths have intermediate radiodensity; they are typically less radiodense than calcium oxalate and struvite uroliths but more so than ammonium urate uroliths (Figures 3 and 4, page 61). In some cases, contrast urethrocystography or ultrasonography may be necessary to visualize uroliths. Cystine uroliths are usually smooth and spherical and range in size from less than 1 mm to greater than 3 cm in diameter. Affected dogs frequently present with multiple cystine uroliths (Figure 5, page 61). Secondary urinary tract infections are uncommon.

Cystine is most soluble in alkaline solutions, and hence cystine uroliths usually form in acidic urine.
normal in affected dogs unless dietary protein is severely restricted. Were it not for the relative insolubility of cystine in urine and the tendency of cystinuric dogs to form uroliths, cystinuria would have no medical consequence. Cystinuria is inherited as an autosomal recessive trait in Newfoundlands and (likely Labrador retrievers) and is associated with a mutation in the renal basic amino acid transporter (rBAT). Testing for this mutation is available, and breeding management in response to such testing may be responsible for the recently observed decrease in cystine uroliths in the U.S. The rBAT gene mutation has not been found in other breeds with cystinuria. The magnitude of the tubular reabsorptive defect in Newfoundlands is more severe than with other breeds and likely explains why cystine uroliths are observed in younger Newfoundlands and the kidneys. Recurrence for cystine uroliths after dissolution or removal is high in all breeds but tends to be highest in Newfoundlands. 

Urine cystine concentrations should be <200 µmol/g creatinine and/or COLA is <700 µmol/g creatinine to prevent recurrence. Urine cystine and/or COLA concentrations can be measured at the School of Veterinary Medicine at University of Pennsylvania, Section of Medical Genetics.

Dissolution of Cystine Uroliths Cystine uroliths can be removed surgically or mechanically (eg, voiding urohydropropulsion, catheter or stone basket retrieval, lithotripsy, dissolved through medical management). High recurrence rates makes medical management to prevent recurrence necessary, even if uroliths are removed. Before initiating

Dachshund, mastiff, Chihuahua, Welsh corgi, bull mastiff, Scottish deerhound, basset hound, Irish terrier, English bulldog, and Newfoundland breeds are predisposed to forming cystine uroliths. Owing to the greater popularity of these breeds in Europe than in the U.S., the prevalence of uroliths varies geographically (>30% in some European studies vs. 1%–3% in the U.S.). The mean age of dogs with cystine uroliths is 4-6 years. Male dogs (98%) are affected to a much greater degree than females (2%), and most cystine uroliths (98%) are found in the lower urinary tract (bladder and urethra). Newfoundlands appear to be an exception as cystine uroliths form in younger (<1 year of age) males and females and can also be found in the kidney. Maned wolves from South America have also been shown to have a high incidence of cystinuria and are predisposed to forming cystine uroliths. Only 0.15% of the feline uroliths analyzed at the GV Ling Urinary Stone Analysis Laboratory at the University of California, Davis, are cystine. Cystine uroliths in cats are found in male and female domestic shorthair and Siamese breeds over a wide age range (4 months–12 years). As is true in dogs, cystine uroliths form in cats with cystinuria.

Pathophysiology of Cystine Uroliths Cystinuria is abnormal and associated with a defect in tubular reabsorption of cystine. This tubular defect may also extend to other dibasic amino acids, including ornithine, lysine, and arginine (with cystine, collectively known as COLA); however, plasma concentrations of these amino acids are typically

COLA = cystine, ornithine, lysine, and arginine; rBAT = renal basic amino acid transporter
Were it not for the relative insolubility of cystine in urine and the tendency of cystinuric dogs to form uroliths, cystinuria would have no medical consequence.

Medical dissolution protocols involve both dietary and drug components. The foundation of medical dissolution is to feed alkalinizing, high-moisture (ideally canned) diets that are low in protein (and therefore amino acids) and salt (natriuresis caused by increased dietary salt results in increased cystine excretion). In addition to dietary changes, N-(2-mercaptopropionyl)-glycine (2-MPG; Thiola, Mission Pharmacal) is administered at 15 mg/kg PO q12h. 2-MPG binds with cysteine in the urine to form a complex that is more soluble than cystine. Finally, urine alkalinizing agents like potassium citrate may be necessary, if diet alone does not maintain a urine pH in the 7 to 7.5 range. Urine should be monitored at least monthly for pH and specific gravity (ideal, <1.020). Imaging to assess urolith size and location is recommended every 4 weeks, and medical management should continue for 4 weeks after uroliths are no longer visible; cystine levels should be monitored during treatment in recurrent cases.

**Prevention of Cystine Uroliths**

Preventing cystine urolith recurrence may be possible with diet alone in some patients. Dietary considerations are similar to those for dissolution (Hill’s Prescription Diet u/d Canine [hillsvet.com], Royal Canin Veterinary Diet Canine Urinary UC Low Purine, Royal Canin Veterinary Diet Canine Vegetarian [royalcanin.us], and Purina Veterinary Diet HA Hypoallergenic Canine Formula [purinaveterinarydiets.com]). If necessary, 2-MPG (15 mg/kg PO q12h) and potassium citrate (0.5 mEq/kg/day PO [starting dose]) can be added to the prevention regimen. Urinalysis and imaging studies should be repeated every 3-6 months or when signs of lower urinary tract infection are present (eg, inappropriate urination, stranguria/dysuria, hematuria).

See Aids & Resources, back page, for references & suggested reading.

**Lateral radiograph of a 5-year-old, castrated English bulldog with multiple cystine uroliths in the kidneys, bladder, and urethra (arrow).**

**Tucked lateral radiograph of the dog from Figure 2 showing additional calcium oxalate urethroliths (arrow).**

**100% cystine uroliths from the dog in Figures 2 and 3 (scale, 1 division = 1 mm).**

Were it not for the relative insolubility of cystine in urine and the tendency of cystinuric dogs to form uroliths, cystinuria would have no medical consequence.
Take the Test!

Quiz yourself on this month’s Clinician’s Brief articles.

1. Conditions that can mimic uncontrolled diabetes mellitus in cats include all of the following except:
   A. Renal disease
   B. Neoplasia
   C. Hypercalcemia
   D. Acromegaly

2. Which of the following is not a common cause of insulin resistance in dogs?
   A. Hypothyroidism
   B. Hyperadrenocorticism
   C. Obesity
   D. Bacterial infection

3. The gold standard for diagnosis of canine distemper virus (CDV) is:
   A. PCR testing
   B. Immunocytology
   C. Virus isolation
   D. Serology

4. Most animals being fed through esophagostomy or gastros- tomy tubes do well with ___ to ___ feedings per day.

5. Leftover food slurries made for enteral feeding should be kept refrigerated and discarded after ______ hours.

6. The only laboratory test that can diagnose iatrogenic hyperadrenocorticism is a(n):
   A. Low-dose dexamethasone suppression test
   B. High-dose dexamethasone suppression test
   C. ACTH stimulation test
   D. Endogenous ACTH measurement

7. The first treatment of choice for adrenal-dependent hyperadrenocorticism is:
   A. Mitotane
   B. Trilostane
   C. Ketoconazole
   D. Adrenalectomy

8. For animals presenting in respiratory distress, thoracic radiographs must be taken immediately to differentiate primary cardiac from primary respiratory disease. True or false?

9. Diets for medical dissolution of cystine in the urine should be:
   A. Alkalizing, high-moisture, low protein, low salt
   B. Alkalizing, high-moisture, low protein, high salt
   C. Acidifying, high-moisture, low protein, low salt
   D. Alkalizing, high-moisture, high protein, low salt


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ENTERAL NUTRITION: STEP-BY-STEP • Allison Wara & Craig Datz

Suggested Reading


HYPERADRENOCORTICISM IN DOGS • Alex Gallagher

References


TOP 5 WAYS TO DIFFERENTIATE PRIMARY CARDIAC FROM PRIMARY PULMONARY DISEASE IN THE EMERGENCY SETTING • Elke Rudloff

References


Suggested Reading


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References and suggested reading for articles in this issue.

**CANINE DISTEMPER VIRUS • Sompong Techangamsuwan & Melissa A. Kennedy**

**Reference**


**Cystine Urolithiasis • Greg F. Grauer**

**References**


Suggested Reading


**Demystifying Diagnostic Tests for Hyperadrenocorticism • Alex Gallagher**

**References**


**Enteral Nutrition: Feeding Tubes • Allison Wara & Craig Datz**

**References**


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