

# Canine Distemper Virus

Somporn Techangamsuwan, DVM, MSc, PhD

Chulalongkorn University

Melissa A. Kennedy, DVM, PhD, DACVM

University of Tennessee

## **P** 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.



A CDV-infected dog with purulent nasal discharge.

- Respiratory, GI, and urogenital epithelium; CNS; and optic nerves are also infected.

### Incidence & Prevalence

- The virus occurs globally, but it is a rare disease in typical pet populations.
- Disease can be common in areas of low vaccine coverage.

**Domestic dogs are considered the reservoir species.**

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### 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.
  - Puppies infected before permanent dentition may have enamel hypoplasia.
- Digital hyperkeratosis may be noted.

### 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



## **Dx** Diagnosis

### Definitive Diagnosis

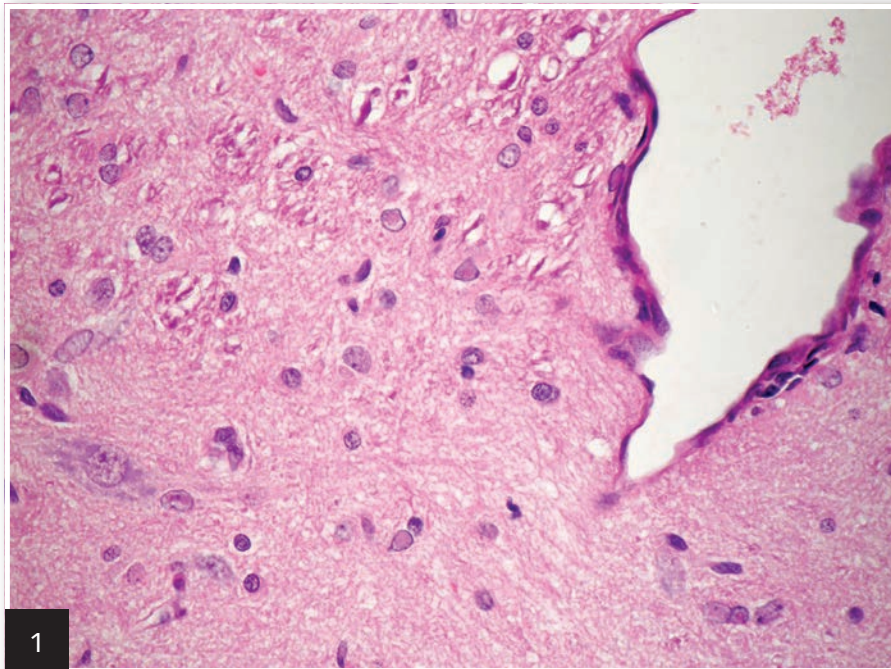
- Diagnosis is established via virus identification in a clinical sample through use of reverse-transcriptase PCR of whole blood, a swab of conjunctiva or tissue, CSF, or urine.
  - Urine is a good choice for PCR testing in patients with CDV encephalitis after resolution of epithelial signs.
  - CDV may be detected in urine for a longer period than other sample types.<sup>1</sup>
  - CDV detection in urine and CSF was equivalent in one study of neurologic cases.<sup>1</sup>
- 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.

### Differential Diagnosis

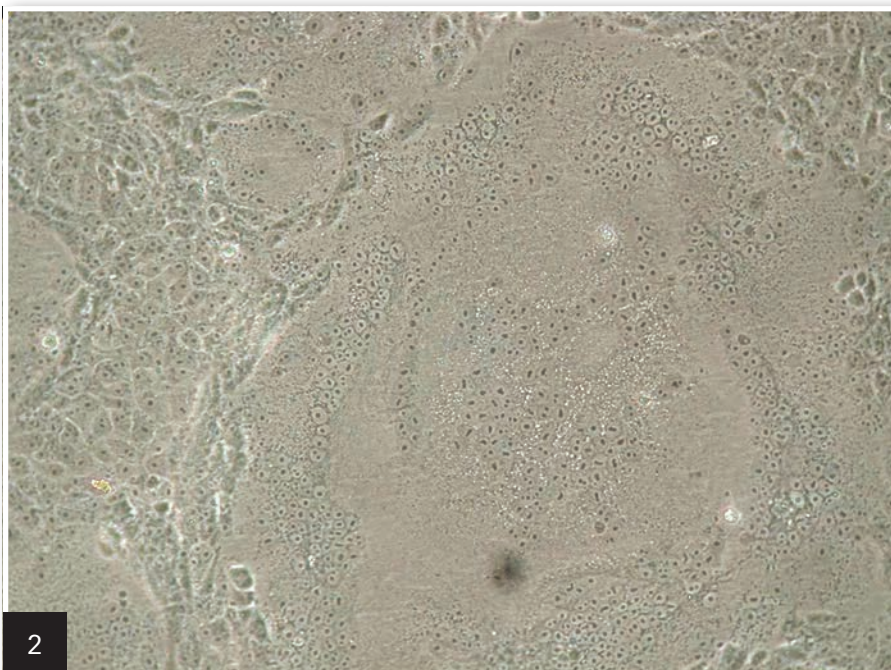
- Distemper is sometimes confused with other systemic infections (eg, leptospirosis, canine infectious hepatitis, rabies, canine infectious respiratory disease complex, Rocky Mountain spotted fever).

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



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



2 Typical cytopathic effect of CDV isolation shows numerous small and large syncytium cell formations.

### 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.
  - 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).

### 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.
  - Neurologic complications include: neuronal degeneration, gliosis, noninflammatory demyelination, perivascular cuffing, nonsuppurative leptomeningitis, intranuclear inclusion bodies (mainly in glial cells; Figure 1, previous page).

## **Tx** Treatment

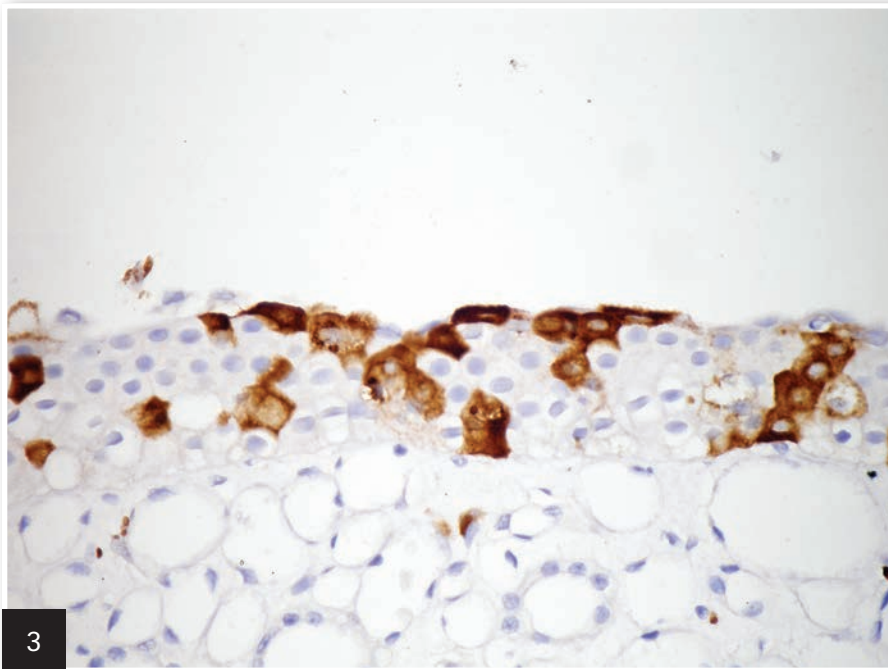
### Inpatient or Outpatient

- 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.

## **Rx** 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.



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

CDV = canine distemper virus, CSF = cerebrospinal fluid, IgM = immunoglobulin M



NADA 141-236, Approved by FDA

**CAUTION**

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

**INDICATION**

vetsulin<sup>®</sup> (porcine insulin zinc suspension) is indicated for the reduction of hyperglycemia and hyperglycemia-associated clinical signs in dogs and cats with diabetes mellitus.

**CONTRAINDICATIONS**

Dogs and cats known to have a systemic allergy to pork or pork products should not be treated with vetsulin<sup>®</sup>. vetsulin<sup>®</sup> is contraindicated during periods of hypoglycemia.

**WARNINGS**

**User Safety:** For use in animals only. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with copious amounts of water for 15 minutes. Accidental injection may cause clinical hypoglycemia. In case of accidental injection, seek medical attention immediately. Exposure to product may induce a local or systemic allergic reaction in sensitized individuals.

**Animal Safety:** Owners should be advised to observe for signs of hypoglycemia (see Owner Information Sheet). Use of this product, even at established doses, has been associated with hypoglycemia. An animal with signs of hypoglycemia should be treated immediately. Glucose should be given orally or intravenously as dictated by clinical signs. Insulin should be temporarily withheld and, subsequently, the dosage should be adjusted, if indicated. Any change in insulin should be made cautiously and only under a veterinarian's supervision. Changes in insulin strength, manufacturer, type, species (animal, human) or method of manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage.

Appropriate diagnostic tests should be performed to rule out endocrinopathies in pets that are difficult to regulate (e.g., hyperadrenocorticism in dogs and hyperthyroidism in cats).

**PRECAUTIONS**

Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia are essential to attain and maintain adequate glycemic control and prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies, and glucocorticoids can have an antagonistic effect on insulin activity. Intact bitches should be ovariohysterectomized. Progestogen and glucocorticoid use should be avoided.

**Drug Interactions:**

In the US clinical effectiveness studies, dogs and cats received various medications while being treated with vetsulin<sup>®</sup> including antimicrobials, antivirals, antifungals, antihistamines, analgesics, anesthetic/tranquilizers, diuretics, bronchodilators, corticosteroids (cats), NSAIDs, thyroid hormone supplementation, hyperthyroid medication (methimazole), internal and external parasitides, anti-emetics, dermatological topical treatments and oral supplements, ophthalmic preparations containing antimicrobials and antiinflammatories, and various vaccines. No medication interactions were reported. This drug was not studied in dogs receiving corticosteroids.

**Reproductive Safety:** The safety and effectiveness of vetsulin<sup>®</sup> in breeding, pregnant, and lactating dogs and cats has not been evaluated.

**Use in puppies and kittens:** The safety and effectiveness of vetsulin<sup>®</sup> in puppies and kittens has not been evaluated.

**ADVERSE REACTIONS**

**Dogs**

In the field effectiveness and safety study, 66 dogs were treated with vetsulin<sup>®</sup>. Sixty-two dogs were included in the assessment of safety. Hypoglycemia (defined as blood glucose < 50 mg/dL) with or without associated clinical signs occurred in 35.5% (22/62) of the dogs at various times during the study. Clinical signs of hypoglycemia were generally mild in nature (described as weakness, lethargy, stumbling, falling down, and/or depression). Disorientation and collapse were reported less frequently and occurred in 16.1% (10/62) of the dogs. Two dogs had a seizure and one dog died during the seizure. Although never confirmed, the presumptive diagnosis was hypoglycemia-induced seizures. In the rest of the dogs, hypoglycemia resolved with appropriate therapy and adjustments in insulin dosage. Seven owners recorded the following observations about the injection site on the home monitoring forms: swollen, painful, sore, and a bleb under the skin.

The following clinical observations occurred in the field study following treatment with vetsulin<sup>®</sup> and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the dogs: hematuria, vomiting, diarrhea, pancreatitis, non-specific hepatopathy/pancreatitis, development of cataracts, and urinary tract infections.

In a 21-day field safety and effectiveness study, 40 dogs, already well controlled on vetsulin<sup>®</sup>, were administered vetsulin<sup>®</sup> using a VetPen<sup>™</sup> insulin pen loaded with a pre-filled 2.7 mL vetsulin<sup>®</sup> cartridge and 29 gauge/12 mm pen needles. All dogs enrolled in the study were evaluated for safety. Loss of diabetic control was reported in 10 dogs, 3 of which were withdrawn from the study. Four dogs' loss of control resolved after dose adjustment while still using the insulin pen. For the remaining 3 dogs, the loss of diabetic control was reported at the end of the study and outcome was not documented. Two dogs had injection site reactions: edema in one dog and two instances of crusting in another. Poor appetite and weight loss was reported in one dog.

**Cats**

In a field effectiveness and safety study, safety data was reported for 78 cats receiving vetsulin<sup>®</sup>. Hypoglycemia (defined as blood glucose < 50 mg/dL) was reported in 61 cats (88 total incidences). Fifteen of the occurrences (involving 13 cats) were associated with clinical signs described as lethargy, diarrhea, decreased appetite/anorexia, vomiting, and hypothermia. One cat had seizures following accidental overdosing by the owner and again during the subsequent dose adjustment period. The cat responded to supportive therapy and had no further hypoglycemic episodes. In all cases of hypoglycemia, the clinical signs resolved following symptomatic treatment and/or dose adjustment. Polyneuropathy was reported in 4 cats. Two injection site reactions were reported: one as a mildly thickened subcutaneous tissue reaction and the second as a mild bruising.

The following clinical observations occurred in the field study following treatment with vetsulin<sup>®</sup> and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the cats: vomiting, lethargy, diarrhea, decreased appetite/anorexia, pancreatitis, dermal events, respiratory disease, urinary tract disorder, renal disease, dehydration, weight loss, polydipsia, polyuria, behavioral change, and ocular discharge/conjunctivitis. In a smaller field effectiveness and safety study, 14 cats were treated with vetsulin<sup>®</sup>. Hypoglycemia was reported in 6 cats (8 total occurrences). Lethargy not associated with hypoglycemia was reported in 4 cats (6 total occurrences). The following clinical observations occurred in the field study following treatment with vetsulin<sup>®</sup> and may be directly attributed to the drug or may be secondary to the diabetic state or other underlying conditions in the cats: foul odor to stool, diarrhea, dull coat, rapid, shallow breathing, stiff gait in rear, gallop rhythm, and pruritus with alopecia.

During the 1998-2007 period, the following adverse events in 50 cats treated with porcine insulin zinc suspension were reported to Intervet International and Intervet Inc: Death, seizures, lack of effectiveness/dysregulation, hypoglycemia, allergic or skin reaction, lethargy, vomiting/diarrhea, injection pain, hyperthermia, nystagmus, PU/PD, and abnormal behavior.

In a 21-day field safety and effectiveness study, 36 cats, already well controlled on vetsulin<sup>®</sup>, were administered vetsulin<sup>®</sup> using a VetPen<sup>™</sup> insulin pen loaded with a pre-filled 2.7 mL vetsulin<sup>®</sup> cartridge and 29 gauge/12 mm pen needles. Loss of diabetic control was reported in three cats all of which resolved after dose adjustment while still using the insulin pen. Hypoglycemia was reported in one cat. The cat recovered with supportive care and dose adjustment.

To report suspected adverse drug experiences, call Merck at 1-800-224-5318.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS, or <http://www.fda.gov/AnimalVeterinary/SafetyHealth>

**Use contents within 42 days of first puncture.**

Additional information about vetsulin<sup>®</sup>, VetPen<sup>™</sup>, and diabetes mellitus can be found at [www.vetsulin.com](http://www.vetsulin.com)

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Summit, NJ 07901

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- 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.



## 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.



## In General

### Relative Cost

- Diagnostics: \$--\$\$
- Treatment and follow-up care: \$\$--\$\$\$

### Cost Key

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

### Prognosis

- Prognosis is guarded.

### Prevention

- Control is accomplished through vaccination.
  - Current vaccines include strains of the American lineage (Onderstepoort 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. ■ **cb**

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