CANINE PARVOVIRUS

UPDATE

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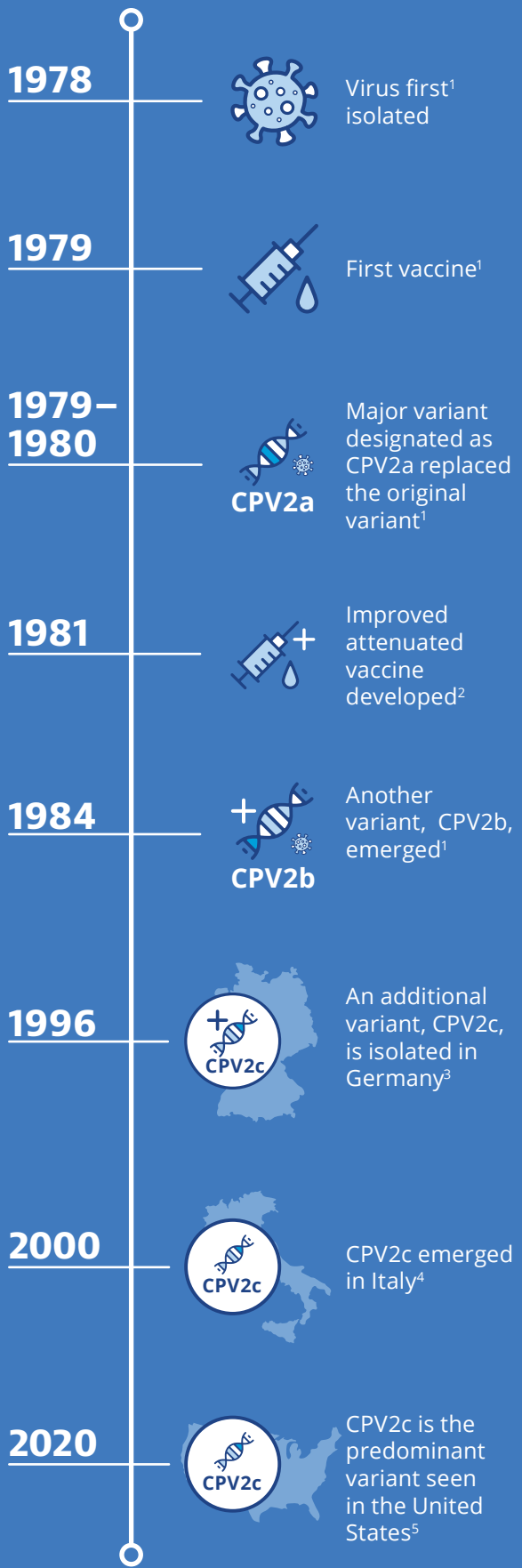
PART 2: THE BIO-PSYCHO-SOCIAL IMPACTS OF PARVOVIRAL DISEASE



PART 1

WHAT IS "PARVO"?

History of Canine Parvovirus

Veterinary medicine faced its own pandemic in the 1970s when a highly contagious novel canine parvovirus (CPV) infected at least 80% of the world's dogs within a year of its emergence.[6]

It is hypothesized that another virus mutated and broadened potential hosts to include dogs. CPV is related to the feline panleukopenia virus (FPV), which was first identified in the 1920s. It's likely that FPV or a similar virus mutated to become CPV.

The new variant, named canine parvovirus 2 (CPV2) in 1978, was genetically distinct from the previously described canine parvovirus CPV1—canine bocavirus or minute virus of canines (MVC)—which was never shown to cause disease.

Very stable in the environment and with efficient fecal/oral or oronasal transmission via contaminated fomites, CPV2 produced high infection and mortality rates when it first emerged.

By 1979 and 1980, a major variant designated as CPV2a replaced the original virus. Later, CPV2b and CPV2c emerged as antigenic variants, with just one capsid protein position difference.

Researchers isolated the virus and developed the first vaccine in 1979. An improved attenuated vaccine came in 1981.

CPV2c is the predominant variant in 2020 in many countries, including the United States. However, leading CPV researchers and clinicians do not consider the distinction of variant to be associated with severity of disease or clinically relevant to case management today.

Causative Agent

Classified as a carnivore protoparvovirus 1, variants of CPV2 are characterized by small,

isometric nonenveloped virus particles containing a single-stranded, negative-sense DNA genome.

CPV enters cells through transferrin receptor attachment and requires targeted cells to be in the S phase of the cell cycle since it cannot turn on DNA synthesis itself. Essentially, it needs rapidly dividing cells to create a disease state in a dog.

CPV initially enters the body via the tonsils or lymph nodes located in the dog's pharyngeal region. Next, it invades lymphocytes and increases replication before being released into the bloodstream. From there, CPV targets rapidly dividing cells such as the bone marrow, lymphatic tissue, and small intestinal crypt epithelium, which leads to suppression of immune function and hemorrhagic enteritis.[7]

As damage to the small intestines increases, the dog's body loses its ability to

- Absorb nutrients
- Prevent and recover fluid loss due to the ensuing diarrhea
- Block bacteria from moving from the digestive tract into other areas of the body[2]

Patient Profile

Unvaccinated dogs of any age with no immunity from prior exposure to the virus remain at risk of infection from CPV, especially when kept together in large numbers. Puppies ages 6 weeks to 6 months, however, face a higher risk of severe illness. Parvovirus disease is most often seen in puppies 6–20 weeks old.

An increased severity in illness can be seen in puppies experiencing the following stressful conditions:

- Weaning
- Overcrowding
- Malnutrition
- Concurrent intestinal parasites or infections[8]

Early in the history of CPV, certain dog breeds were described with an increased risk:

- American pit bull terriers
- Doberman pinschers
- English springer spaniels
- German shepherds
- Rottweilers[8]

Titer testing. Vaccination does not equal immunization. Even puppies who are "fully vaccinated" may not be immune to infection, principally because acquired maternal antibodies can bind and neutralize vaccine antigens.[9] Titer testing (serology) is crucial to finding cases where immunization hasn't occurred. Sometimes, revaccination is the solution for puppies or young dogs found to have titer levels below the threshold for immunity. In a small number of cases, however, extra, lifelong preventive precautions may be needed for dogs deemed nonresponders to CPV vaccination. The World Small Animal Veterinary Association recommends titer/serology testing puppies at least 4 weeks after primary vaccinations are completed at 16 weeks or older to check puppies' immune status.[10]

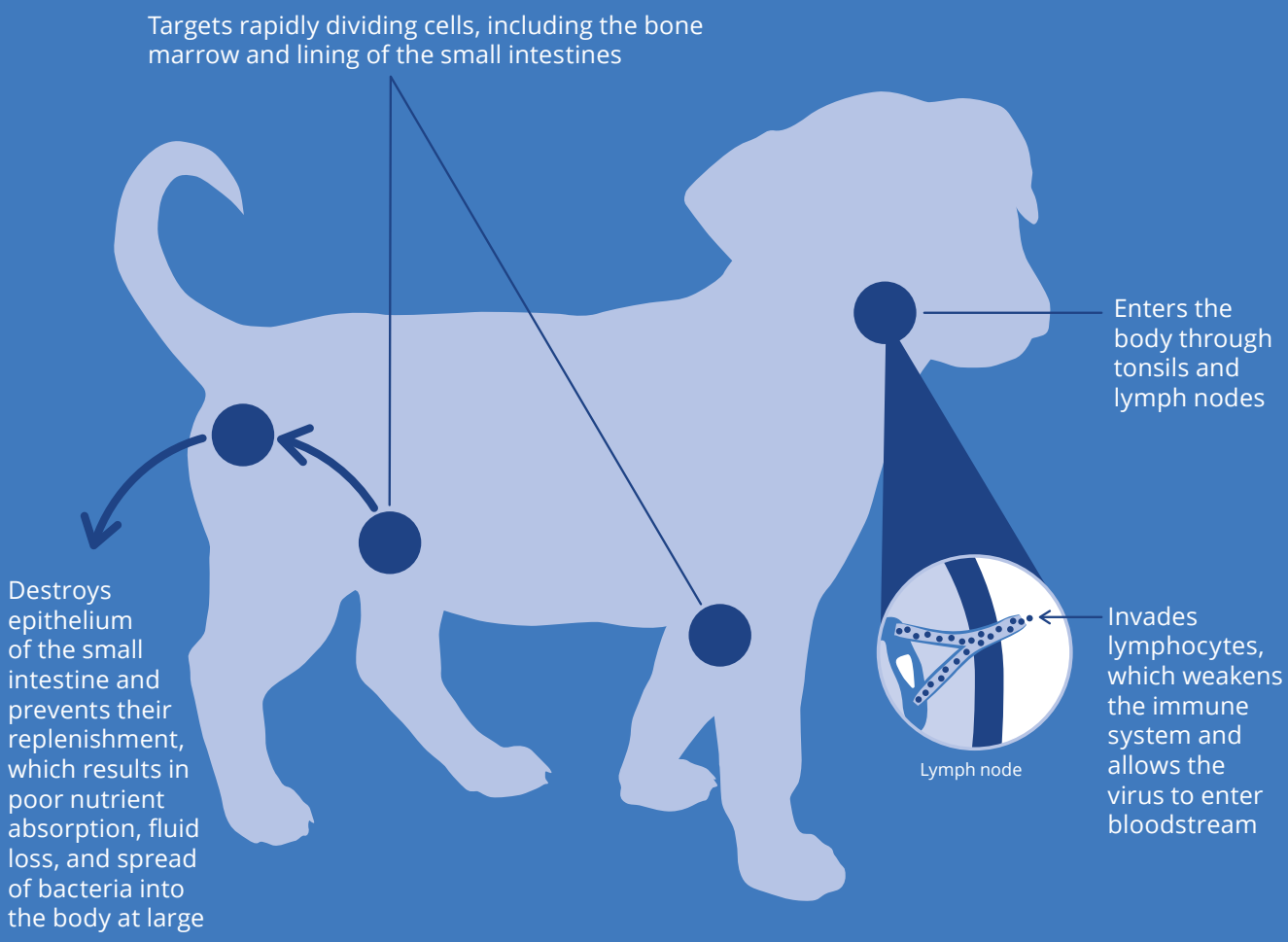
Transmission

Dogs acquire CPV infection through direct oral or nasal contact with feces containing the virus shed by other infected dogs or by contact with contaminated fomites.

CPV is long-lived in the environment. Outdoors, it can persist for many months, potentially even a year or more. Indoors, at room temperature, it can persist for at least two months.[8]

Based on geographic variations, some areas experience a seasonal increase in prevalence. For example, in a retrospective case-control study, researchers found that dogs were three times more likely to be admitted with CPV enteritis in July, August,

How Canine Parvovirus Attacks the Body[7]



Clinical Signs[2]

CPV typically presents with the following clinical signs beginning 2–14 days from exposure:

- Lethargy
- High fever
- Vomiting
- Sudden-onset diarrhea, often profuse and bloody
- Hypersalivation secondary to nausea
- Abdominal pain
- Depression
- Anorexia

Cause of Death[2]

Cause of death in patients with CPV typically is a result of

- Dehydration
- Shock
- Sepsis

and September.[11] However, parvo remains a concern any time there is a large-scale change in pet owners' ability to obtain regular vaccinations.

CPV is resistant to changes in temperature and pH as well as many detergents and disinfectants. Solutions containing quaternary ammonium compounds have limited ability to inactivate a nonenveloped virus such as CPV. Instead, disinfection protocols for CPV use solutions with oxidizing activity such as a 3% dilution of either of the following:

- Accelerated peroxide compounds
- Bleach (sodium hypochlorite)

Diagnosis

Because gastrointestinal complaints are common and nonspecific, diagnosis begins with systemic assessment to see if clinical signs can be pinned on the gut or another part of the body that is manifesting as gastrointestinal complaints.

Clinical history. Such an assessment relies heavily on the patient's signalment and clinical history:

- Age
- Vaccination status
- Vaccination status of the dam, if the patient is young or presents along with sick littermates
- Housing environment
- Clinical signs, including type, timeline of onset, and severity

Testing Accuracy and Pros/Cons

Discussions of diagnostic test accuracy frequently cover specificity and sensitivity.

Specificity gives clinicians information necessary to rule *in* a disease diagnosis by knowing the true negative rate.

Sensitivity, on the other hand, gives clinicians information necessary to rule *out* a diagnosis by knowing the true positive rate.

Type of Test	Pros	Cons
Point-of-care test (ELISA/SNAP—surface protein antigen)	• Quick, in-hospital results • More affordable • Real-time data on virus shedding	• Less sensitive than PCR tests
Reference lab test (PCR—polymerase chain reaction)	• More sensitive than a SNAP test • More useful to CPV researchers	• Slower turnaround time • With ongoing treatment, patient may have recovered or disease may have progressed significantly by the time results are available
Serology test	• Useful in assessing the presence of protective immunity • Useful in the management of outbreaks in animal shelter	• Not, by itself, diagnostic for active infection

Physical exam. CPV patients often show discomfort on abdominal palpation. Depending on the severity of disease, some patients will feel doughy or sticky during abdominal palpation.

Initial screening. An in-hospital CPV antigen test uses a rapid enzyme immunoassay to detect CPV antigen in the dog's feces.

Some teams administer the test in the client's car—assuming the patient arrives in stable condition where it's safe to wait for results.

Clinical Progression and Prognoses

Subclinical cases, particularly in unvaccinated adult dogs may be difficult to detect.

Parvovirus cases that typically are seen in veterinary practice may arrive with a variety of clinical signs and levels of severity. On arrival, triage efforts may designate mild, moderate, or severe cases. However, initial presentation does not indicate how severe the disease may become. Mild cases have the potential to escalate into severe cases with significant clinical intervention required. This is one of many reasons hospitalization and frequent reassessment remain a best practice.

Dehydration is the first enemy. Dogs showing signs of hypovolemia require aggressive fluid resuscitation. In cases where the patient is not immediately showing signs of hypovolemic shock, IV fluids can be calibrated to restore fluid balance over 12–24 hours.

Survival rates range from 68% to 92% with appropriate supportive care. Dogs who recover may develop long-term immunity.[8] Antibody titers may be measured in adult dogs to determine the frequency of parvovirus vaccination.

Severity	Observations
Mild	Some vomiting or diarrhea but the dog remains bright, alert, and happy
Moderate	Serious hemorrhagic diarrhea, some vomiting, lethargy, anorexia, moderate dehydration, possible secondary bacterial infection
Severe	Extreme hemorrhagic diarrhea, repeated vomiting, anorexia, lethargy, dehydration, and signs of shock and sepsis

Treatment Levels	Estimated Cost of Care
Mild—may be a candidate for at-home treatment and support after initial veterinary contact and intervention (See page 10 for outpatient protocols.)*	$
Moderate—requires hospitalization, IV fluids, and medications	$$
Severe—requires intensive care hospitalization with IV fluids and medications, feeding tube, etc. for many days	$$$+

* Initially mild cases can progress into moderate or severe cases quickly, so careful monitoring and good communication are important.

PART 2

THE BIO-PSYCHO-SOCIAL IMPACTS OF PARVOVIRAL DISEASE

Parvovirus cases take a tremendous toll on everyone involved.

Impact on Veterinary Practices

Parvovirus is challenging to veterinary practices on several fronts.

Clinical. Parvo cases require intensive monitoring and frequent treatments—and can go from bad to worse quickly.

Psychosocial. Clients often span a wide variety of socioeconomic backgrounds, which can result in veterinary team members editing recommendations and protocols in an effort to balance optimal patient care and client capabilities. Hospitalization is generally recommended,[12] which can be cost-prohibitive for some owners. The financial burden may lead some owners to elect euthanasia.[13]

When parvovirus infection is due to a lack of preventive care, it can lead to a range of client emotions, including guilt and embarrassment. Owners of puppies who received recommended vaccinations may feel angry and confused about how the infection occurred. Clients may vent their frustrations and feelings on social media, which can create additional stress on the veterinary team.

Facilities and staffing. Many practices simply aren't set up or staffed for managing the isolation and ICU needs of parvo cases, which is why transferring patients to 24/7 emergency/specialty facilities is often recommended.

Impact on Pet Owners

Parvovirus is challenging for clients, too.

Emotional rollercoaster. Families bond quickly with a new puppy, and the uncertainty of a long, healthy path ahead for their new family member can be crushing.

Lack of control. If the family chooses inpatient care, it isn't easy to hand over a young pet for round-the-clock care, with limited access to progress information and visitation.

Fear of failure. If the family chooses outpatient care, the pressure of learning and performing clinical tasks, frequent progress appointments, patient ups and downs, and likely fear the puppy may not survive can overwhelm even experienced veterinary clients.

Financial worries. Many families are unprepared for a large veterinary bill and may struggle to pay for treatment. Some owners may elect to euthanize the puppy if they are unable to pay for longer, in-hospital treatment.

Impact on Caregivers

Providing the round-the-clock care often required by parvo patients can come at more than a financial cost.

Private practice. Many caregivers develop a unique bond with their parvo patients. The cautious elation that comes with a patient's survival can be dampened by fatigue from emotional and clinical concentration.

Shelter settings. The sheer volume of parvo cases in shelter settings may result in immediate euthanasia in communities where shelters don't have the resources to provide treatment.

In locations where shelters do provide care to parvo puppies, teams must focus on saving those they can and taking solace in knowing they gave the others the best chance possible, providing love and compassion along the way.

Impact on Pets

Based on the known damage caused by a parvoviral infection, researchers have looked at possible long-term effects on dogs who survive the infection. One study found that dogs who survive a CPV infection have a significantly higher risk for developing chronic gastrointestinal disease.[14]

Preventive Measures and Veterinary Hospital Infection Control

To protect more puppies and dogs in their communities and as noted in the *2022 AAHA Canine Vaccination Guidelines*[15], veterinary teams

Must continue to recommend the CPV vaccine as a core vaccination

In addition, handle and store vaccines properly to ensure efficacy.

Follow infection-control strategies as stated in the *2018 AAHA Infection Control, Prevention, and Biosecurity Guidelines*[16]

Triage potential parvovirus cases over the phone. Avoid contaminating the main entrance or lobby

Transport parvovirus patients directly into the isolation area

Use proper personal protective equipment

Appropriate PPE is critical to decrease further transmission of CPV throughout the hospital

Adhere to proper donning and doffing procedures when entering and exiting the isolation area

Use strict cleaning and disinfection protocols

Prepare solutions fresh daily

Remove all organic matter from surfaces first

Apply disinfecting solution and let it remain wet for the proper contact time. Depending on concentration, bleach may require up to 15 minutes of contact time

Overview of Current Patient Care Options

For more than 40 years, veterinary practitioners used supportive care strategies for parvovirus patients because there were no available treatments for the disease itself. However, Canine Parvovirus Monoclonal Antibody (CPMA), the first and only USDA-conditionally approved monoclonal antibody treatment that targets canine parvovirus, now provides more specific treatment.

The primary goals of treatment include:

- Neutralization of canine parvovirus by selectively binding and blocking the virus from entering and destroying enterocytes
- Restoration of fluid, electrolyte, and metabolic abnormalities and maintenance of fluid needs due to ongoing losses
- Prevention (or treatment) of secondary bacterial infection[8]

Inpatient Care Overview

While CPV cases may initially present along a spectrum of severity, cases may rapidly devolve. That is why CPMA should be administered as early in the disease course as possible. Patients should also be hospitalized with supportive care to monitor and assist their recovery. When canine parvovirus patients are admitted, the first step is to restore fluids.

Positive and Negative Prognostic Indicators for Parvovirus Infection in Dogs[17]

Associated with Good Prognosis	Associated with Poor Prognosis, Including Longer Hospitalization or Death
Normal leukocyte count (>4,500/µL) and normal lymphocyte count (>1,000/µL) 24 hours after hospital admission	Already in hypovolemic shock on arrival
Survival of the first 3–4 days	Systemic inflammatory response syndrome (SIRS)
	Leukopenia and/or lymphopenia + neutropenia at hospital admission
	Hypocholesterolemia
	Higher serum C-reactive protein (CRP) concentration 12 and 24 hours after hospital admission
	High serum cortisol and low serum thyroxine concentration 24 and 48 hours after hospital admission
	Development of intussusception

One Shelter's Parvo Protocols[18]

Veterinary shelters often see a higher number of parvo cases than typical private practices. Especially in locations with high puppy intake numbers, isolation areas and specific protocols are required to prevent transmission from infected puppies to healthy, adoptable puppies.

Austin Pets Alive (APA) treats 600-700 parvo puppies per year. A retrospective study showed an 86.6% survival rate for puppies treated between June 2009 and December 2019.[18]

APA's protocols include the following:

- IV fluids for puppies showing signs of poor perfusion and hypovolemic shock
- Subcutaneous fluids twice a day if IV fluids aren't needed
- Combinations of affordable antibiotics

The facility's parvo team administers point-of-care tests in the parking lot and sets up its isolation ward in a separate section of kennels.

Parvo puppies go up for adoption after clinical signs have resolved, appetites return, and puppies have had two normal stools.

Additional inpatient care protocols build upon that first step as follows:

- Administer CPMA to stop additional destruction from CPV
- Monitor and treat patients for hypokalemia and hypoglycemia
- Provide antiemetic therapy for protracted vomiting, if applicable
- Administer colloid therapy or fresh frozen plasma if GI protein loss is severe (while the plasma provides serum protease inhibitors to counter systemic inflammatory response, convalescent or hyperimmune serum has not been shown to provide passive immunization)
- Introduce antibiotic therapy as appropriate
- Use of enteral nutrition has been associated with earlier clinical improvement, weight gain, and improved gut barrier function (feeding tube may be required)[8]
- Provide appropriate pain management

Treatments to avoid:

- The administration of antidiarrheals is not recommended because retention of intestinal contents and compromised gut integrity may increase bacterial translocation risks
- Antiviral drugs have not been shown to decrease hospital stays, case severity, or mortality rates[4]

Outpatient Care Overview

Outpatient care may be considered due to financial constraints, lack of critical care facilities, veterinary staffing shortages, or a client's desire to provide nursing care at home.

However, these outpatient protocols require extensive commitment to at-home care, good communication with the veterinary practice team, daily assessment by the veterinary team, and a clinical case suited to this option.

In one study, the outpatient protocol was deemed a success in 80% of the cases—compared to 90% of patients treated with traditional inpatient protocols.[9] In another study, 75% of the outpatient protocol dogs survived more than three days after initial diagnosis.[19]

A 2020 retrospective study of outpatient treatment cases in a shelter-based low-income clinic showed that 83% of patients survived.[20]

While sample sizes have not been large enough to analyze patient age for protocol success, trends suggest that younger dogs or those with low body weight may not tolerate outpatient care and, therefore, may not be good candidates.[20]

The outpatient protocol is comprised of the following steps:

1. Initial stabilization in a veterinary setting, including
   a. Placing an IV catheter for intravascular volume resuscitation
   b. Checking an initial electrolyte panel for abnormalities, especially hypokalemia and hypoglycemia
   c. Providing appropriate IV fluid therapy until hypovolemia, hypoglycemia, and hypokalemia have resolved. This may require several hours to achieve. Please refer to the *AAHA Fluid Therapy Guidelines for Dogs and Cats* for guidance on calculating an appropriate fluid rate, available at aaha.org/fluid-therapy.
   d. Administering CPMA

2. Electrolyte and Dextrose supplementation
   a. Blood glucose and electrolytes checked daily by veterinarian along with a physical examination
      i. IV or *per os* dextrose supplementation for dogs with a glucose <80 mg/dL
      ii. IV or PO potassium supplementation for dogs with a serum K^+ <3.4mEq/L

3. Subsequent outpatient protocol at home, including
   a. Subcutaneous (SQ) fluid therapy
   b. Parenteral antibiotic therapy while at the veterinary hospital, during one of the recommended daily visits or long acting parenteral antibody
   c. Parenteral antiemetic therapy
   d. Syringe feeding of small amounts of convalescence diet q6h at 1 ml/kg PO, as tolerated
   e. Pain management if abdominal pain is suspected on physical exam

4. Outpatient protocol failure for dogs with worsening symptoms defined as
   a. Progressive dehydration (loss of ≥10% body weight from admission or ≥8% dehydration on two serial measurements, based on physical exam findings)
   b. Hyperlactemia (≥4 mmol/L)
   c. Decline in mentation to stuporous/obtunded
   d. Fever (>104°F)
   e. Other subjective criteria used by the attending veterinarian[21]

Advancements in Parvovirus Therapies

In recent years, advancements have been made in parvovirus treatment options that provide improved clinical outcomes.

Antibodies. While convalescent or hyperimmune serum has given mixed results,[22,23] treatments have been developed that use targeted antibodies to prevent CPV from entering cells and causing infection. Convalescent plasma contains many different antibodies with varying activities, properties, and antigenic targets. Monoclonal antibody therapy uses a uniform, biosynthesized population of antibodies with known activities, properties, and the same antigenic target.

Company-funded trials were conducted to assess the safety and efficacy of a monoclonal antibody therapy that blocks CPV's entry into a dog's cells. In a randomized blinded placebo-controlled treatment efficacy study, dogs were challenged with CPV-2b on study day zero. By day 4, all dogs tested parvo positive via the IDEXX SNAP test and received either CPMA or a placebo. Most dogs were displaying clinical signs at the time of diagnosis. The placebo-control dogs all developed parvovirus infection and had a 57% mortality rate. Dogs in the CPMA-treated group experienced less severe and/or shorter duration of diarrhea, fever, vomiting, CPV-2 fecal shedding, and lymphopenia, and no dogs in this group died.[24]

A field safety study of 391 pet dogs across the US showed that CPMA was well tolerated in healthy dogs ranging from 3 weeks to 15 years of age and weighing from 0.6 to 59.2 kg (1.3 to 130 lb), and by SC and IV administration routes.[24]

Monoclonal antibody treatments are thought to work similarly to maternal antibodies and are anticipated to wear off. At that time, it is critical to establish, or resume, a regular vaccination schedule for parvo.

A Brighter Future

CPMA may lessen many of the impacts of parvovirus and help provide a brighter future for veterinary practices, pet owners, caregivers, and puppies.

Veterinary practices. CPMA treatment may lessen the severity and duration of clinical signs, which can lessen the burden on veterinary teams. Potentially better clinical outcomes can lead to happier clients, which may boost veterinary teams' well-being.

Pet owners. Less severe disease, shorter hospital stays, and a greater likelihood of survival can help support the human-animal bond and may reduce the incidence of euthanasia based on financial concerns or a poor prognosis.

Caregivers. Less intensive treatment can help lessen veterinary fatigue and may mean that shelters that were not previously equipped to handle parvo cases can now provide treatment.

Pets. Although it is uncertain whether parvovirus causes chronic gastrointestinal disease, if CPMA is given early in the course of treatment and severe disease does not develop, this could potentially reduce the likelihood of long-term effects.

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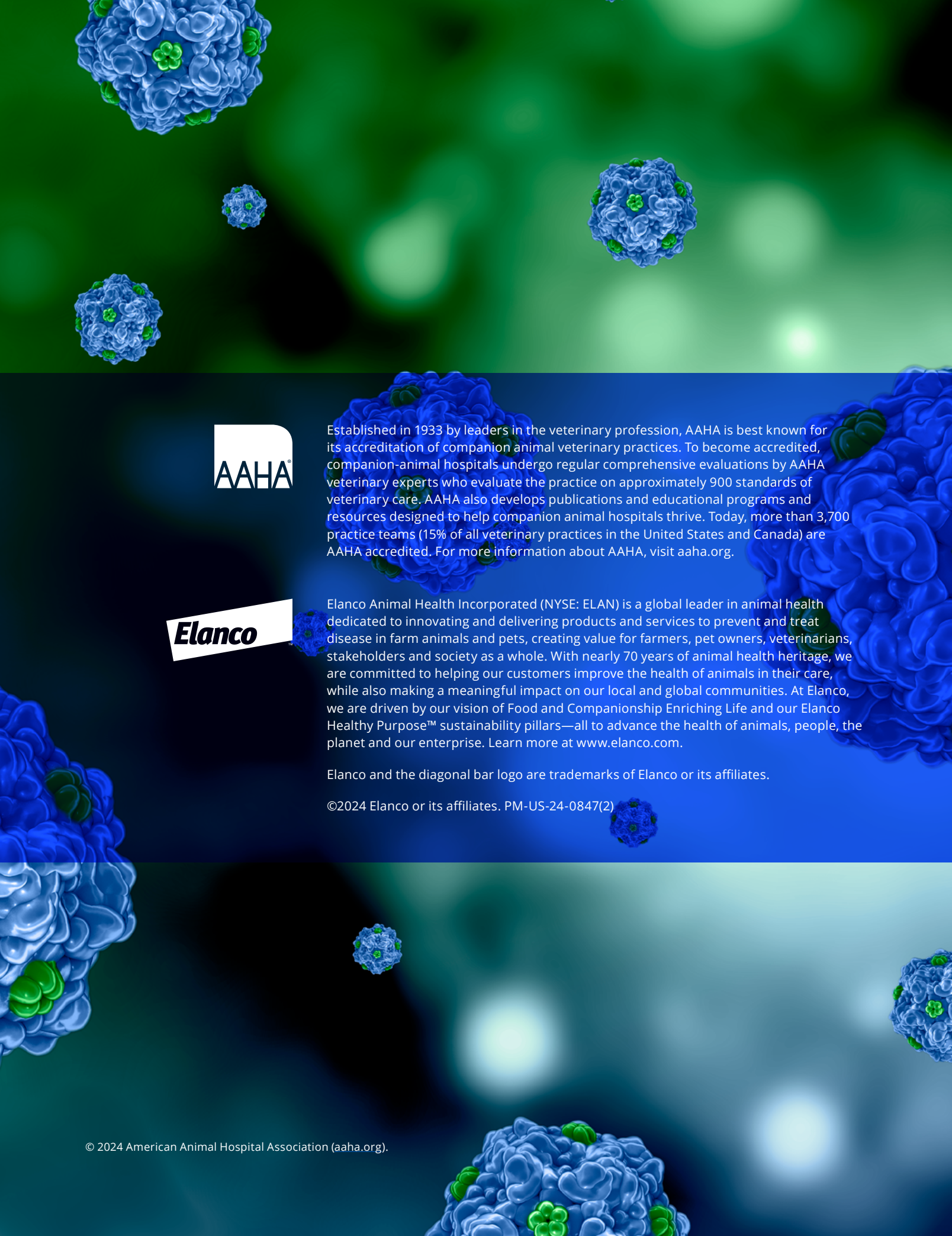

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