Parvovirus in Raccoons

Karen Bailey
Kentucky Wildlife Center, Inc.
kywildlife.org
Background

- Mother was a rehabber growing up
- MBA Vanderbilt
- Licensed: Kentucky Department of Fish and Wildlife Resources
- Certified Wildlife Rehabilitator (CWR)
- Member IWRC, NWRA, KWRA (board member)
- President and Founder- Kentucky Wildlife Center, Inc. (501 c 3)
DISCLAIMER:
No part of this presentation is intended to provide veterinary advice or recommendations of any kind. Medications and Protocols administered by KWC are used under the advisement of our veterinarian of record.

Consult your own veterinarian before using any medication and do so only under his direct supervision.
“Not to hurt our brethren of fur, feather, or fin is not enough. We have a higher mission to be of higher service whenever they require it.”

St. Francis of Assisi
“Confusion is that wonderful state of mind right before clarity.”

Mandy Evans
Virology Simplified

- A virus is the simplest organism that can technically be called alive
- Parvovirus consists of a capsid (protein coat) and a single strand of DNA
- Virus attaches to a host cell and injects its own DNA
- Viral DNA tells the host cell to stop what it’s doing and start mass producing more virus
- Thousands of new viral organisms are replicated that can infect more cells
Parvovirus Overview

- Smaller than most viruses: name comes from the Latin parvus (small)
- Consists of a protein coat (capsid) and a single strand of DNA
- Virus capsids are the primary determinants of host range
- Not enveloped in fat like most viruses
- Extremely stable in the environment
- Resistant to most disinfectants
- Attack rapidly dividing cells: intestine, bone marrow, lymph nodes
- Highly contagious
History of Parvovirus

- Feline Panleukopenia Virus (FPLV) is also known as Feline Parvovirus (FPV) or Feline Distemper
- FPV and Raccoon Parvovirus (RPV) isolates are indistinguishable. Mink Enteritis Virus (MEV) is a minor variant
- Canine parvovirus (CPV) probably derived by mutation from FPV or a closely related virus and first emerged in 1978 in dogs in Europe and quickly spread around the world
- Since 1978, CPV has gone through antigenic variations resulting in variant viruses and demonstrating the virus’s ability to rapidly evolve
- These variations have not influenced the efficacy of vaccination
- Raccoons were not susceptible to the original strains of CPV

Host Range Similarities

- Clinical presentation is almost identical in affected hosts
- Gross and microscopic lesions in all species are similar
- This is important to raccoon rehabilitators because we can extrapolate a lot of information from research of other animals

Pathophysiology of Parvovirus

- Transmitted by oral exposure to feces of infected animals
- Attacks rapidly dividing cells beginning with the lymph nodes in the throat
- Followed by rapid viremia leading to systemic infection
- Virus attacks bone marrow causing a decrease in white blood cell count leading to a compromised immune system
- Primary site of viral replication is within the intestinal crypts resulting in enteritis and diarrhea
- The intestinal barrier is compromised resulting in translocation of bacteria into the bloodstream leading to septicemia
- Animals die of dehydration, septicemia, or endotoxemia
Anatomy of a Parvoviral Infection

- Villi: tiny finger-like protrusions that increase the surface area available for absorption of fluid and nutrients.
- Villi possess Microvilli which further increase surface area.
- Cells of the villi are short-lived and rapidly replaced by new cells.
- Source of the new cells is the rapidly dividing area at the base of the villi known as the crypts of Lieberkuhn.
- Parvovirus attacks right at the crypt.
- Without new cells from the crypt cells, the villi become blunted and unable to absorb nutrients.
- Causes diarrhea and nausea leading to rapid dehydration.
- Barrier that separates intestinal bacteria from the bloodstream breaks down.
- Bacteria enters the bloodstream resulting in secondary infections and sepsis.

Source: Parvovirus Information Center: VeterinaryPartner.com
Survival

- Depends on how quickly it's diagnosed, virulence of the strain, size of virus exposure, age, health & immune status of the animal, and how aggressive the treatment protocol is.
- The goal is to keep the patient alive long enough for the immune system to recover and respond - antibodies are produced everyday that can bind and inactivate the virus.
- Accomplished through supportive and symptomatic care: fluid therapy, antibiotics, antiemetics, etc.
- Survivors have life-long immunity.
Prevention and Control

- Practice of shelter medicine protocol in rehabilitation facilities
- Vaccination to reduce the number of susceptible animals
- Quarantine
  - Long enough to encompass the incubation period
  - Long enough for development of antibodies post-vaccination
- Minimize environmental contamination
Shelter Medicine

- Animal shelters are similar to rehabilitation facilities
- High-density, high-risk, high-stress population
- High likelihood of exposure with possibility of devastating consequences
- Must be considered when developing vaccine protocol
Vaccine Types: Killed vs. Modified Live

- Killed vaccines are less effective and take longer to induce an immune response than MLV
- Current research shows that Duration of Immunity (DOI) after vaccination with MLV is 7 years or longer based on challenge and serological studies (CDV and FPV)
- MLV core vaccines are much less likely to cause adverse reactions than killed vaccines
- MLV vaccines are more effective against waning maternal antibodies

Source: Journal of Small Animal Practice © 2007 WSAVA
Vaccine Failure

- Maternal Antibody Interference
  - depends on titer of colostral antibody and the amount of antibody absorbed after birth
  - most common reason for vaccine failure
  - reason boosters are needed with last dose > 16 weeks in raccoons

- Vaccine is Poorly Immunogenic
  - manufacture (type of strain, passage history, production errors)
  - administration of vaccine to animal
  - incorrect storage, transportation, handling

- Animal is a Poor Responder to the Vaccine
  - animal fails to develop an antibody response
Vaccination of Sick & Injured Animals

- EVERY animal over 4-5 weeks of age should be vaccinated on intake, regardless of health status
- Vaccines aren’t likely to be harmful, and the risk of exposure to deadly viruses is high in rehab facilities
- It’s possible (but unlikely) that a sick animal may not elicit an immune response. But, it’s highly unlikely that the vaccine will adversely affect the animal. More importantly, there is a good chance the animal will gain protection.

Immunity Onset

- MLV vaccines provide rapid immunity in the absence of maternally derived antibodies (MDA).
- With MLV and recombinant vaccines for canine distemper, immunity develops within hours after vaccination (in the absence of MDA).
- 98%-99% of dogs vaccinated with MLV CPV-2 vaccine were protected when challenged 3 days post-vaccination (in the absence of MDA).
- Cats showed immunity to FPV when exposed almost immediately after MLV vaccination.

Humoral Response and Protection from Experimental Challenge Following Vaccination of Raccoon Pups with a Modified-Live Canine Distemper Virus Vaccine (Pare, et al)

- Used Galaxy-D in the study (Modified Live Vaccine for Canine Distemper)
- No local or systematic adverse reactions in any of the raccoons
- Study used 47 wild caught baby raccoons divided into 6 groups. Of the 47 pups, 31 were seronegative & 16 were seropositive
- Some of the seronegative raccoons developed titers as early as 1 week PV and all vaccinated seronegative raccoons showed rises in titers between 2-4 weeks PV and remained high throughout the follow-up period
- Study suggests that after 5 months of age, a raccoon could benefit from a single dose of vaccine (if booster is unfeasible). Immunity from MLV Canine Distemper vaccine is long-lasting in the absence of maternal antibodies.
Maternal Antibodies

- All of the seropositive raccoon pups were from wild unvaccinated mothers.
- Maternal antibodies in all seropositive raccoons declined gradually to negligible levels by the time they had reached 20 weeks of age.
- Study showed that maternal antibodies will nullify or interfere with active immunization in raccoon pups until they reach 14–16 weeks of age.
- Vaccination failed to elicit a response before the 3rd vaccination (16 weeks of age) in 7 of the 8 raccoons with maternal antibodies.
- The immune status of raccoon pups is rarely, if ever, known.
- Vaccination protocol should extend to 16–18 weeks of age.

Challenge Study

- 20 raccoons were randomly selected for the challenge study.
- All 16 vaccinated raccoons survived the challenge with no clinical signs of disease.
- 3 of 4 unvaccinated, seronegative raccoons developed clinical signs significant enough to warrant euthanasia. The 4th raccoon had sub-clinical lesions on necropsy suggesting that it is likely that it would have developed neurological symptoms later.
Vaccine Protocol

- Essential to preventive care
- Goal: Vaccinate PRIOR to exposure.
- Vaccinate immediately upon intake if old enough
- Under no circumstance would the risk of adverse reaction outweigh the benefit
- We start vaccination protocol at 4 weeks of age and continue until 16-20 weeks of age
- Revaccinate every 2-3 weeks based on risk
- Decision is unique to each rehabber
  - number of animals admitted
  - current outbreaks in your area
Vaccine Protocol for Raccoon Rehabilitators

- Vaccine selected should be based on similarity of the hosts (FPV vaccine for RPV and CPV vaccine for mutated strains of CPV in raccoons)
- Use of these vaccines in wildlife is off-label
- Long history of use in wildlife with low risk of complications
- The few studies of parvovirus vaccination in wild animals suggest that the response is comparable to that in domestic animals
- Vaccination protocol should be based on the principles applied to the vaccination of domestic carnivores
- Rabies, Canine Distemper and Parvovirus are the most important infectious diseases in raccoons and should be included in all vaccination protocols

Relevance to Raccoon Rehabilitators

- Current research definitively shows that there are multiple strains of parvovirus that can cause clinical disease in raccoons
- RPV which is antigenically similar to FPV
- Recent research has identified a mutated variant of CPV that can infect raccoons
- Important considerations when developing vaccination protocols in the rehabilitation setting
Vaccines used by Kentucky Wildlife Center

- Chosen for safety and efficacy
- Protocol developed with our veterinarian of record
- Combination is needed to protect against the most common infectious diseases seen in raccoons (canine distemper, the multiple variants of parvovirus, and rabies)
- These are not the only vaccines. If you are using something that works.....continue.
Merial Recombitek C4/CV

- Modified Live Virus, Canarypox vector
- Combo vaccine that protects against Canine Parvovirus and Canine Distemper
- High titer/low passage
- Very Safe
- It can be used in young animals and in wildlife
Merial PureVax Feline 4

- Modified live virus vaccine
- Combo vaccine provides protections against Feline Panleukopenia
We Do Not Use Distox-Plus (Killed Vaccine for MEV)

- MEV is closely related to FPV and RPV
- We use MLV vaccine for FPV and CPV
- Evidence of cross-species protection
- MLV are more effective against waning maternal antibodies
- Inactivated vaccines may interfere with antibody response of MLV vaccines
Summary of two studies that influenced our decision to eliminate MEV vaccine from our Vaccine Protocol for Raccoons

(1) Full protection in mink against mink enteritis virus with new generation canine parvovirus vaccines based on synthetic peptide or recombinant protein (Langeveld, et al. 1995)
  - Two recently developed vaccines—one based on synthetic peptide and one based on recombinant capsid protein—fully protected dogs against heavy challenge
  - Antigenic similarity between CPV, MEV, FPLV, and RPV suggests that the new vaccines could protect mink, cats, and raccoons against their respective host range variants
  - Both CPV vaccines were fully protective in mink against MEV

Conversely

(2) The Failure of an Inactivated Mink Enteritis Virus Vaccine in Four preparations to Provide Protection to Dogs Against Challenge with Canine Parvovirus2 (Carman, et al. 1982)
  - The inactivated MEV vaccines failed to provide protection in dogs against CPV-2 challenge
Differential Causes of Diarrhea

- Overfeeding
- Introduction of formula or food too quickly
- Change in formula or food
- Medication
- Stress
- Poor hygiene or sanitation
- Spoiled formula or food
- Parasites
- Disease - bacterial or viral
- Toxins
Symptoms of Parvoviral Enteritis

- Diarrhea
- Vomiting
- Dehydration
- Fever
- Depression
- Anorexia
- Rapid weight loss
- Shock
- Hypoglycemia
- Acute death

Note: photo is an example of shock, not parovirus
Clinical Significance

- Animals may be found moribund (in dying state) or dead without noticeable symptoms
- Symptoms generally develop 4-5 days post-exposure
- Animals that resume eating within 3-4 days are likely to survive
- Most animals that are going to die succumb within 4-5 days
- Juveniles have higher mortality rates than adults

Treatment Protocol:
Aggressive Supportive Care

Medications and Protocols administered are used under the advisement of our veterinarian of record. Consult your veterinarian before using any medication.
Treatment of Parvoviral Enteritis

- Standard (Essential) Care
  - Fluid Therapy
  - Antibiotic Therapy
  - Management of Symptoms
    - Antiemetics
    - Pain Medication
    - Gastroprotectants
  - Antiparasitic Therapy

- Adjunctive Therapies
  - Supplements (Vitamins, Probiotics)
  - Tamiflu (oseltamivir)
  - Early Enteral Nutrition (EEN)
  - Plasma Transfer
Fluid Therapy: Overview

Determine How Much Fluid to Give

- Calculate Deficit: Most parvoviral patients are 8-10% dehydrated

- Determine Maintenance:
  - 70-90 ml/kg/day (Mitchell)
  - 50 ml/kg/day (IWRC)

Neonates require 2 to 3 times the fluid of adults (IWRC)

- Adjust for ongoing losses: diarrhea, vomiting
Subcutaneous Injection (SQ)

- Warm the fluids
- Administer every 4-6 hours until diarrhea and vomiting have stopped
- Lactated Ringers Solution (LRS)
  (don’t give dextrose SQ)
- Wide Safety Margin
Intravenous Injection (IV)

- Necessary for animals in severe shock
- Catheter is placed by our veterinarian
- We use LRS with added Dextrose and Vitamin B Complex
Oral (PO)

- Always warm the fluids
- In dehydrated animals, administer SQ before giving oral fluids.
- Administer no more than 5% of body weight at any one time.

*Never attempt to use a stomach tube without proper training*
Fluid Therapy - Keep It Simple

- Know the basics, but don’t get caught up in the numbers! The deficit, ongoing losses, age adjustment are ESTIMATES! The most important thing is to give fluids!
- Reassess regularly. When in doubt - Continue!

It truly can make the difference whether or not your patient survives!
Antibiotics

- Necessary to prevent secondary infections
- Do not use oral antibiotics because the GI tract is damaged
- Use a combination of 2 antibiotics to provide broad spectrum coverage against gram negative, gram positive and anaerobic bacteria that originate in the intestines
- (1) Beta Lactam antibiotic: ampicillin, cefazolin, penicillin and
- (2) Aminoglycoside: gentamicin, amikacin or Flouroquinolone: Enrofloxacin

Source: Treatment of Parvoviral Enteritis. Douglass K. Macintire, DVM, Auburn University College of Veterinary Medicine
Antibiotics Commonly Used in Parvoviral Treatment Protocol

Best to combine a Beta Lactam with either Aminoglycoside or Flouroquinolone

Beta Lactam Antibiotics
- Penicillins: broad spectrum activity against Gram-positive, Gram-negative, and anaerobic bacteria.
- Cephalosporins: Classified by generation. Spectrum of activity against Gram-negative bacteria increases with each generation, but decreases for Gram-positive bacteria. All can be used against anaerobes with varying results.

Aminoglycosides
- Synergistic activity when used with Beta Lactam Antibiotics
- Excellent against Gram-negative bacteria
- Use is contraindicated in dehydrated animals- can be nephrotoxic (make sure the animal is well hydrated)

Flouroquinolones
- Enrofloxacin (Baytril): May cause cartilage abnormalities if used in high doses for extended periods in young animals. Doses higher than 5 mg/kg can cause blindness in cats. No research on safety margin in raccoons. We have used 5 mg/kg in raccoons for short periods with no observed side effects.
- Broad spectrum against Gram-positive and Gram-negative, but poor activity against anaerobic bacteria
Antiemetic (Anti-nausea) Medications

- Cerenia (Maropitant)
- Reglan (Metoclopramide)

It may be helpful to administer antiemetic drugs (Reglan) 30 minutes before giving any oral medication (such as Tamiflu) if vomiting is present.
Pain Management

- NSAIDs: Meloxicam (Metacam), Ketoprofen (Ketofen)
  - mild to moderate pain
  - make sure the animal is well hydrated

- Opioids: Butorphanol (Torbogesic), Buprenorphine
  - moderate to acute pain
  - controlled substances

- Develop protocols with your veterinarian
- Wild animals are adapted to mask pain and discomfort
- Parvoviral enteritis can be very painful
Meloxicam (Metacam)
- New Manufacturer Warning: Repeated use of meloxicam in cats has been associated with acute renal failure and death
- Not sure of the pharmacological significance in the use of raccoons
- All NSAIDS should be used with caution in dehydrated animals
- Consider alternatives in raccoons with parvo
Gastroprotectants
Parvo can cause ulceration of the esophagus, stomach, and small intestine

Famotidine has longer duration of action and fewer drug interactions than other gastroprotectants such as Cimetidine
Antiparasitic Therapy

- Parasites can increase the severity of parvovirus
- Raccoons should be dewormed on intake and at regular intervals anyway due to the zoonotic potential of *Baylisascaris procyonis*
- Fecal examination is indicated to rule out or identify parasites
- Ponazuril to prevent opportunistic parasitic infections
Ponazuril for the Treatment of Coccidia

- Dose: 50 mg/kg PO once daily for 1-5 (may repeat in 1 week)
- 50 mg/ml solution = 10 ml paste + 20 ml water
- Dose and concentration are both 50, so the calculations are easy!
- It has been used extensively in shelters

Source: Maddie’s Shelter Medicine Program
Cornell University College of Veterinary Medicine
Probiotics
Vitamin Supplements
Zinc Supplementation

- Recommended in treating acute diarrhea by the WHO
- Affects immune function, intestinal structure, & epithelial recovery
- Used in conjunction with oral rehydration
- In numerous clinical trials, children had a significant faster recovery
- We use the recommended dosage in dogs 1.5-2.5 mg/kg zinc gluconate PO TID (Plumb’s Veterinary Drug Handbook)
- We mix zinc in Lixotinic or in oral electrolytes
- Use is anecdotal in treating parvoviral enteritis
Tamiflu (Oseltamivir)

- Human drug used off-label to treat parvoviral enteritis
- Use is controversial
- Decision must be made with your veterinarian
- Information provided is for reference purposes only and does not constitute a recommendation for or against its use
Pharmacology of Tamiflu in the Treatment of Parvovirus

- Originally developed to treat human influenza virus
- Tamiflu is a neuraminidase (NA) inhibitor
- CPV does not rely on NA for replication, so any beneficial effects would not be due to direct antiviral action
- Suspected beneficial mechanism of action in treating parvoviral enteritis is the inhibition of bacterial translocation through the gut epithelial cells

Study Overview

Use of oseltamivir in the treatment of canine parvoviral enteritis

- Dose: 2 mg/kg, PO, q 12h diluted in water 1:1
- Dogs that received oseltamivir had increased weight gain compared to dogs in the control group which showed significant weight loss
- Dogs that received oseltamivir did not demonstrate a decline in WBC. Dogs in the control group showed a significant decline in WBC. A higher WBC could be protective against the negative effects of sepsis
- Suspected mechanism of action is by blocking bacterial translocation through NA inhibition decreasing disease severity both locally in the gastrointestinal tract and systemically
- No major adverse side effects associated with the use of oseltamivir
- Recommends further investigation

Directions for Use

- Take (1) 75 mg capsule of Tamiflu and mix into 10 ml of juice, etc.
- Keep refrigerated. Shake Well
- Give .1 ml/lb every 12 hours for 10 treatments.
  (If you don’t get a response after the first dose, double the starting dose)
- Minimum dose should be .2 ml (even in small individuals)
- Do NOT exceed 12 hours between dosing. If you do, restart for another 10 treatments

Source: Dr. Jack Broadhurst. A New Treatment For Parvoenteritis
Early Enteral Nutrition (EEN)

- Improved recovery time and decreased morbidity
- Early reintroduction of food does not seem to make symptoms worse even in severely affected animals
- Must weigh the risks and benefits in the presence of vomiting
- Anitemetics (such as Metoclopramide) may be beneficial if administered 30 minutes prior to feeding
- Feed small amounts, several times a day
- Nutrition is necessary for recovery
Study Overview
Effect of Early Enteral Nutrition on Intestinal Permeability, Intestinal Protein Loss, and Outcome in Dogs with Severe Parvoviral Enteritis.

- Conventional treatment of parvoviral enteritis recommends “gut-rest”. Lack of controlled clinical studies to support this
- The most important stimulus for intestinal mucosal growth, repair, and integrity is the presence of nutrients in the intestine
- Documented benefits of EEN include:
  - reduced intestinal mucosal permeability
  - increased weight
  - reduced incidence of bacteremia, endotoxemia, and septicemia
  - reduced incidence of multiple organ failure
  - improved immune status
  - improved clinical symptoms: appetite, attitude, resolution of vomiting & diarrhea
  - reduced catabolism and malnutrition preventing additional intestinal inflammation
  - significantly higher survival rates
Stomach Tubing
(Oral Rehydration, Enteral Nutrition, Oral Medications)

- Measure from tip of nose to last rib
- Mark with tape or marker
- Use appropriate size tube—don’t go too small! (esophagus is larger than trachea)
- Make sure the animal is sternal, nose up
- Gently glide, never force—should slide easily
- If you’re not sure, pull out and start over
- Give 5% of bodyweight, start with less
- Remeasure tape regularly and adjust for growth

*Don’t try without proper training!*
Current Research at KWC
Plasma Transfer in Raccoons
Use of plasma in neonates for the suspected failure of passive transfer (photo of plasma donor and recipient)
Use of plasma from hyper immunized donors for the treatment of parvoviral enteritis
Euthanasia

- Hardest part of being a rehabber
- Develop protocol with your veterinarian
- Consider long-term quality of life, risk to other animals in your care, likelihood of recovery, amount of suffering involved, releasability
- Black and white decisions are always easier than the gray ones
- Try to view it as a kind alternative
- Trust your gut—experience helps. In hindsight, most animals that I thought I should euthanize but didn’t, ended up dying or being euthanized anyway.

Butorphanol & Xylazine are used to sedate prior to euthanasia
Transmission

- Sick animals can pass billions of infective virus per gram of feces
- Transmission is by the fecal-oral route
- High potential for contamination of environment
- Easily spread by fomites (inanimate objects) such as clothes, shoes, feeding utensils, litter, bedding, etc.
- Possibility of transmission by insects
Prevention and Disease Outbreak Management

- Isolate sick animals
- Quarantine exposed animals for at least 2 weeks
- Clean and disinfect the entire facility
- Wear protective clothing
- Launder clothing, bedding, towels, etc. in hot water with detergent and bleach and dry on high heat. Don’t overload!
- Make sure each room has its own cleaning tools
Label and Disinfect Feeding Utensils
Make sure you use a parvocidal disinfectant and make sure the surface is clean (remove organic matter). The disinfectant should remain in contact for 10 minutes.
Proper Management to Reduce Risk of an Outbreak

- Quarantine new intakes
- Vaccinate on intake if old enough
- Reduce Stress: provide nest boxes for hiding and sleeping, provide enrichment, reduce noise, reduce exposure to strangers and domestic animals
- Segregate by conspecifics: by litter or age group
- Feed the best diet possible
- Keep cages and enclosures clean
- Deworm regularly
Burnout and Compassion Fatigue

No matter what you do or how hard you try.....some animals are not going to make it!

“We can do no great things, only small things with great love.”

Mother Teresa
Be a better rehabber today than yesterday
High learning curve in wildlife rehabilitation
Forgive yourself when you make mistakes
Never stop learning
Keep an open mind
Network with other rehabbers
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The End!