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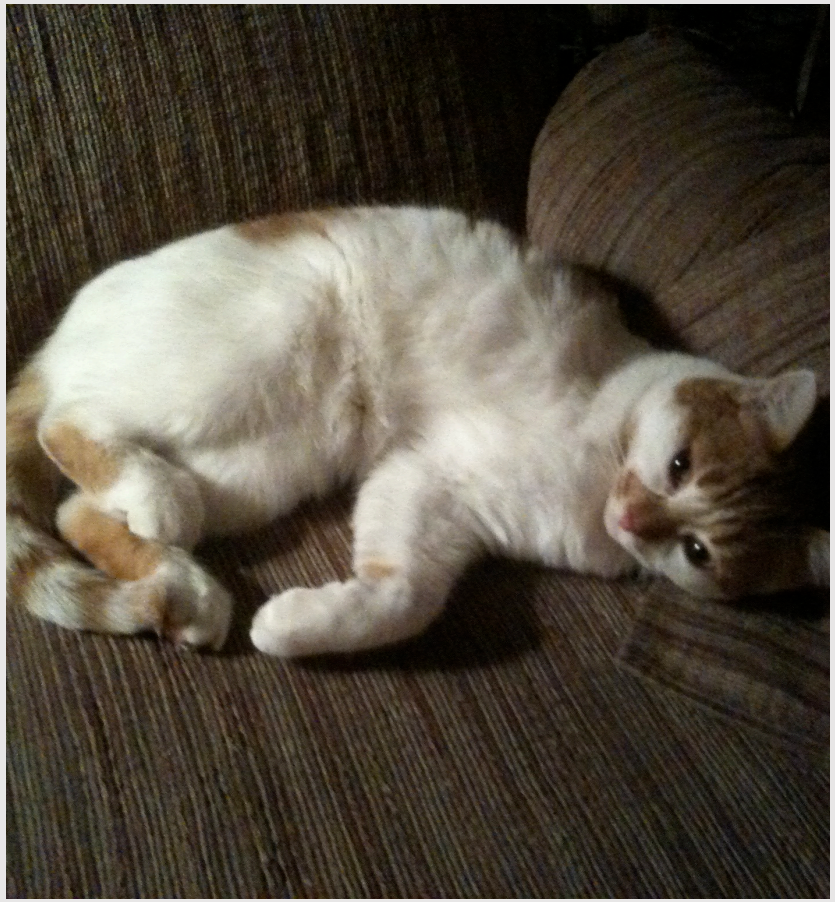



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LECTURE 10: PARVOVIRIDAE

Russ Fraser, Fall 2023

Questions?

Housekeeping

- Questions from last time?
- Quiz next week
  - Content
- Case study review

Parvoviridae: General characteristics (p30-31)

Size	25 nm
Morphology	Naked
	Icosahedral
Genome	linear, ssDNA
Site of Replication	• Nucleus • Requires S phase (active division)

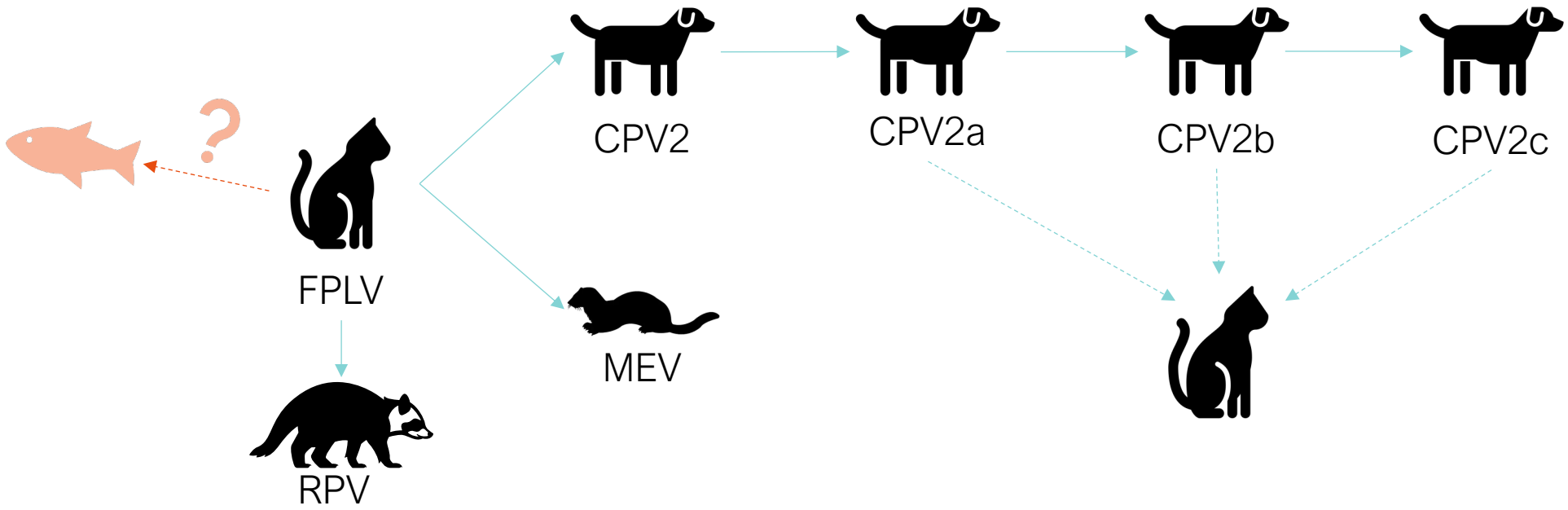
Properties	• Very stable in the environment
	  • Persists for years
	  • Bleach for disinfection
	• Intranuclear inclusion bodies (rarely noted)
	• Release by cell lysis

Parvoviridae

Virus	Disease manifestation
Feline panleukopenia virus	Panleukopenia, enteritis, cerebellar hypoplasia, abortion
Canine parvovirus (2a, 2b, 2c)	Lymphopenia, enteritis, myocarditis (rarely)
Porcine parvovirus	Stillbirth, mummification, embryonic death, & infertility (SMEDI)
Mink enteritis virus	Leukopenia, enteritis, abortion
Aleutian mink disease virus	Chronic immune complex disease; intestitial pneumonia in neonates
Rodent parvoviruses (mice & rats)	Persistent infection; congenital fetal malformations
Goose parvovirus	Hepatitis, myocarditis, myositis
Duck parvovirus	Hepatitis, myocarditis, myositis
Chicken & turkey parvoviruses	Enteritis
Equine parvovirus-hepatitis, (EqPV-H)	Hepatitis (Theiler's disease)?

Parvoviruses: evolution and phylogenetics

- MEV & CPV are host range mutants of FPLV
- CPV emerged in 1974 & spread globally in 1978.
- Since 1980, antigenic variants (CPV-2a & CPV-2b, & recently CPV-2c) have emerged & have completely replaced the original CPV.



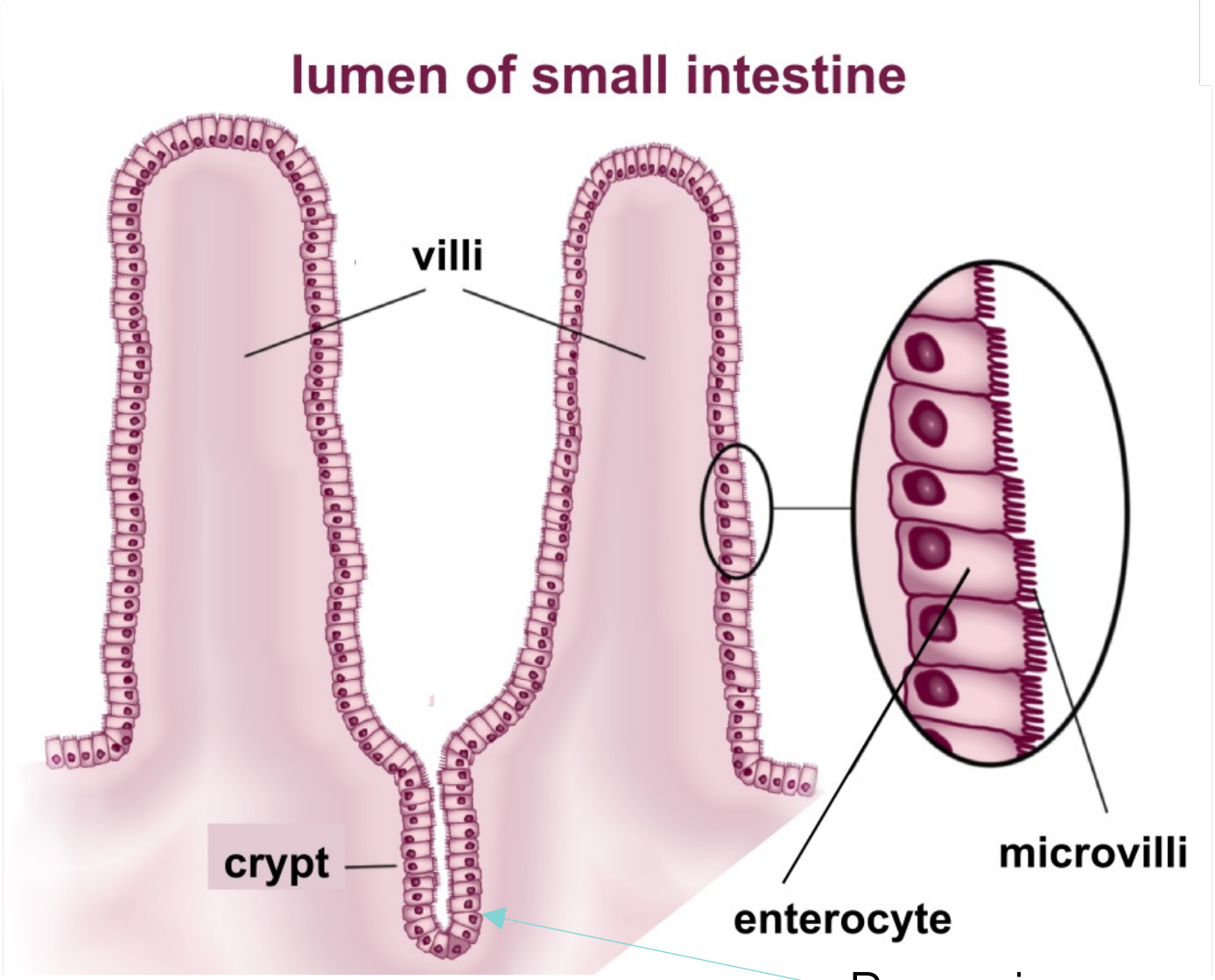
Parvoviridae: General characteristics (page 34)

- Parvoviruses are good immunogens.
- A rapid immune response follows natural infection.
- Recovered animals are immune for life.
- Maternal antibody in dog & cat is passed via placenta (10%) & colostrum (90%)

Parvoviridae: General pathogenesis (p33-34)

- Virus requires cellular proteins only present in S/G2 phase of cell cycle
    - Virus replicates in rapidly dividing cells
    - Virus is released by cell lysis → clinical signs
    - Lesions occur in tissues that have rapidly dividing cells
        - Bone marrow
        - Gastrointestinal crypt cells (NOT PIGS)
        - Fetal tissue (NOT DOGS)
        - Cerebellum (CATS < 4 weeks)

Parvoviridae: General pathogenesis

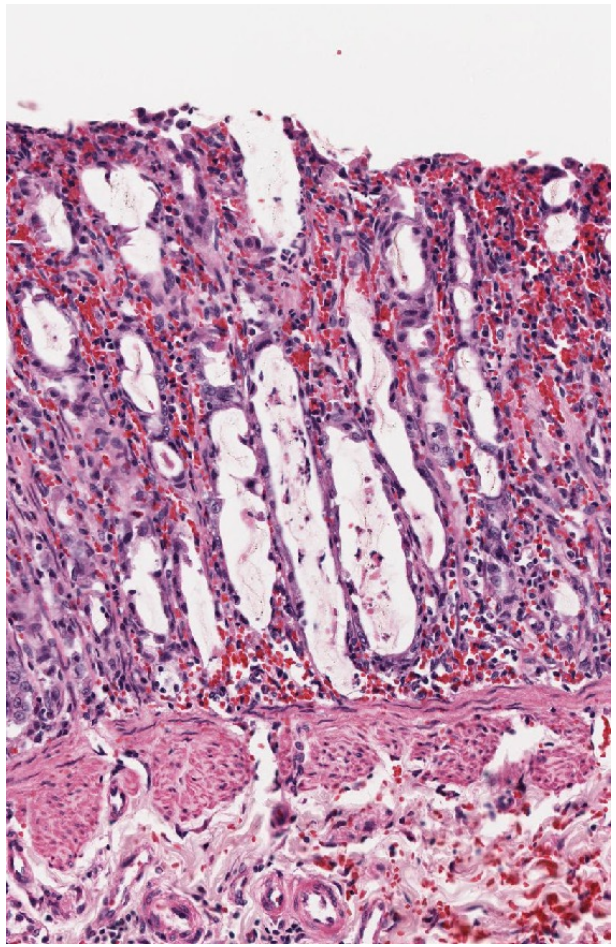


https://upload.wikimedia.org/wikipedia/commons/thumb/0/0e/Villi_&_microvilli_of_small_intestine.svg/1024px-Villi_&_microvilli_of_small_intestine.svg.png

Paroviridae: General pathogenesis



Normal



Feline panleukopenia virus



Feline panleukopenia virus

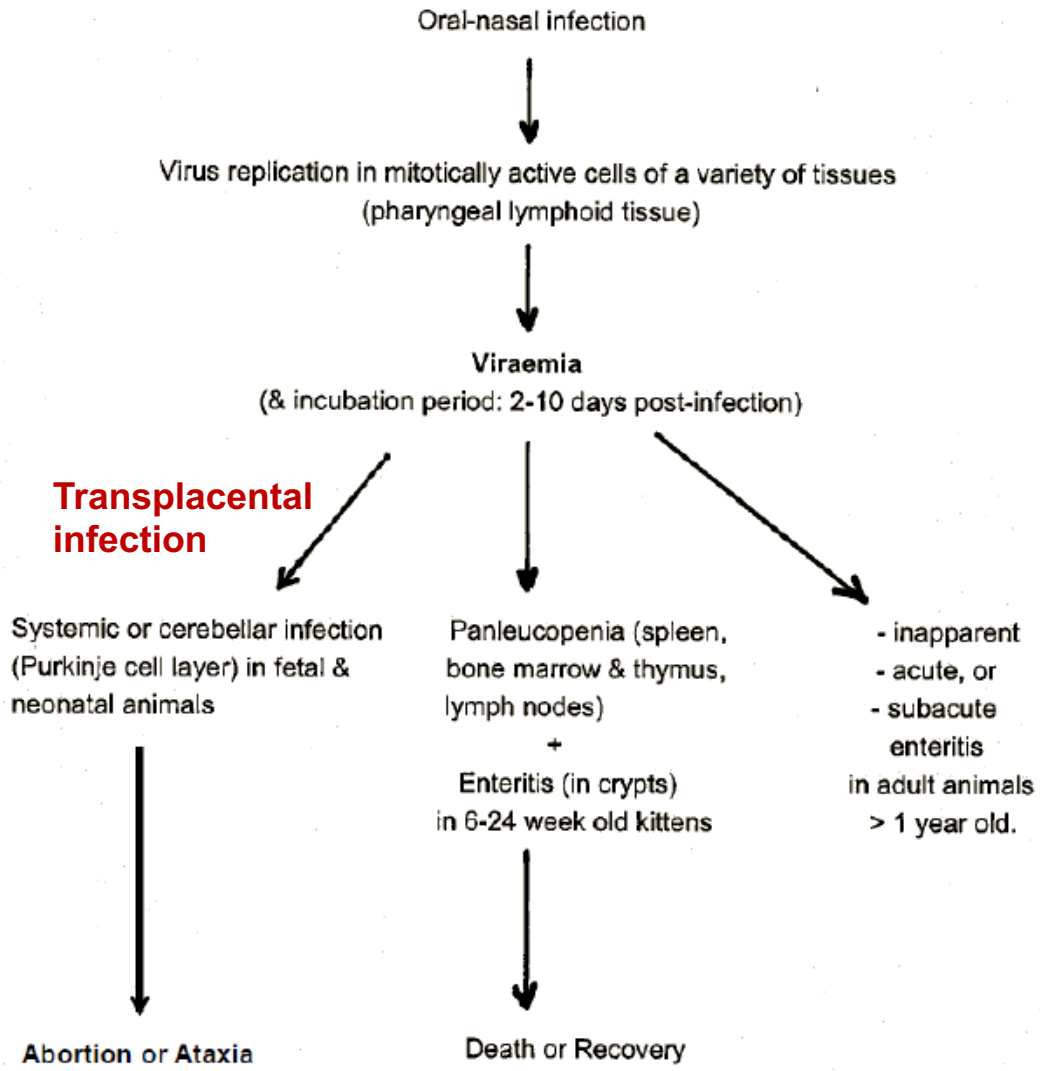
Feline distemper, cat distemper, “panleuk”

Feline panleukopenia virus (pages 34-37)

- One of the most significant viral diseases of cats.
- Transmission occurs transplacentally & horizontally (via fecal-oral route).
- Host range: all felines.
- Clinical disease is most commonly seen when maternal antibodies wane.
- Recovered cats continue to shed virus for up to 6 weeks after recovery.
- Virus persists in premises for ≥ 1 year.
  - It is extremely resistant to environmental conditions: can be transmitted by objects that come in contact with cats, including people who have handled infected cats.



Feline panleukopenia virus: pathogenesis



Feline panleukopenia virus: clinical presentation



Pregnant cats

Abortion/resorption

Birth of mummified fetuses

Infertility



Kittens -2 to 4 weeks old

Nonprogressive ataxia & hypermetria

Head tremors



Kittens 3-5 months old

Depression, anorexia, lethargy,

Fever (>40°C)

Repeated vomiting

Profuse bloody diarrhea

Dehydration

Profound leukopenia

± Death

Feline panleukopenia virus

- Marked ataxia secondary to cerebellar hypoplasia



https://www.youtube.com/watch?v=J2ZKOhzf-w8

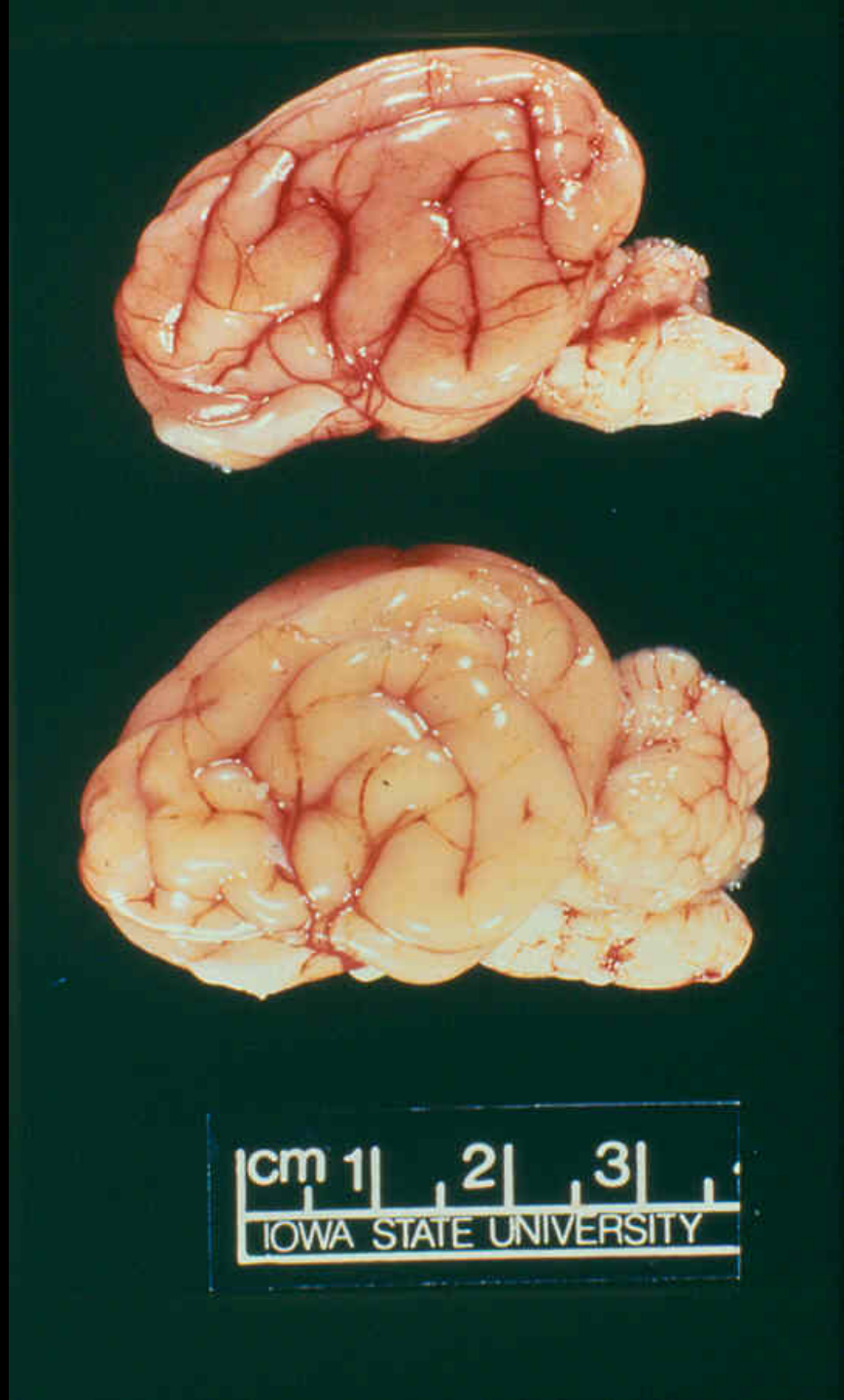
Feline panleukopenia virus: gross lesions

- Marked cerebellar hypoplasia caused by FPLV infection anywhere from 2 weeks before birth to 4 weeks after birth.



Feline panleukopenia virus: gross lesions

- Marked cerebellar hypoplasia caused by FPLV infection anywhere from 2 weeks before birth to 4 weeks after birth.



Feline panleukopenia virus: gross lesions

- Dilated intestinal tract.
- Ecchymotic or petechial hemorrhages on serosal surface of intestinal tract
- Bloody feces.
- Often subtle.



Feline panleukopenia virus: gross lesions

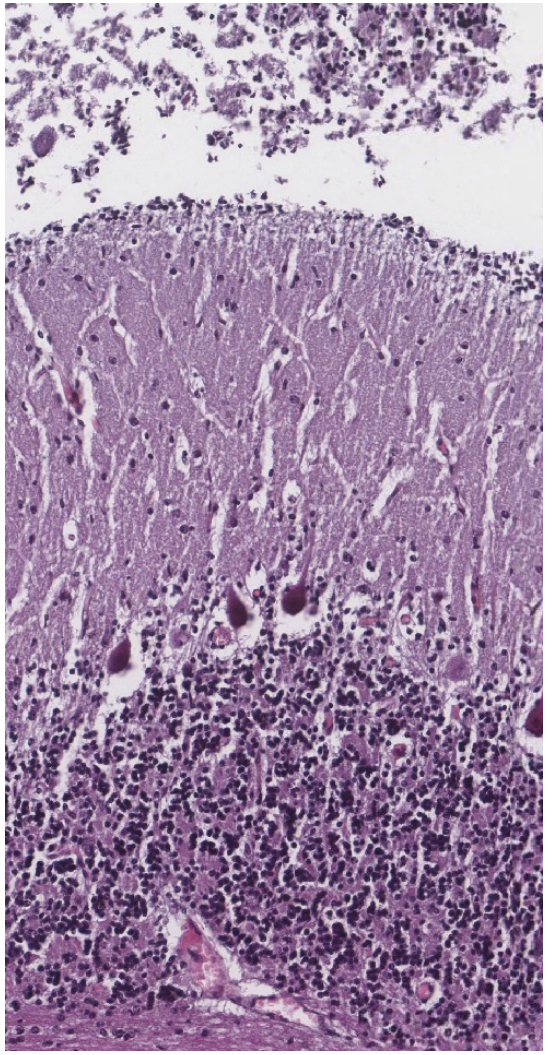


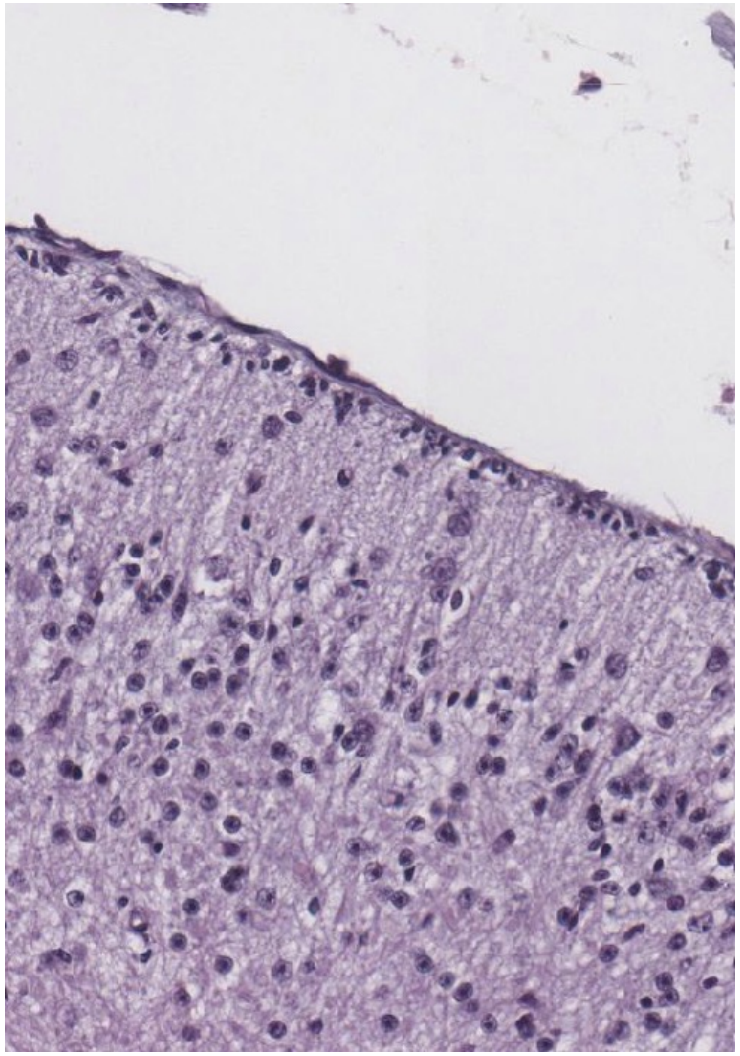


Feline panleukopenia virus: histopathology

- Destruction of Purkinje cell layer of cerebellum (late prenatal or early neonatal ≤ 4wks of age).
- Lymphoid depletion in bone marrow, spleen, thymus, lymph nodes, & Peyer's patches.
- Shortening & blunting of intestinal villi (jejunum & ileum)
  - Mucosal crypts are dilated & distended with mucus & cellular debris.
- Rarely, large eosinophilic intranuclear inclusion bodies

Feline panleukopenia virus





Histopathology of normal and hypoplastic cerebellar folia demonstrating profound Purkinje cell loss, granular cell layer disruption and loss, and attenuation of the molecular cell layer

Feline panleukopenia virus: diagnosis (pages 36-37)

- Presumptive diagnosis:
  - unvaccinated kitten with diarrhea & transient leukopenia.

- Differential diagnosis:
  - FeLV, salmonellosis, feline enteric coronavirus
  - Up to 20% of parvovirus enteritis in cats is due to CPV-2a & CPV-2b

- Confirmatory diagnosis:
  - Virus detection in feces by
    - PCR
    - ELISA
    - EM
    - FA on tissues
    - Virus isolation

Feline panleukopenia virus: treatment & control

- Symptomatic:
  - Fluid therapy (to replace lost electrolytes & to counteract dehydration)
  - Antibiotics protect against possible bacterial infection (sepsis).

- Control:
  - Good hygienic practices to reduce environmental contamination: virus is inactivated by common household bleach.

  - Vaccination:
    - There can be maternal antibody interference.
    - Good vaccination protocol (start at 6-8 weeks, every 3-4 weeks following).
    - Vaccinate kitten before introducing it to infected premises.

  - Good management practices in catteries: separate cats by age, have strict hygiene, quarantine any new cats.



Canine parvovirus

"parvo"

Canine parvoviruses (pages 37-44)

- There are three different types of parvovirus that occur in the dog:

- *Carnivore bocaparvovirus 1* (previously called Canine minute virus, Canine parvovirus type 1 or CPV-1):
  - now reclassified in genus ***Bocaparvovirus***
  - is widespread, & pathogenic to puppies below 3 weeks old; & might cause abortion in pregnant bitches.

- Canine parvovirus (previously called Canine parvovirus type 2 or CPV-2):
  - Is considered a strain of feline panleukopenia virus in the genus ***Protoparvovirus***
  - Causes enteritis in dogs similar to FPL in cats (but not abortion or ataxia)
  - Causes myocarditis in puppies ≤ 8 weeks old.

- Canine adeno-associated virus or CAAV:
  - Non-pathogenic
  - Belongs to the genus ***Dependoparvovirus*** (has defective replication)
  - Depends on adenovirus for its replication.

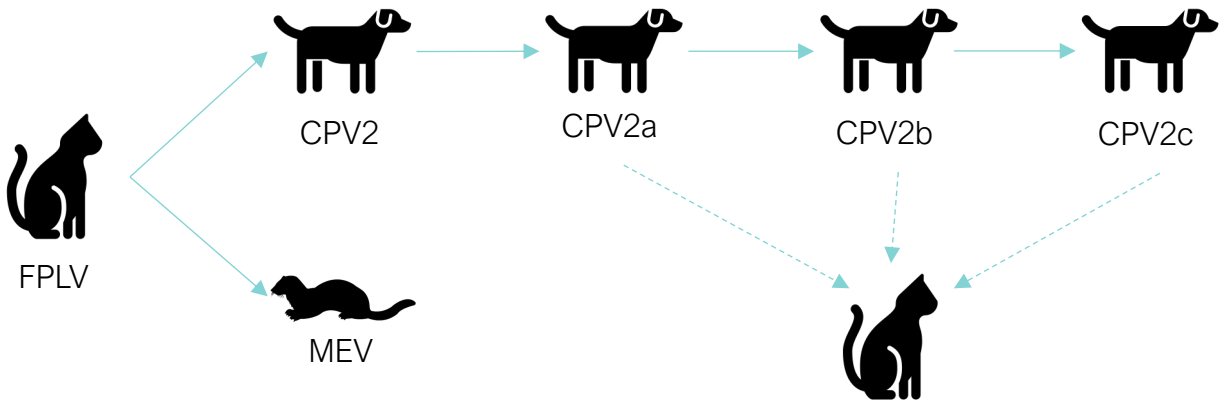


Canine minute virus

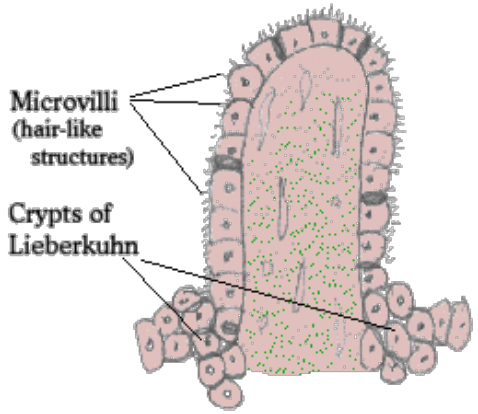
- Most infections are likely subclinical
- Has since been shown to be pathogenic for puppies:
  - causes fatal disease (respiratory illness or diarrhea) in nursing puppies 5-21 days old.
  - transplacental infections with fetal deaths & abortions have only been demonstrated experimentally. (Note: CPV does not cause abortion in dogs).
- Clinical signs:
  - sudden death between 1-3 weeks of age,
  - vomiting, diarrhea (even in puppies with maternal antibodies to CPV),
  - dyspnea, & crying in puppies.
- Diagnosis:
  - Routine diagnostic tests are not widely available, but
  - Virus is readily isolated using Walter Reed canine cell line and can be identified by immunofluorescent staining.

Canine parvovirus 2

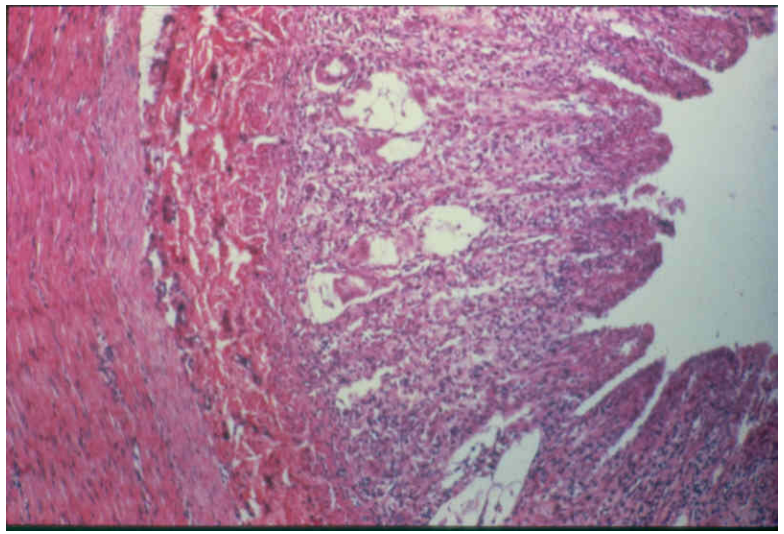
- Host range: all members of the family Canidae (dogs, wolves, coyotes) are susceptible to natural infection with CPV.
- The newer antigenic variants of CPV, CPV-2a, CPV-2b, & CPV-2c:
  - Are more virulent
  - Have shorter incubation period
  - Cause more severe disease (haemorrhagic enteritis or collapse of the animal).
  - CPV-2c was 1st reported in the US in 2006, where it is now the commonest variant of CPV.
  - The variants replicate & sometimes cause disease in cats (feline CPV infections are rare in Europe & USA; current FPLV vaccines protect against these new CPV variants).



Canine parvovirus 2

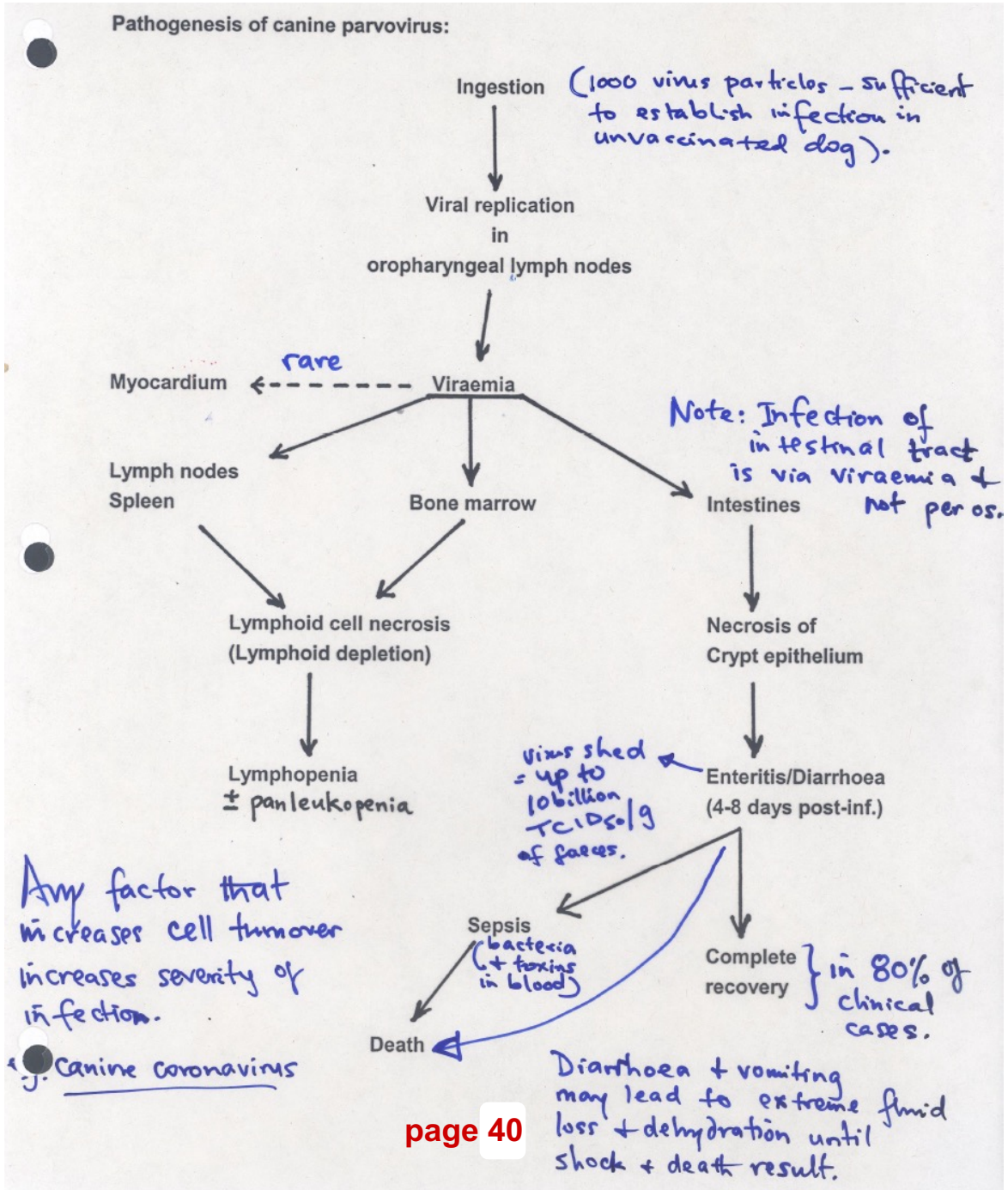


Normal Intestinal Villus



Necrosis of intestinal epithelial cells in crypts of Lieberkuhn, and fusion and blunting of the villi.

- Pathogenesis of CPV in the dog is similar to that of FPLV
  - Abortion & cerebellar hypoplasia do not occur
  - Myocarditis can occur in dogs < 1 week old, but is now seen only rarely. Why?
- Clinical disease is most commonly seen in puppies 8-12 weeks old when maternal antibodies wane
- Dogs in single dog households & adult dogs may only develop a subclinical infection.



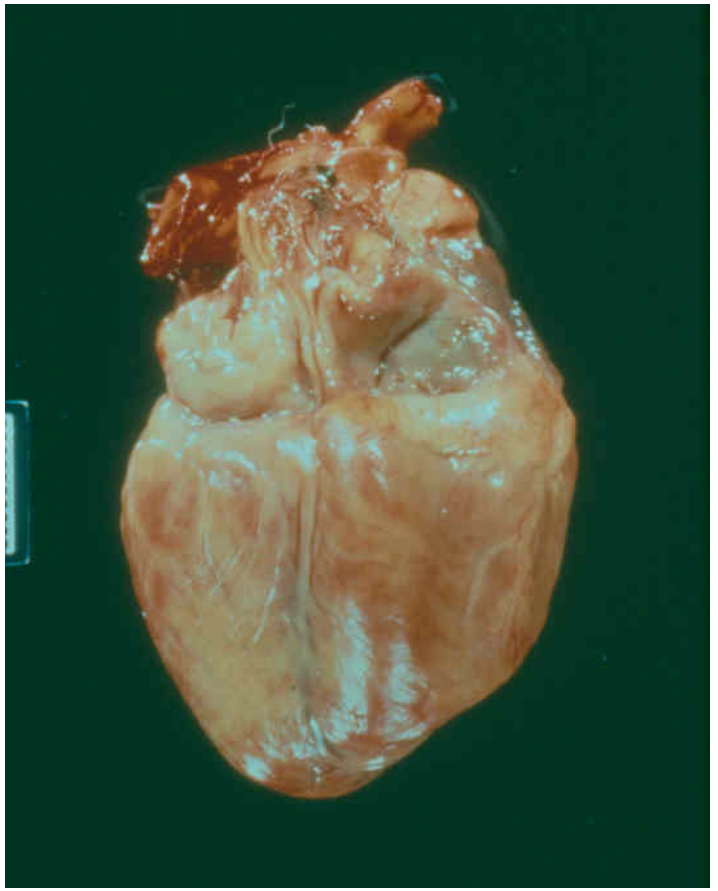
Virus reaches the intestinal tract via viraemia; therefore mucosal immunity (intestinal IgA) has no role in protective immunity.

Canine parvovirus 2: pathogenesis

- Similar to cats.
- Cerebellum unaffected
- Myocardium can be infected in dogs < 1 week

Canine parvovirus 2: clinical signs

- Myocarditis in dogs < 1 week old (now rare due to widespread vaccination of dogs):
  - Sudden death in pups
  - Survivors have signs of congestive heart failure (exercise intolerance, coughing, dyspnea) months/years later.
- Lymphopenia & +/- panleukopenia
  - Susceptibility to secondary infections
- Enteritis:
  - Acute fever, vomiting & diarrhea (hemorrhagic in 50% of cases).
- Note: less severe cases are more common & may pose a diagnostic challenge.



Canine parvovirus 2: clinical signs (page 41)

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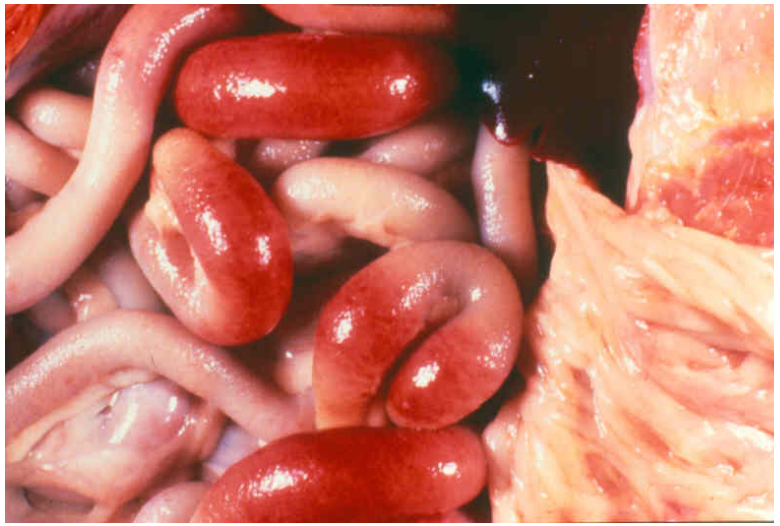
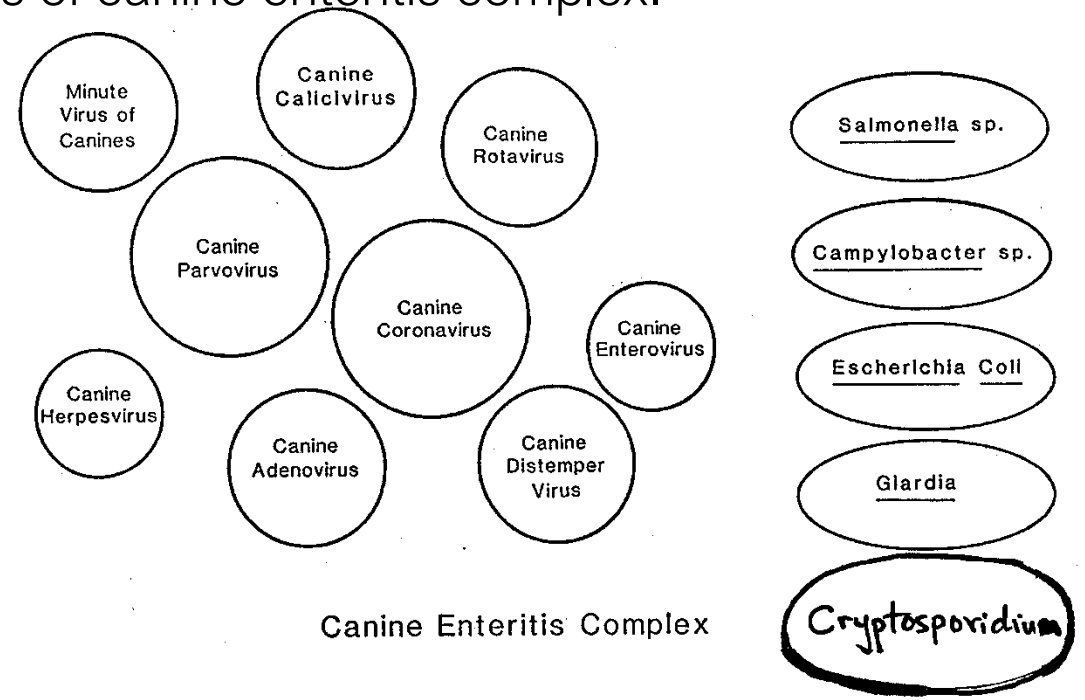


Canine parvovirus 2: diagnosis

- Note: the less severe cases present a problem because there are many causes of enteritis in a dog.

- Differential diagnosis:
  - consider the agents of canine enteritis complex.



Canine parvovirus 2: diagnosis

- Differential diagnosis:
  - consider the agents of canine enteritis complex.

- Confirm diagnosis in feces by:
  - ELISA (SNAP test)
  - PCR
  - EM [CPV is indistinguishable from Minute virus of canines & CAAV]
  - HA & HI with pig or cat RBCs
  - Virus isolation



Canine parvovirus 2: control

- Treatment & control of sick animals are as for FPLV in cats (page 37).
- Control:
  - Good management practices (in kennels: isolate puppies at 4-6 weeks of age until their vaccination series is complete).
  - Good hygienic practices
  - Disinfection with household bleach
- Vaccination:
    - MLV-CPV vaccine is a “core vaccine”
    - Remember: Maternal antibody interference is the commonest cause of “vaccine” failure in puppies ≤ 22wks old.
- Breed predispositions?

Canine parvovirus 2

“certain breeds of dogs have been suspected to be poor-responders. It is believed (but unproven) that the high susceptibility to CPV-2 recognized in certain Rottweilers and Dobermanns during the 1980s (regardless of their vaccination history) relates in part to a high prevalence of non-responders (Houston *et al.* 1994).In the USA today, these two breeds seem to have no greater numbers of non-responders to CPV-2 than other breeds, possibly because carriers of the genetic trait may have died from CPV-2 infection. Some dogs of these breeds may be low or non-responders to other antigens. For example, in the UK and Germany, the non-responder phenotype remains prevalent amongst Rottweilers for CPV-2 and recent studies have shown this breed to have a higher proportion of animals failing to achieve the titre of rabies antibody required for pet travel”

☹

WSAVA Guidelines for the vaccination of dogs and cats, 2016

Canine parvovirus 2: control

- Any commercially available CPV vaccine can protect dogs against <u>all subtypes of CPV</u>





Porcine parvovirus

Porcine parvovirus: general

- Virus is widespread (prevalence in USA herds is 90%)
  - 50% of gilts near breeding age are seropositive
- Virus is a major cause of infertility in pig herds.
- Neonatal & postnatal infections are mostly subclinical (i.e., there is no clinical enteritis)
  - Clinical disease is only in pregnant pigs which manifest abortion and SMEDI syndrome.
- Clinical signs of SMEDI are most noticeable at 1st introduction of virus in seronegative herd with many pregnant sows.
- With time, losses are less obvious.

Porcine parvovirus: clinical signs

- SMEDI
  - Stillbirth
  - Mummification
  - Embryonic Death
  - Infertility
- Sows are usually not symptomatic



Porcine parvovirus: clinical signs

- SMEDI
  - Stillbirth
  - Mummification
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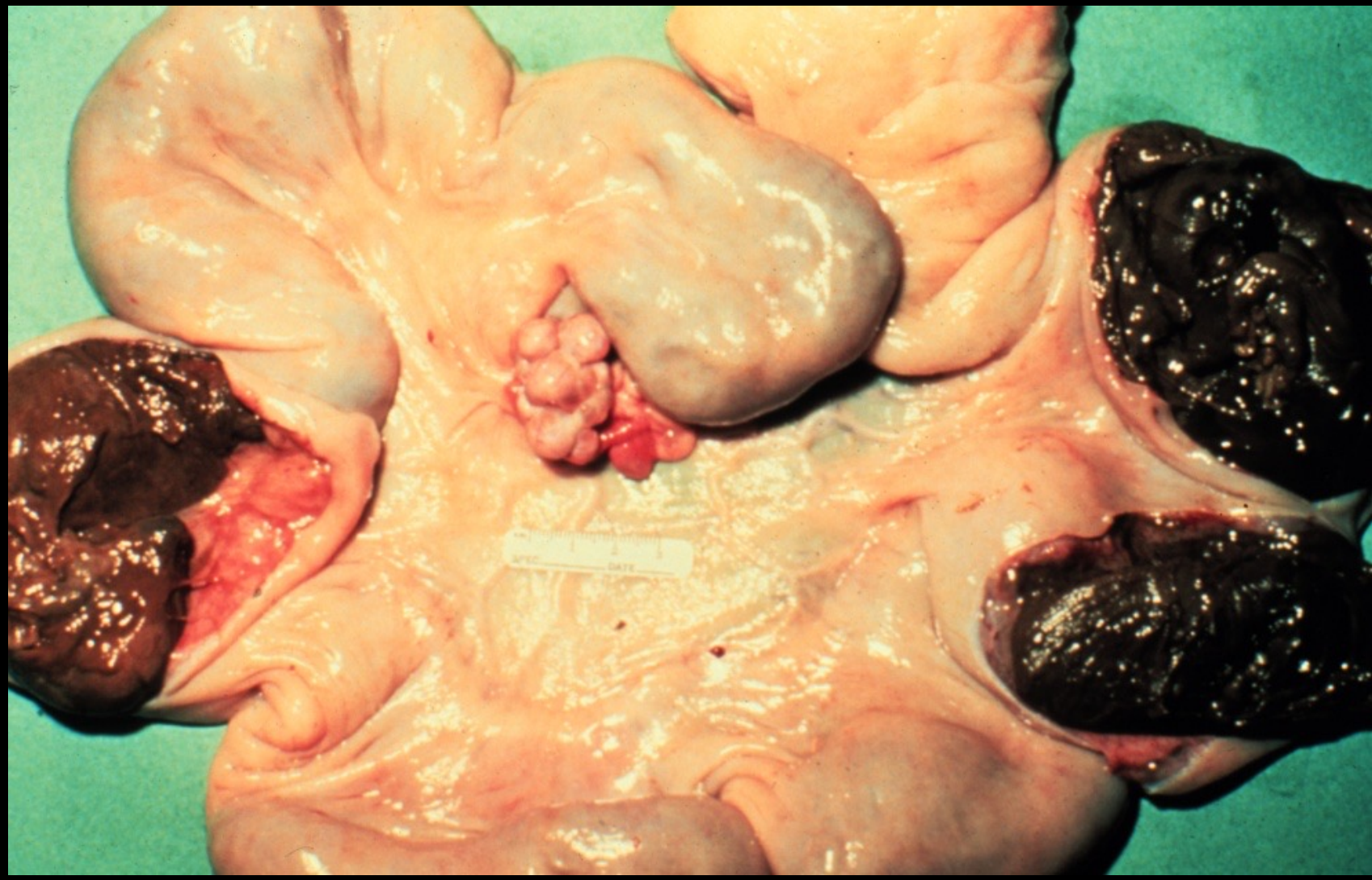
  - Infertility
- Sows are usually not symptomatic



Porcine parvovirus: diagnosis (pages 45-46)

- DDx: viral causes of abortion & infertility in pigs
  - Pseudorabies
  - Hog cholera/classical swine fever/porcine pestivirus
  - PRRS

- History: ↓ litter size, ↑ mummies + embryonic deaths, lack of illness in sows → suspicious for parvovirus

- Confirm diagnosis by:
  - PCR (lung from aborted fetuses)
  - Immunofluorescence (lung from aborted fetuses)

Porcine parvovirus: control

- No treatment.
- Vaccination with MLV
- Good management practices:
  - Avoid introduction of virus to pregnant sows
  - All progeny in affected litter should be disposed of as they are persistently infected.



Aleutian mink disease virus

Mink parvoviruses (pages 46-48)

- There are two different types of parvovirus (belonging to two different genera) that occur in the mink:
    - Mink enteritis virus (similar to FPLV but does not cause cerebellar hypoplasia in mink kits).
    - Aleutian mink disease virus (has a different pathogenesis to other parvovirus diseases).
        - Is one of the most important diseases of the mink industry.
        - There are commercial mink ranches in USA & Canada (particularly in Nova Scotia, Newfoundland, Ontario, & British Columbia)

Aleutian mink disease virus: transmission

- Virus is present in blood, bone marrow, spleen, feces, urine and saliva of infected mink.

- Direct transmission or indirect transmission are possible
  - e.g. equipment/feed/water, etc.

- Vertical transmission is also important.

Aleutian mink disease virus: pathogenesis

- Is most severe in mink recessive for the Aleutian coat colour
  - But affects all mink.



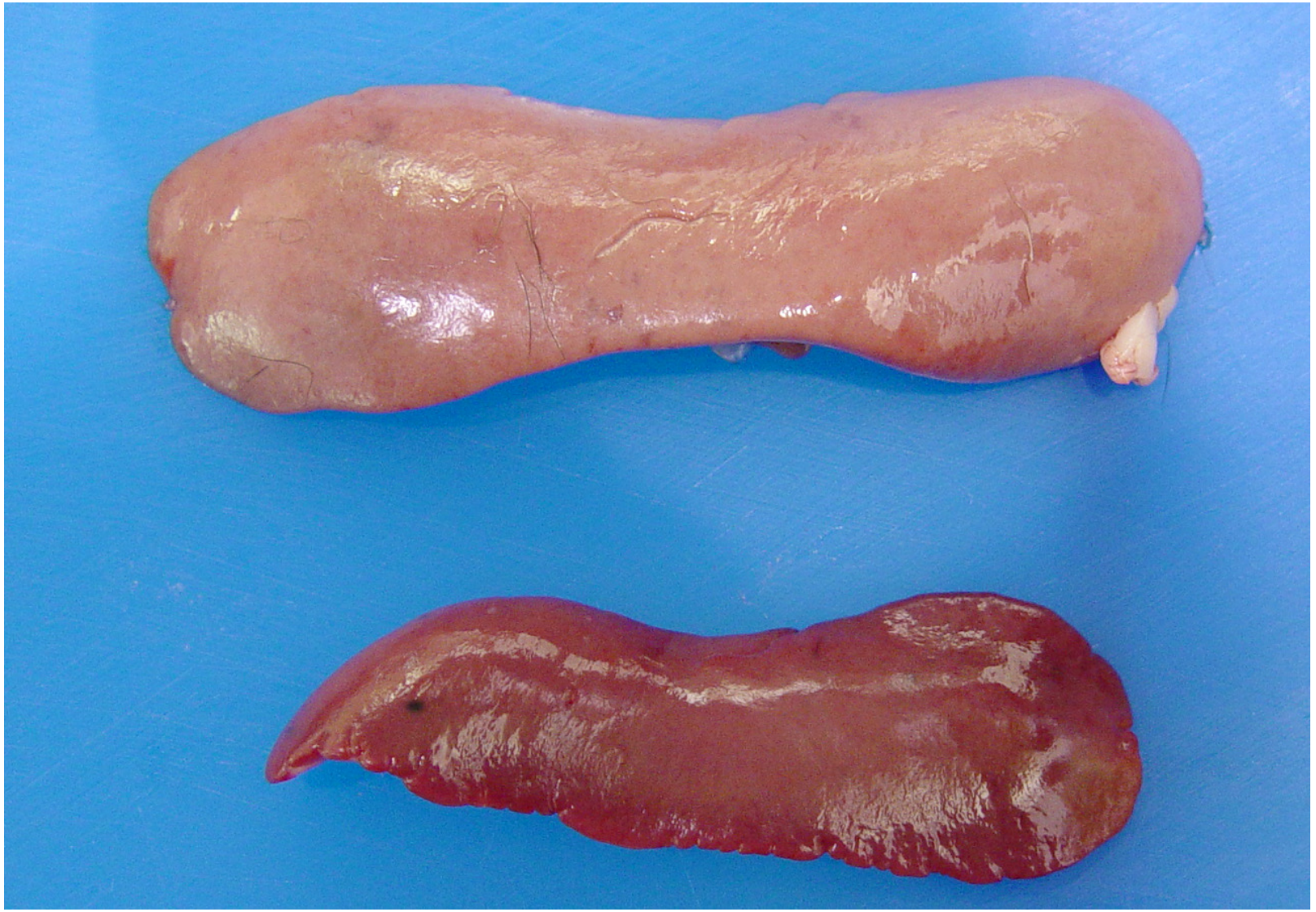
Aleutian mink disease virus: pathogenesis

- Adults:
  - Slowly progressive disease (months - year)
    - During this time the animal is asymptomatic but sheds virus
  - Infection → plasmacytosis → ↑ ↑ antibody production
    - Antibodies are not neutralizing
  - ↑ Antibodies + antigen → Ab-ag complex → deposition in glomeruli, vessels, and other organs → glomerulonephritis, vasculitis

Aleutian mink disease virus: clinical signs

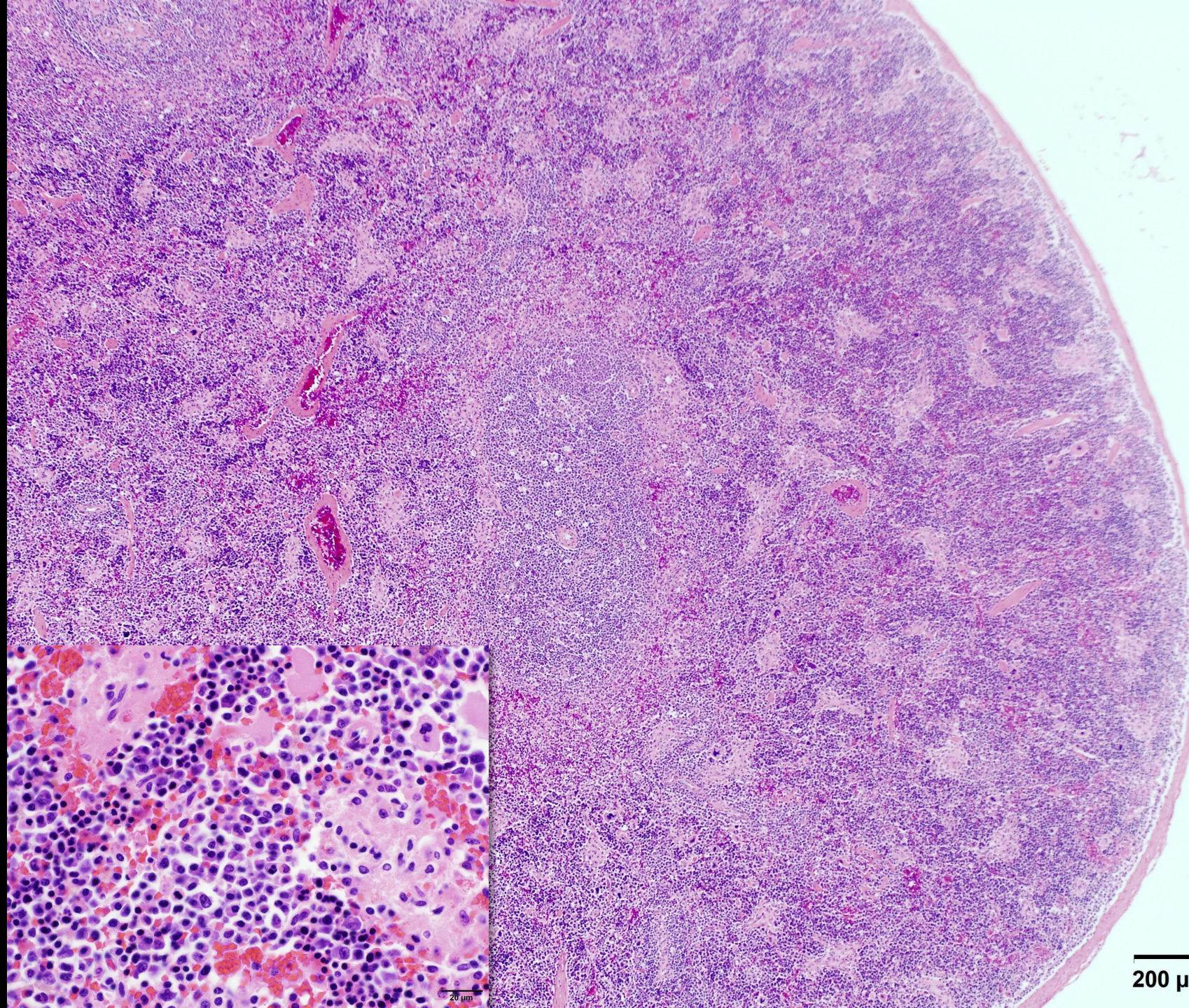
- 3 types of infections occur:
  - Adult mink infections:
    - Anorexia and chronic wasting
    - Splenomegaly and lymphadenopathy
    - Systemic plasmacytosis
    - Elevated serum IgG levels
    - Glomerulonephritis, arteritis, & focal hepatitis
    - Splenomegaly & lymphadenopathy
    - Death.
  - Neonatal infections:
    - Very severe acute interstitial pneumonia, usually fatal within 3 weeks.
  - Transplacental infections:
    - Minks are asymptomatic but live long enough to reproduce (& they are most important in perpetuating disease on farm).

Aleutian mink disease virus: lesions



Aleutian mink disease virus: lesions

- Histopathology:
  - ↑ ↑ plasma cells in various organs



Aleutian mink disease virus: diagnosis & control

- Diagnosis
  - Detection of antibody in serum
  - PCR

- Control
  - No vaccine
  - Test and cull
  - Closed farm
  - Quarantine incoming animals



Equine parvovirus

Equine parvovirus

- Active area of research.
- Equine parvovirus-hepatitis (EqPV-H) is a newly identified etiology of equine serum hepatitis (i.e., Theiler's disease or idiopathic acute hepatitis).
- Disease is acute hepatitis that occurs in horses 30-70 days after administration of equine blood products, typically hyperimmune equine plasma or serum (most commonly associated with administration of tetanus antitoxin).
- Etiology, mechanism of transmission & pathogenesis of this disease had remained unknown since 1919.
- Other viruses (flavivirus) are also associated with Theiler's disease

Equine parvovirus

Based on strong evidence indicating that EqPV-H causes hepatitis in horses, veterinarians should consider this virus an important differential diagnosis in such cases.

Ramsauer AS, Badenhorst M, Cavalleri JV. Equine parvovirus hepatitis. Equine Vet J. 2021 Sep;53(5):886-894. doi: 10.1111/evj.13477. Epub 2021 Jul 4. PMID: 34101906; PMCID: PMC8457058.