Lecture 17: Paramyxoviridae



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Russ Fraser, Fall 2023

Housekeeping

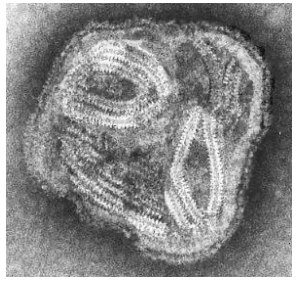
- Cows with LSDV can have lesions and be debilitated for months – do they remain infectious for that entire period?
- From the OIE/WOAH:

> "LSDV is very resistant to inactivation, surviving in necrotic skin nodules for up to 33 days or longer, desiccated crusts for up to 35 days, and at least 18 days in air-dried hides"

> "Skin nodules, scabs, and crusts contain relatively high amounts of LSDV. Virus can be isolated from this material for up to 35 days and likely longer"

Paramyxoviridae

Size	150 – 300 nm
Morphology	Enveloped
	Pleomorphic
Genome	• ss, -ve sense RNA • Linear • 13-19 kb
Site of Replication	• Cytoplasm
Properties	• Mature by budding • IN and IC inclusions • F protein has a polybasic cleavage site (like AIV) that affects pathogenicity (particularly NDV) • Mainly cause respiratory disease



Paramyxoviridae

- Canine distemper virus
- ★Newcastle disease virus

- Bovine parainfluenza virus 3
- Canine parainfluenza virus 5
- Hendra and Nipah viruses

- ★Rinderpest
- Peste-des-petits-ruminants

- (Measles)
- (Mumps)





Avian paramyxovirus 1

Newcastle disease virus

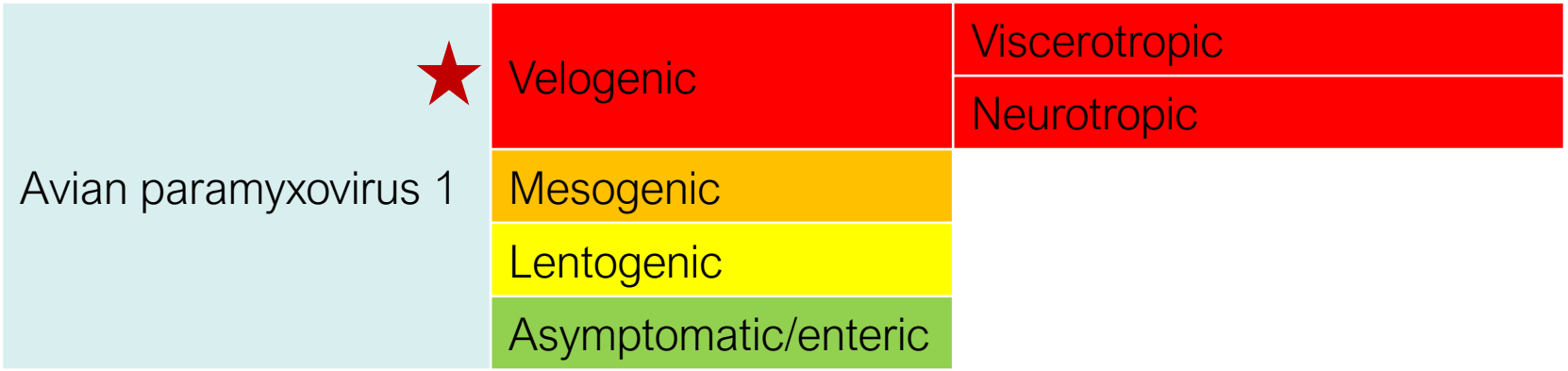
Avian paramyxovirus 1

- One of the most contagious viruses of birds
- Can infect most, if not all, bird species



Avian paramyxovirus 1

- There are numerous strains of avian paramyxovirus 1
- Divided into ‘pathotypes’:



- Like avian influenza virus, not all strains of avian paramyxovirus 1 are reportable
- These reportable strains are also known as Newcastle disease virus
  - They are, by definition, virulent.
  - The non-reportable (lentogenic, asymptomatic) strains are no longer referred to as NDV – they are avian paramyxovirus 1

Avian paramyxovirus 1

- For the purposes of the Terrestrial Code, Newcastle disease (ND) is defined as an infection of poultry caused by Newcastle disease virus (NDV), which is an avian paramyxovirus serotype 1 (APMV-1) that meets one of the following criteria for virulence:
  - The virus has an intracerebral pathogenicity index (ICPI) in day-old chicks (*Gallus gallus*) of 0.7 or greater
  - Multiple basic amino acids have been demonstrated (either directly or by deduction) at the C-terminus of the fusion protein.

Avian paramyxovirus 1

- Low-virulent and avirulent strains are maintained in waterfowl and poultry
- NDV are maintained and spread in domestic poultry
  - Cormorants have also been implicated as a reservoir in NA
- Mutations in the F protein can lead to an avirulent enzootic strain → NDV
- Significant economic importance



Avian paramyxovirus 1: transmission

- Primary transmission is via inhalation or aerosols and/or dust particles or ingestion of contaminated feed/water.
- All secretions and excretions contain virus
- Shed for up to 4 weeks in survivors
  - Some Psittacine birds may shed for > 1 yr without clinical signs
- Relative stability of the virus facilitates mechanical spread from farm-to-farm
- Vertical transmission is rare



Avian paramyxovirus 1: pathogenesis

Lentogenic, asymptomatic →

Inhalation

↓

Replication in epithelium of the airways and intestine

Avian paramyxovirus 1: pathogenesis

NDV →

Pathogenicity is determined by the presence of a polybasic cleavage site in the F protein

Inhalation

↓

Replication in epithelium of the airways and intestine

↓

Viremia

↓

Spleen, LN, BM

↓

Secondary viremia

↓

Lung, intestine, CNS

Inflammation, necrosis, and destruction of lymphoid tissue

Avian paramyxovirus 1: clinical signs

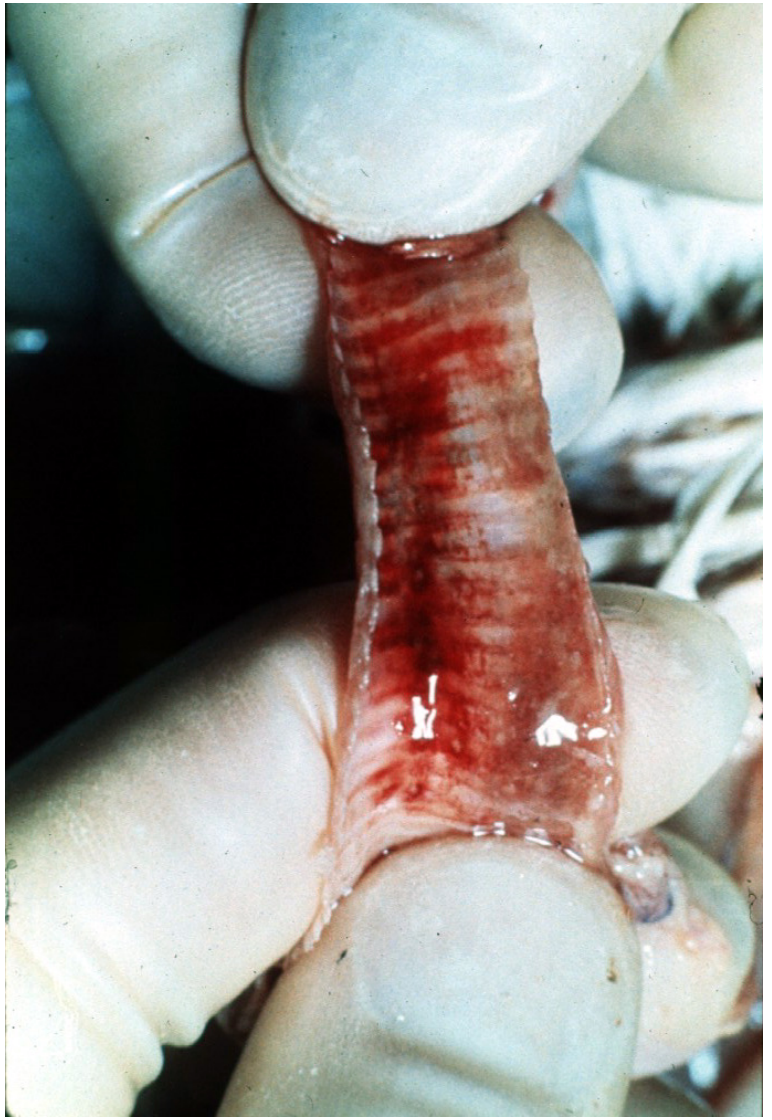
- Clinical signs are variable, and depend on the infecting strain, immune status, and age of host
- Typical incubation period is ~ 2 – 10 days. Spread in flock is rapid.

Velogenic-viscerotropic	Velogenic-neurotropic	Mesogenic	Lentogenic	Asymptomatic
• ~100% mortality • ↑ RR, dyspnea • Anorexia, huddling • Periorbital edema • ± neuro signs • ± diarrhea • ↓↓ Egg production	• Respiratory disease ↓ • Paresis • Paralysis • ~ 50% mortality • ↓↓ egg production	• Respiratory disease • ↓ egg production • Low mortality • Rarely, neuro signs	• Usually asymptomatic unless complicated by secondary bacterial infection → respiratory disease	• Usually asymptomatic, occasionally mild enteric disease

Few gross lesions

Avian paramyxovirus 1: gross lesions





Avian paramyxovirus 1: gross lesions





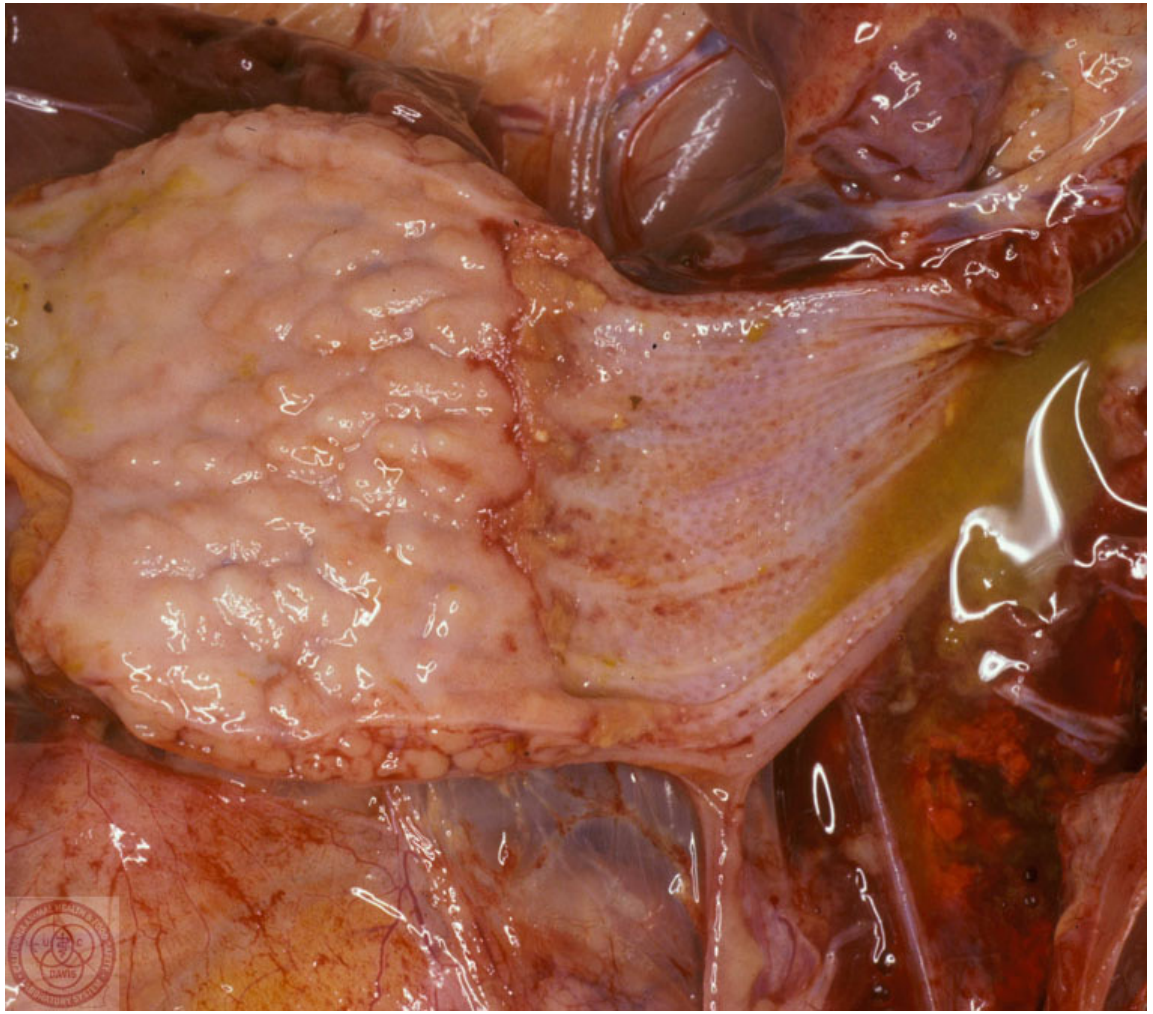
Avian paramyxovirus 1: gross lesions





Avian paramyxovirus 1: gross and histo

- Hemorrhage and necrosis particularly at junction of esophagus-proventriculus and proventriculus-gizzard
- Multifocal hemorrhage in small intestine
- Hemorrhages can also be seen in the subQ, muscles, pericardium and myocardium
- The lesions in the CNS include encephalomyelitis, neuronal necrosis, perivascular cuffing, and interstitial inflammatory infiltration



Avian paramyxovirus 1: diagnosis

- Differential diagnosis:
  - Avian influenza
  - Marek's disease (neurolymphomatosis), Infectious bronchitis, ILT

- Confirmatory diagnosis:
  - PCR
    - Careful in vaccinated flocks
  - Virus isolation & determination of virulence of field isolate – *this is technically the requirement for case confirmation by the CFIA*.

Avian paramyxovirus 1: control

- Control:
  - Reportable disease: velogenic strains are exotic to US & Canada.
    - In case of outbreak, quarantines are set up & all poultry on affected farm are slaughtered with compensation. Farm is disinfected & restocked after 21 days.
  - Vaccination is with live lentogenic/asymptomatic strains
    - Vaccination is commonly practiced.
  - Increase biosecurity on farm (NCD virus is highly infectious).

- Zoonotic
  - NDV can cause self-resolving conjunctivitis in humans.



APHIS, USDA



Canine distemper virus

"hard pad disease", distemper

Vyacheslav Oseledko / AFP via Getty

Canine distemper virus

- Virus belongs to genus Morbillivirus.
- This is one of the most important viral disease of dogs (d/t guarded prognosis)
- Rare due to wide use of vaccination.
- Host range:
  - All Canidae (virus is enzootic in wild Canids)
  - Raccoon, ferret, mink, skunk
  - Large cats (lions, leopards, cheetahs, tigers)
  - Not domestic cats
- Young dogs < 3-6 months old (after loss of maternal antibody – if dog is not vaccinated) are most susceptible.

TABLE 3-1

Terrestrial Carnivores Susceptible to Canine Distemper[a,b]

Order	Description
Ailuridae	Lesser panda
Canidae	Coyote, dingo, raccoon dog, wolf, fox
Mustelidae	Ferret, marten, mink, otter, wolverine, badger
Mephitidae	Skunk
Procyonidae	Coati, kinkajou, raccoon
Ursidae	Bear, giant panda
Viverridae	Binturong, fossa, linsang, civet
Herpestidae	Mongoose, meerkat
Felidae (large species)	Cheetah, lion, jaguar, margay, ocelot

[a]Subclinical infections occur in noncarnivores including the Asian elephant and Tayassuidae (peccaries). Information from Ref. 20 and 217.
[b]See also Table 100-10 for vaccination recommendation for these animals.

Green's Infectious Disease of the Dog and Cat

Canine distemper virus: transmission

- Primarily aerosolized respiratory secretions
  - Oronasal/inhaled
- Can be found in almost any secretion or excretion
- Virus is relatively susceptible to environmental degradation
  - Can persist in colder temperatures
  - Close contact is generally required



Canine distemper virus: pathogenesis

1. Infection of URT and tonsils

   Particularly macrophages

2. Primary viremia

3. Spleen, Kupffer cells, GALT, mesenteric LNs

   Cells with SLAM receptor:

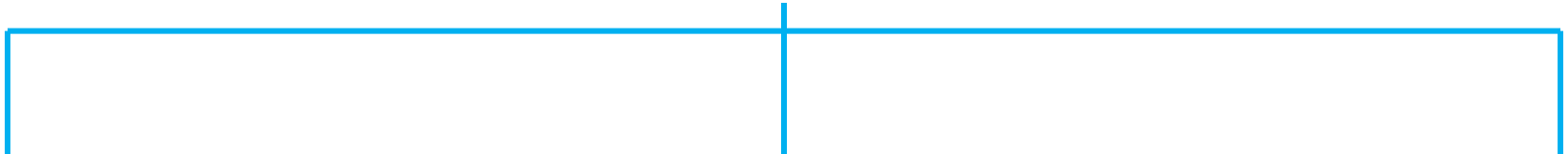
   Activated lymphocytes, macrophages, dendritic cells, thymocytes

   → Marked immunosuppresion d/t destruction of lymphocytes

4. Secondary viremia

5. Epithelial cells of the respiratory tract, urogenital tract, GI tract, skin, and endo/exocrine glands

   Uses a different receptor for epithelial cells – nectin-4



😀

Good immune response:

Clear the virus, little to no signs of illness

😐

Intermediate response:
Spread within these organs and clinical signs which *may* resolve

May involves CNS

😭

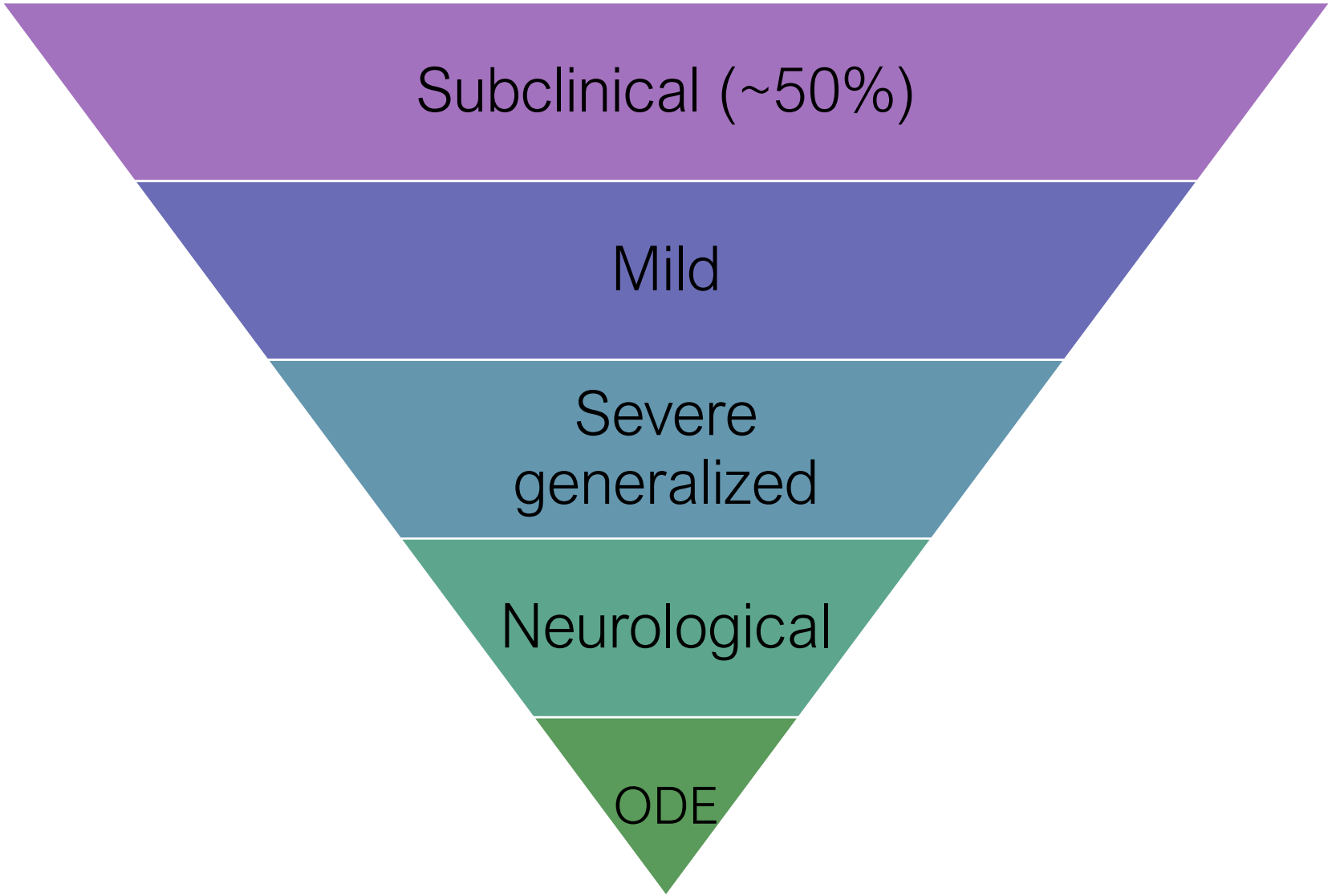
Poor response:

Severe disease reflective of infection of the above organs

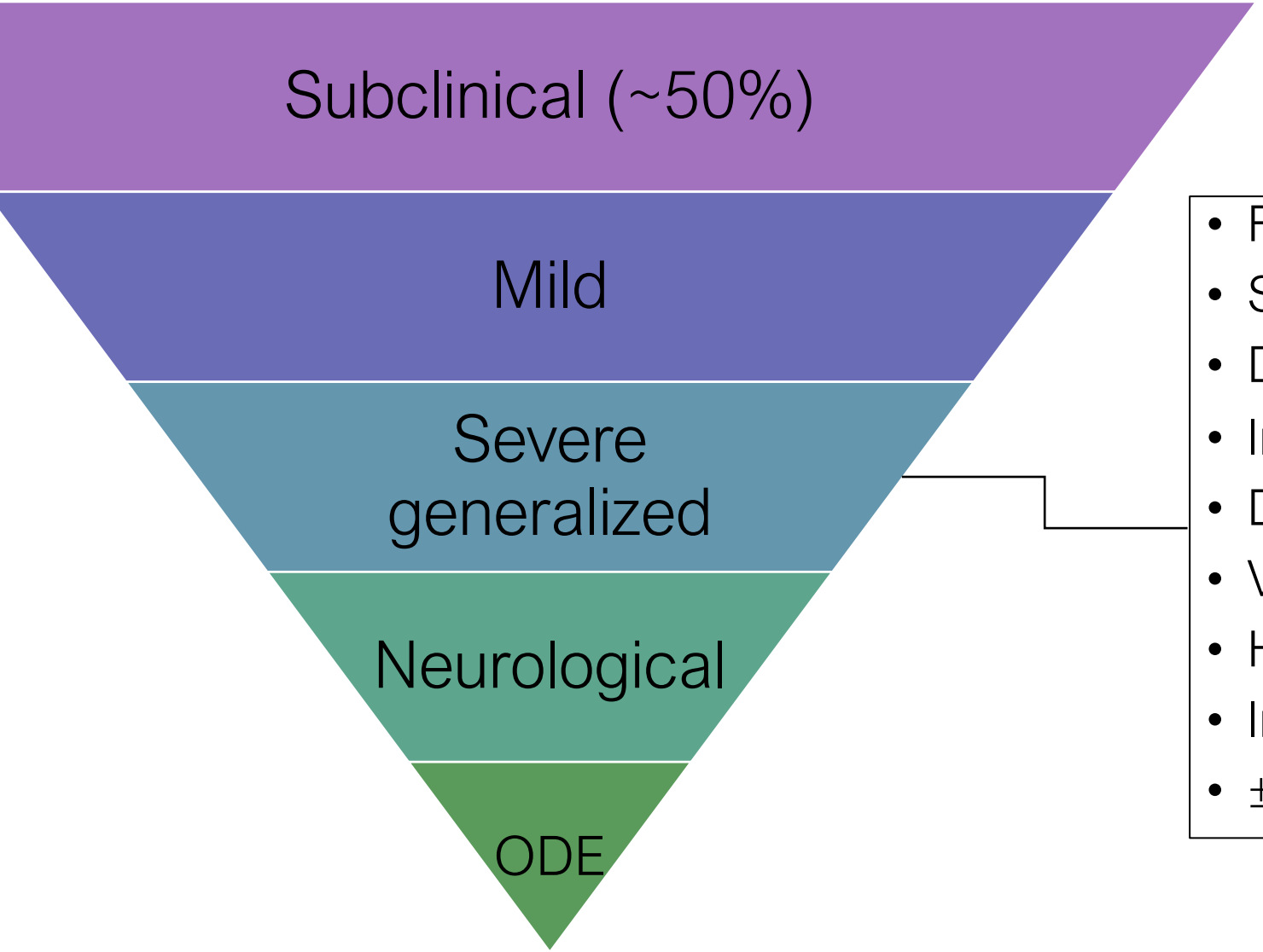
CNS involvement likely

Death likely

Canine distemper: clinical signs

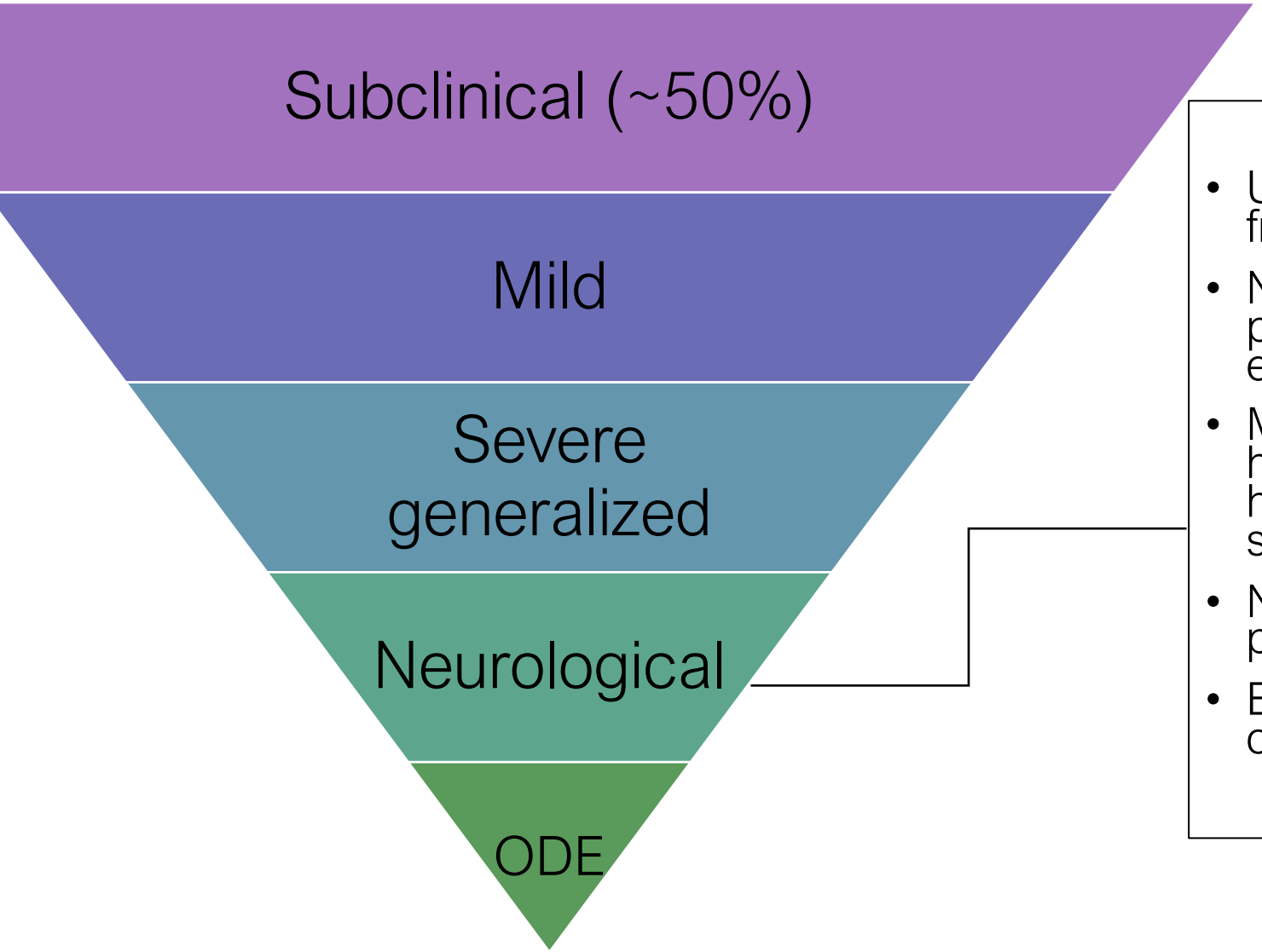


Canine distemper: clinical signs



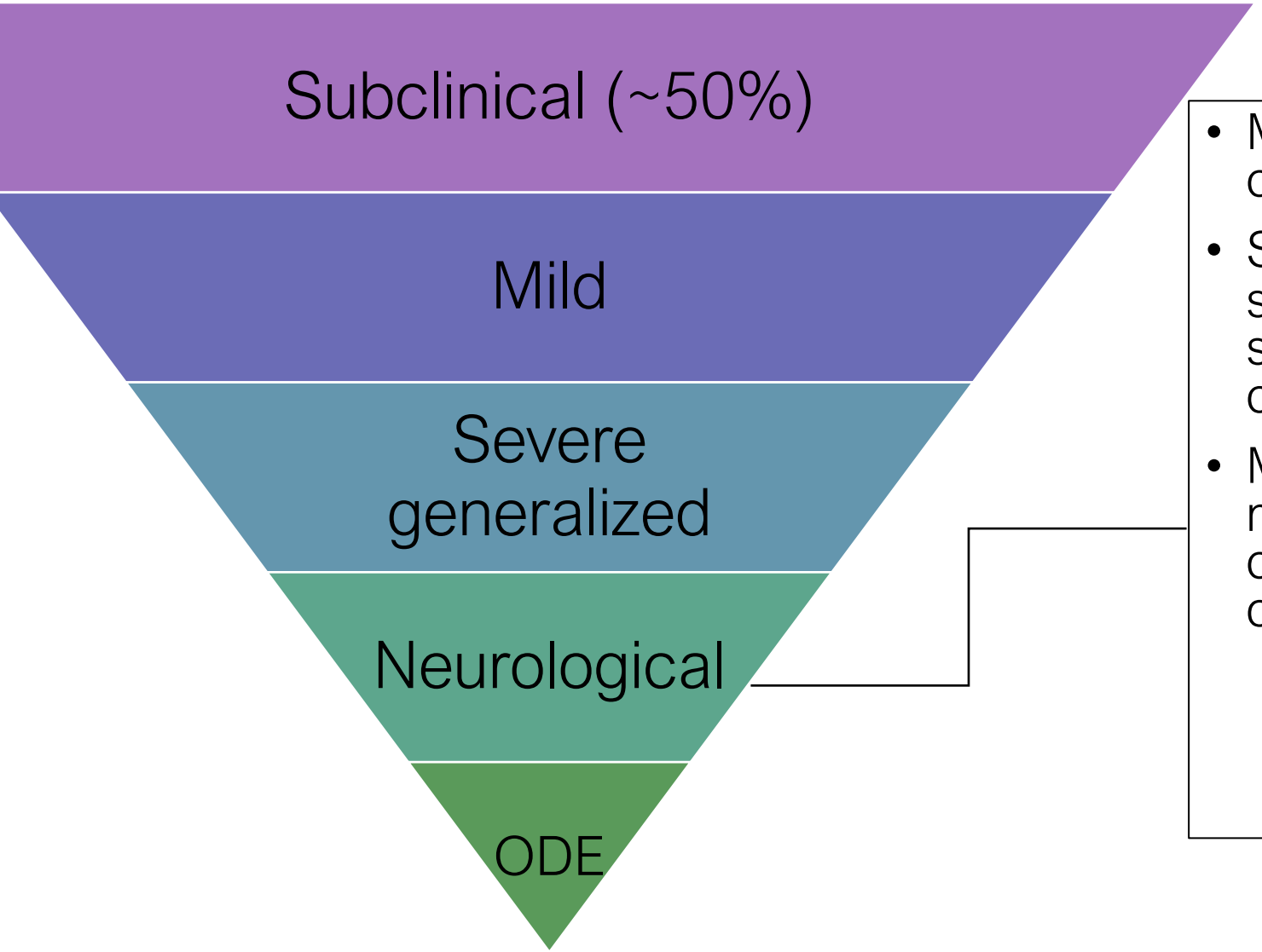
- Fever (biphasic)
- Serous-mucopurulent conjunctivitis
- Dry → productive cough
- Increased lung sounds
- Depression, anorexia
- Vomiting and diarrhea
- Hyperkeratosis esp of feet and nose
- Immunosuppresion
- ± Death

Canine distemper: clinical signs



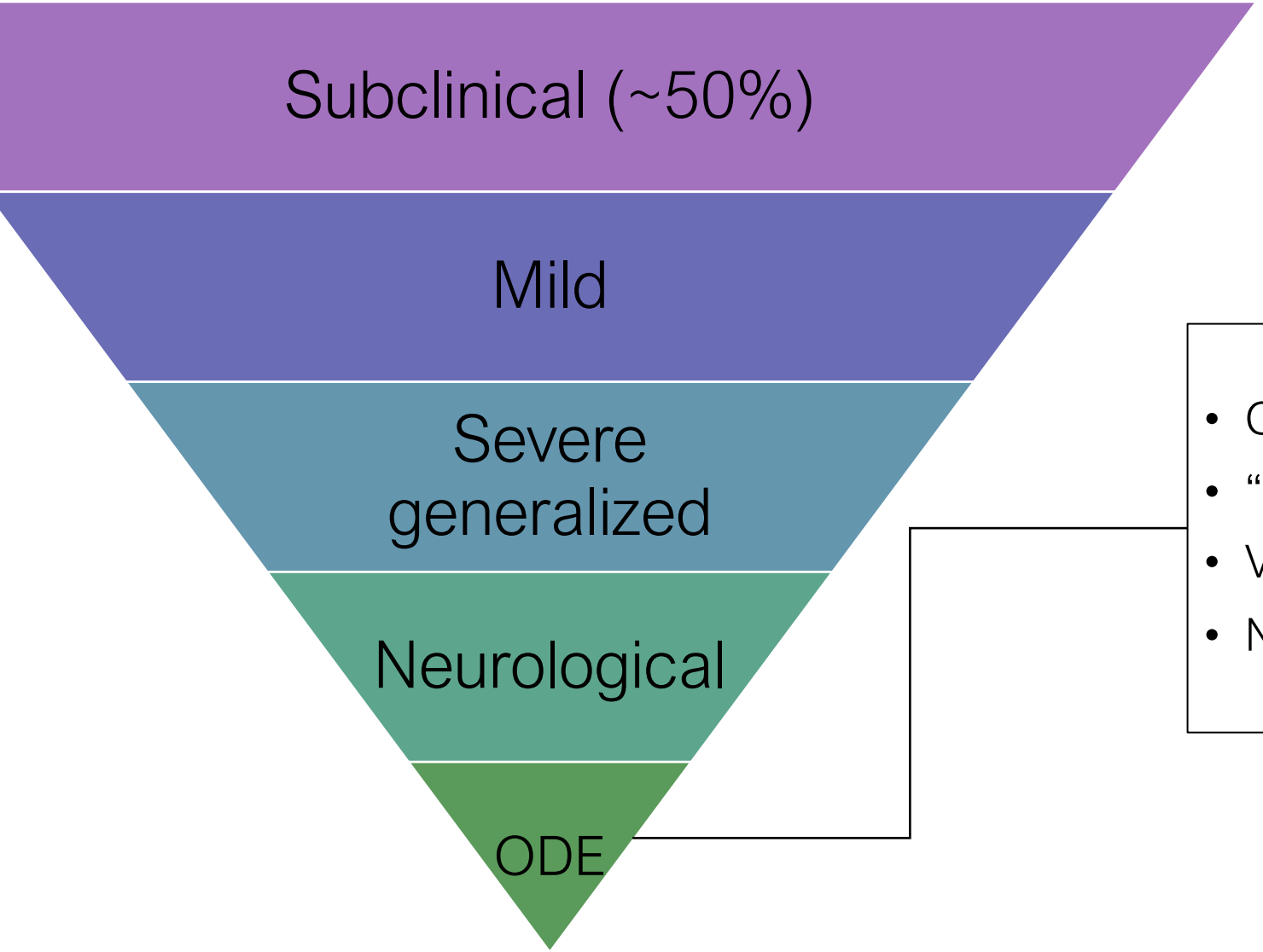
- Usually begin 1 to 3 weeks after recovery from systemic illness
- Neurologic signs frequently develop in the presence of nonexistent or very mild extraneural signs.
- Mature or partially immune dogs that have been previously vaccinated and have no history of systemic disease can suddenly develop neurologic signs.
- Neurologic signs are typically progressive.
- Exact signs are dependent on what area of the CNS is involved

Canine distemper: clinical signs



- Meninges: Hyperesthesia and cervical or paraspinal rigidity
- Seizures, cerebellar and vestibular signs, paraparesis or tetraparesis with sensory ataxia, and myoclonus are common.
- Myoclonus (involuntary twitching of muscles in a forceful simultaneous contraction) can be present without other neurologic signs.
  - More commonly occur while dog is sleeping.
  - Considered specific for CDV infection

Canine distemper: clinical signs



- Chronic, relapsing neurological disease
- “Chewing gum” seizures
- Very rare and poorly understood
- Not restricted to old dogs

Canine distemper virus: gross



FIG. 3-4 Nasal hyperkeratosis in a dog with systemic distemper. (Photograph by Craig Greene © 2004 University of Georgia Research Foundation Inc.)



FIG. 3-5 Digital hyperkeratosis ("hard pads") in a dog dying of distemper encephalomyelitis. (Photograph by Craig Greene © 2004 University of Georgia Research Foundation Inc.)

Canine distemper virus



FIG. 3-6 Enamel hypoplasia characterized by irregularities in the dental surface in an older dog that survived neonatal distemper. (Photograph by Craig Greene © 2004 University of Georgia Research Foundation Inc.)

Canine distemper virus: diagnosis

- Suspect canine distemper in any puppy with compatible clinical signs:
  - ANY neurological disease
  - Respiratory disease with mucoid conjunctivitis
  - GI signs
- Differentials (viral) include CAV-1, -2, and CPV2
- Detection of virus can be challenging if MLV is present (i.e. days-weeks after vaccination)
  - PCR is most commonly used
    - Virtually any secretion can be tested
    - Combining several (e.g. blood, urine, TTW, nasal/conjunctival swab) increases sensitivity
  - Other modalities are available but are not as frequently used.

Control of Canine distemper virus (pages 160-161)

- Recovered animals are immune for life
  - Rare possibility they will develop old-dog encephalitis
- Effective control is by vaccination with attenuated vaccines
  - Avoid interference from maternal antibody
  - Do not vaccinate < 6 weeks old (risk of vaccine-induced encephalitis)
  - Recombinant canarypox vaccine is recommended for ferrets



Peste des petits ruminants (PPR)

And a soupcon of rinderpest.



Rinderpest

- Highly infectious disease of many species
- Ruminants, in particular cattle, are the most significant host
  - Domestic pigs can develop clinical signs and be a reservoir.
- Transmission is oronasal via aerosols or direct contact
  - All secretions contain the virus
- Transmission between farms/herds was typically via due to animals in a prodromal phase, in which clinical signs were not present but virus was being secreted.
- Maintained by wildlife.

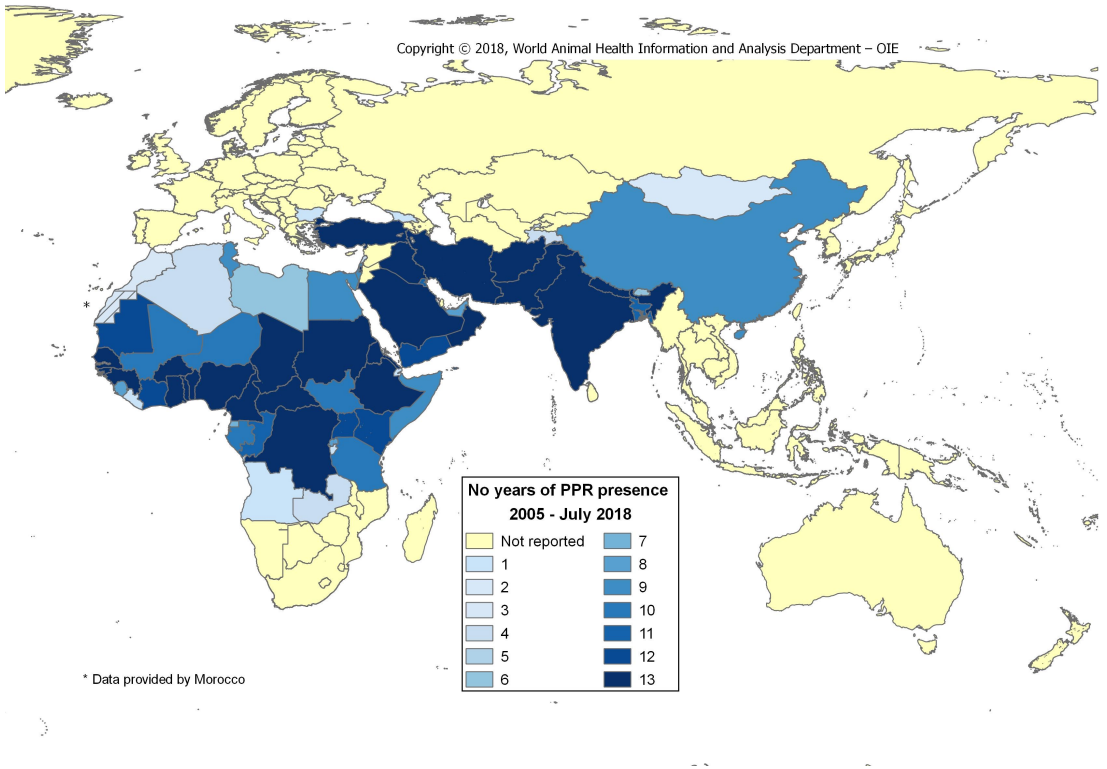
Rinderpest: continued

- In naïve herds/young animals:
  - Abundant mucoid oculonasal d/c
  - Extensive coalescing erosion and ulceration of the oral mucosa
    - Extensive drooling
  - Severe, bloody diarrhea
  - Marked fever, anorexia
  - ± Death
- In populations in which the virus was established, disease was typically milder.

- Immunity following infection or vaccination is lifelong
  - Allowed for the eradication of the disease, declared in 2011.

PPR: general characteristics

- Closely related to rinderpest.
- Highly contagious disease of **sheep and goats.**
  - Goats more severely affected than sheep
  - CFR - up to 85 % in goast, usually < 10 % in sheep
- Morbidity is usually high
- Economic impact is severe in endemic countries



PPR: transmission

- Generally requires close contact
- Aerosols are possible
- There is a period prior to the onset of clinical signs in which animals are **asymptomatic but shedding high levels of the virus**.



PPR: pathogenesis

- Similar to CDV
- Profound lymphopenia and immunosuppresion is a significant contributor to disease

PPR: clinical signs

- Acute pyrexia and depression
- Serous to mucuoid nasal d/c
- Erosions and ulcers in the oral cavity with hypersalivation/drooling
- Pneumonia is common
- ± Bloody diarrhea in later stages
- ± Death



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PPR: diagnosis and control

- PCR is the mainstay of diagnosis
- Trade restrictions are in place
- Eradication program is-going:
  - Vaccine is available (and works)
  - No wildlife reservoir



Respirovirus and *Rubulavirus*

Bovine parainfluenza virus-3 (PI-3)

- Virus occurs worldwide in cattle; 60-90% of cattle in general cattle population are seropositive.

- Host range: cattle, sheep, wild ruminants
  - Infection of calves & lambs is mild or asymptomatic unless complicated by secondary bacterial infection, leading to “shipping fever”.

- Exclusively a disease of the respiratory tract
  - Does not become systemic
  - Spread via aerosolization

Bovine parainfluenza virus-3 (PI-3): pathogenesis

Inhalation

↓

Necrosis + inflammation of small airways, particularly epithelial cells but also macrophages

↓

Interference with mucociliary apparatus and alveolar macrophages → secondary infections

Bovine parainfluenza virus-3 (PI-3): clinical signs

- **Most** cattle will have asymptomatic or mild infection

- Pneumonia (cough, rapid respiration)
- Mucoid nasal discharge
- Anorexia, fever, & general malaise

Bovine parainfluenza virus-3 (PI-3)

- Diagnosis:
  - Because several viruses can predispose to shipping fever, laboratory confirmation is important:
    - Virus isolation is from nasal secretions & lung tissue;
    - PCR
    - Seroconversion in a paired serum sample to PI-3 is diagnostic.

- Control:
  - Attenuated & inactivated PI-3 vaccines are available.
  - Vaccines in US & Canada are multivalent, incorporating PI-3, IBR, BRSV
  - Minimize stress during management & marketing of cattle.

Canine parainfluenza virus-5 (PI-5)

- Virus belongs to genus Rubulavirus

- One of the causes of “Kennel cough” syndrome
  - Other viral agents?
  - Usually initial infection is viral, followed by bacteria (mainly Bordetella)

- PI-5 virus destroys ciliated epithelial cells, predisposing animal to secondary infections.

Canine parainfluenza virus-5 (PI-5)

- Crowding, poor ventilation, young age are risk factors.

- Clinical signs:
  - Nasal discharge
  - Coughing
  - Fever

- Diagnosis:
  - PCR
  - Demonstration of seroconversion to PI-5 is diagnostic.

- Common component of multivalent vaccines.