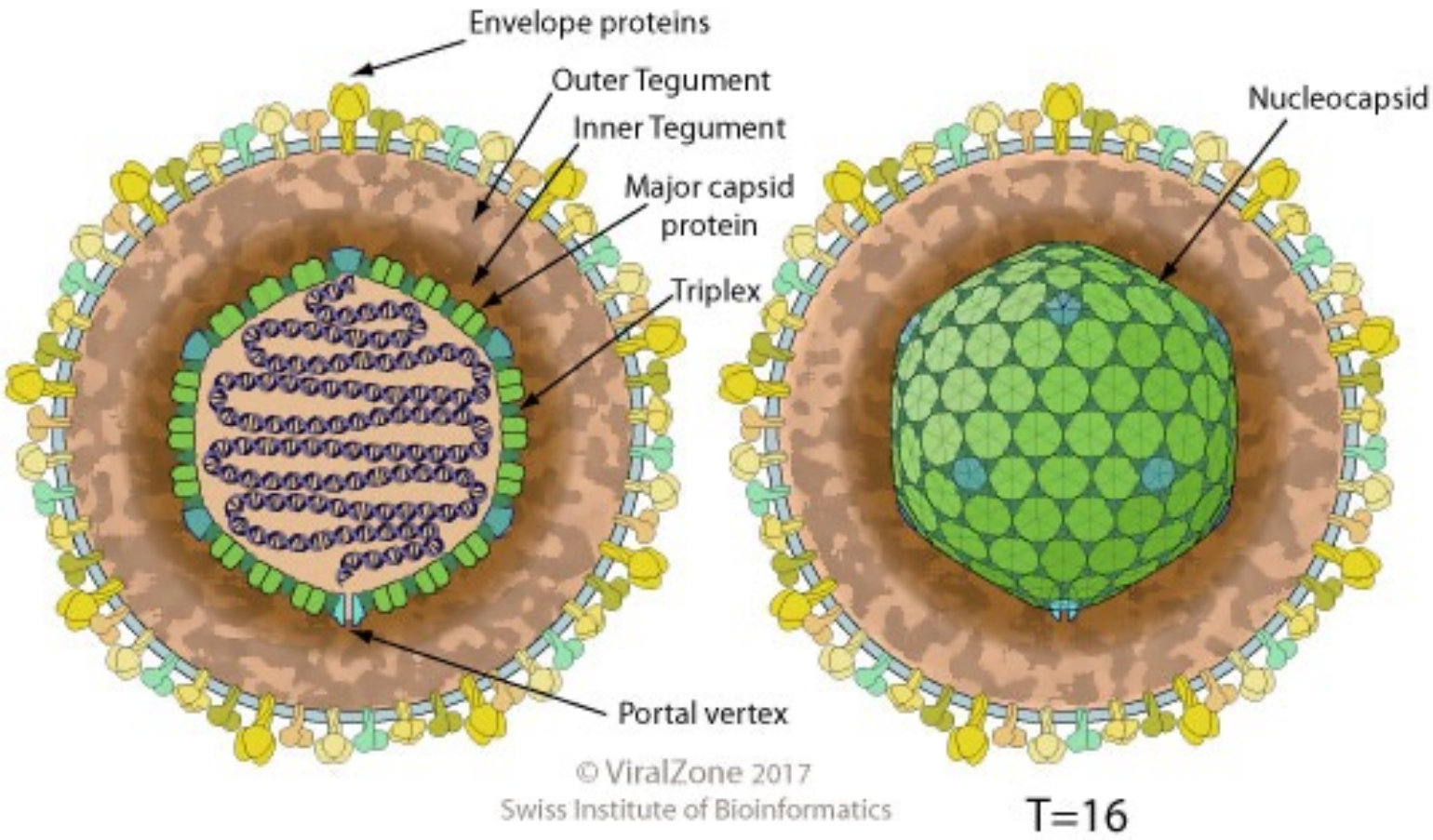
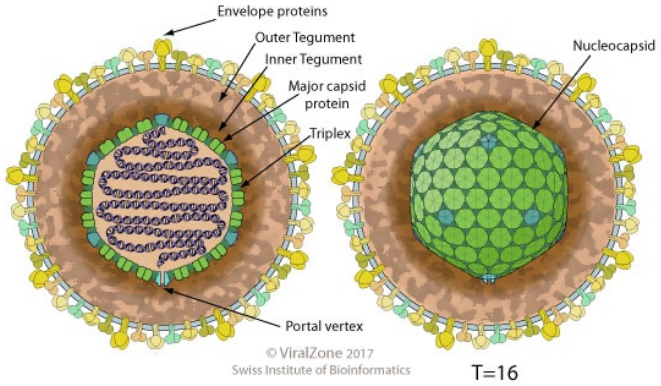


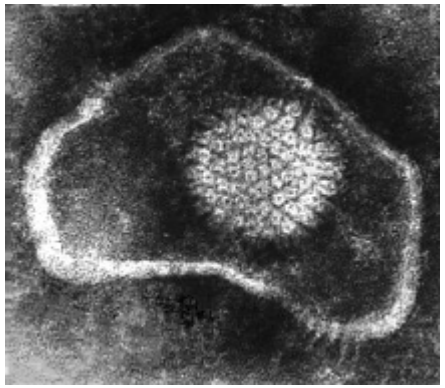
LECTURE 8: HERPESVIRIDAE I

Russ Fraser, Fall 2023

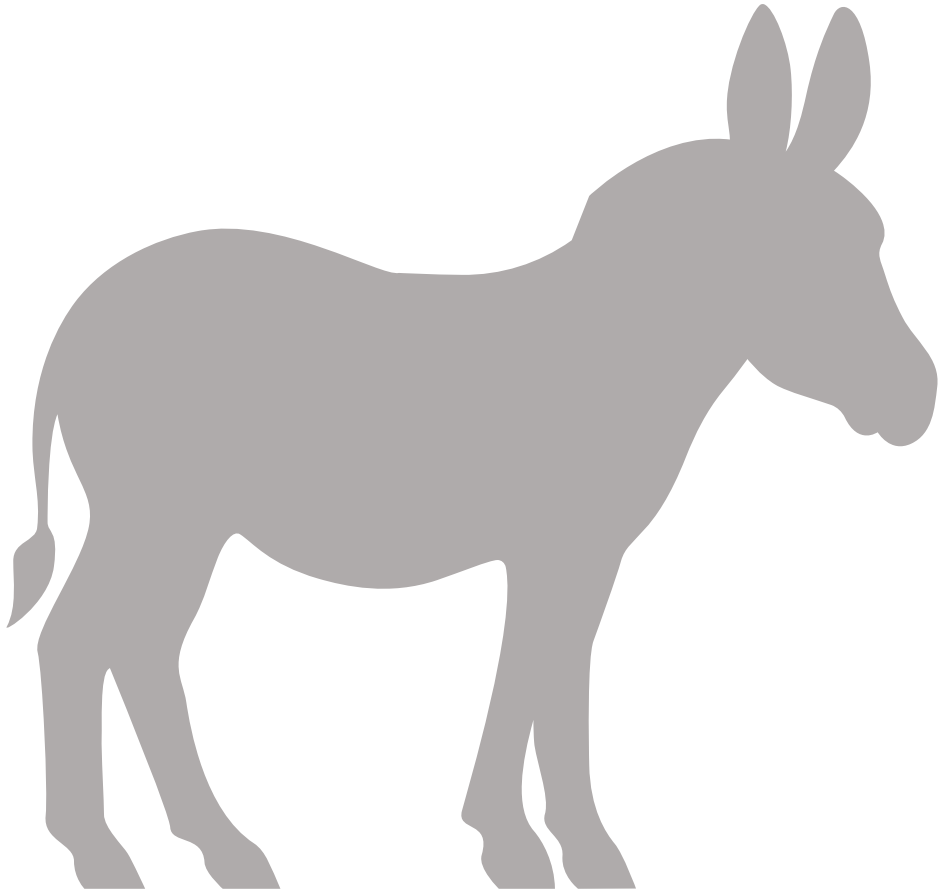
Herpesviridae: general

Size	200 – 300 nm
Morphology	Enveloped
	Icosahedral, thick tegument
Genome	linear, dsDNA, 108-300 kbp
Site of Replication	Nucleus
Properties	• Eosinophilic intranuclear inclusions • Buds from nuclear membrane • Unstable in the environment • Often cause respiratory disease • Some are oncogenic (e.g. Marek's) • Hallmark is latency





Herpesviridae: latency



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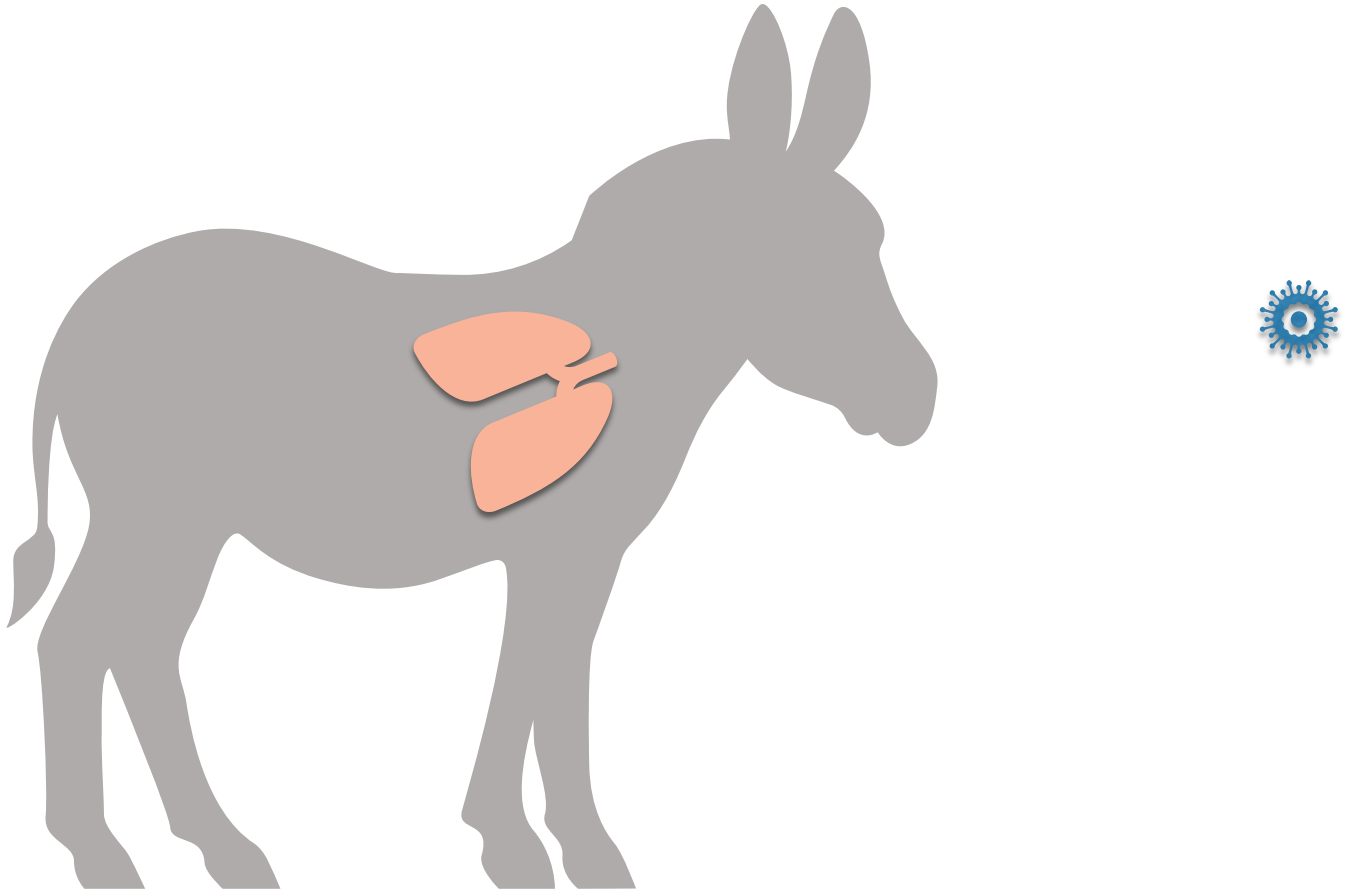
Herpesviridae: latency



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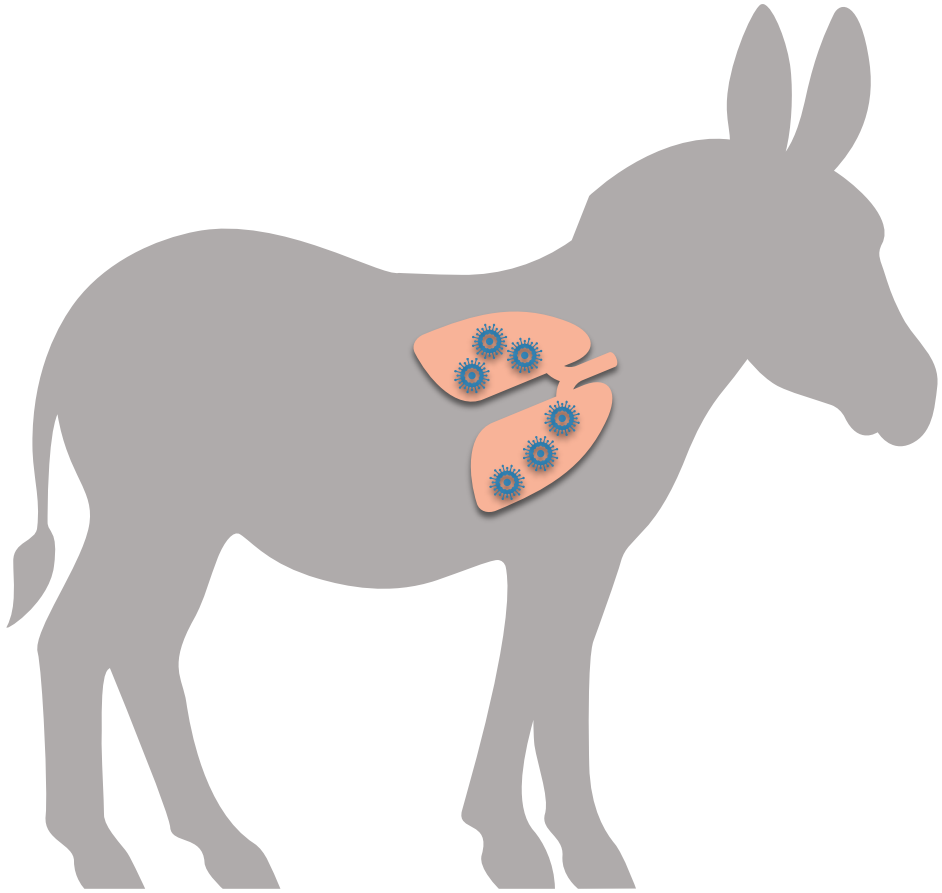
Herpesviridae: latency



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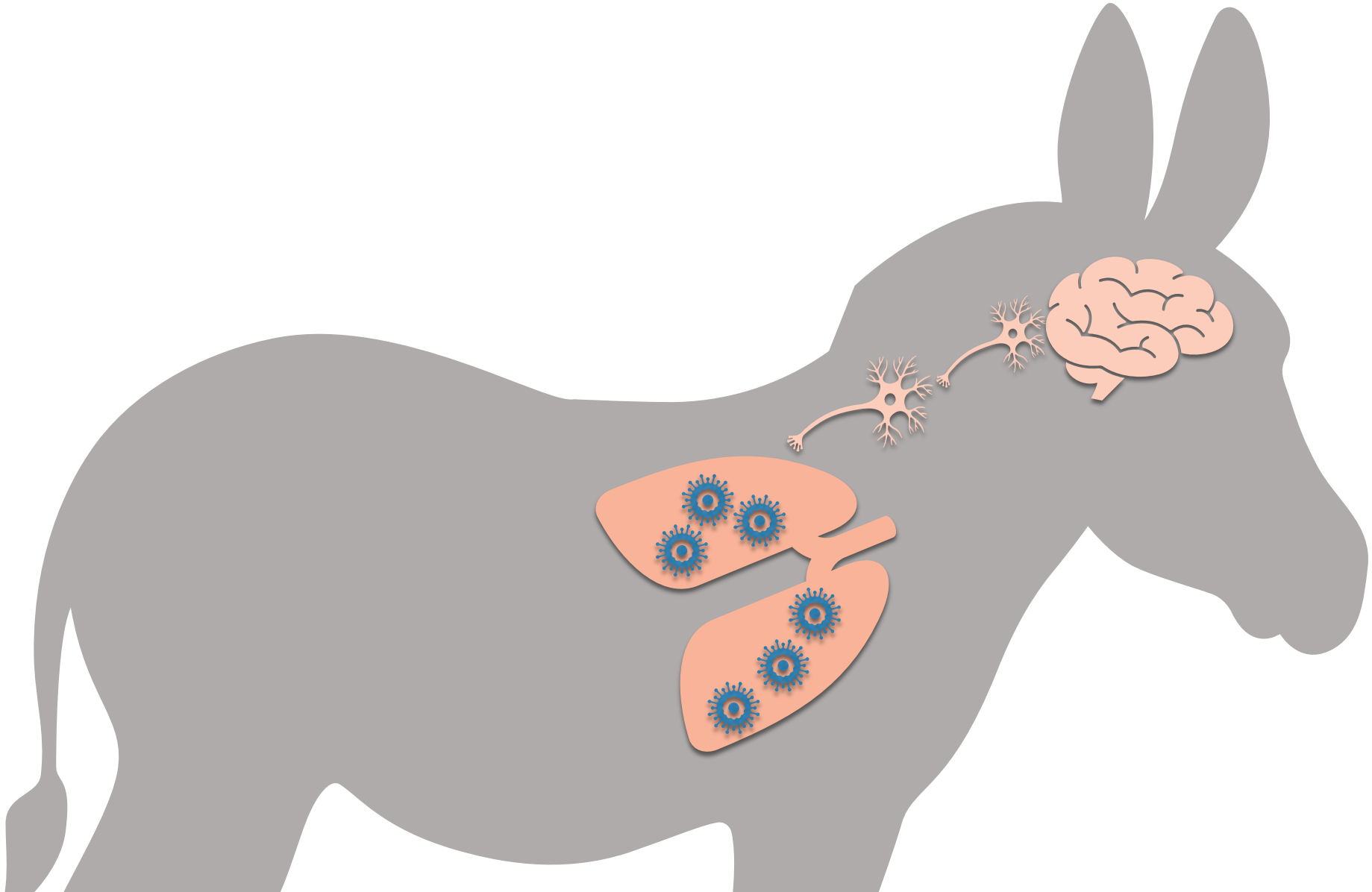
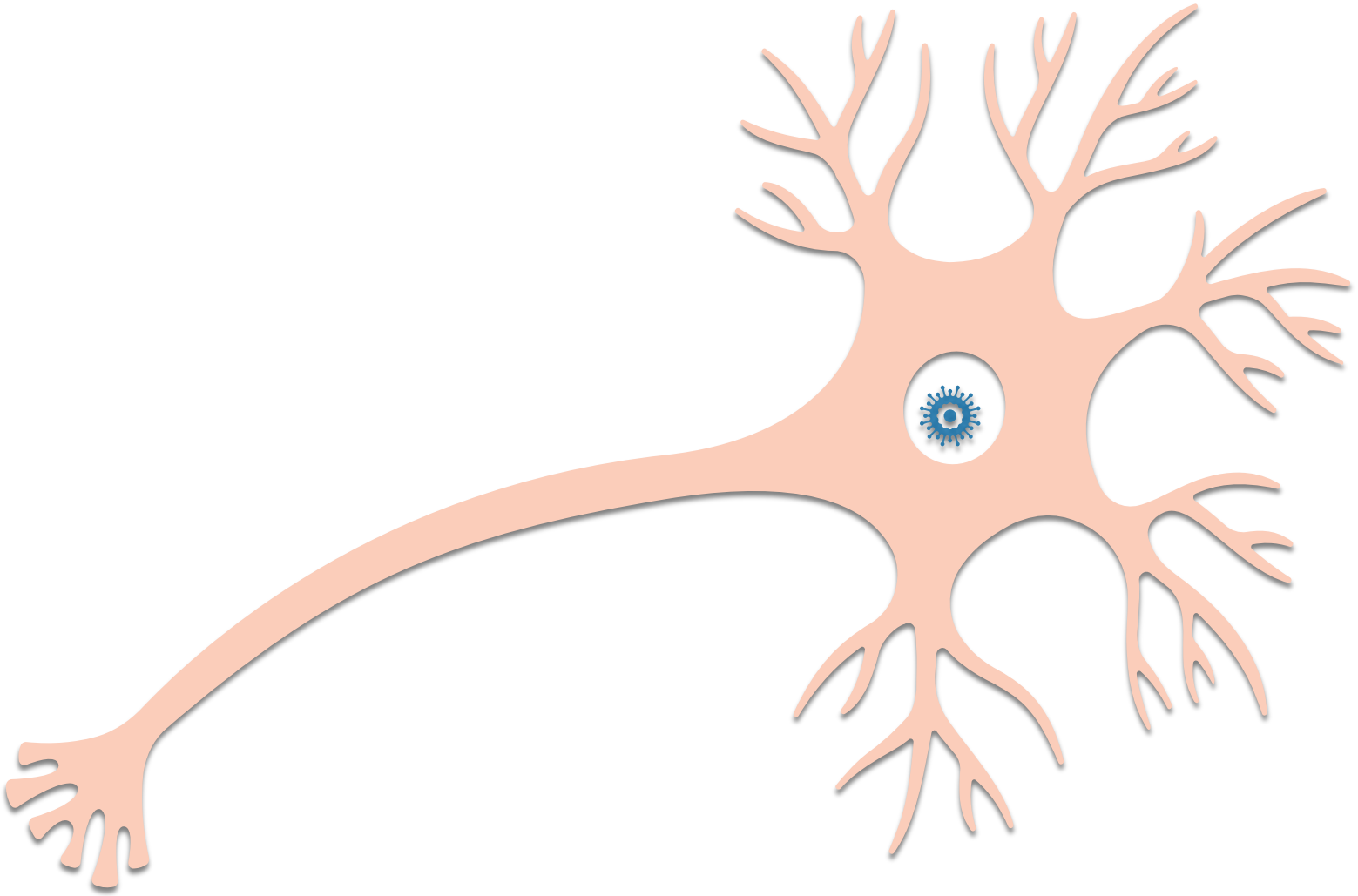
Herpesviridae: latency

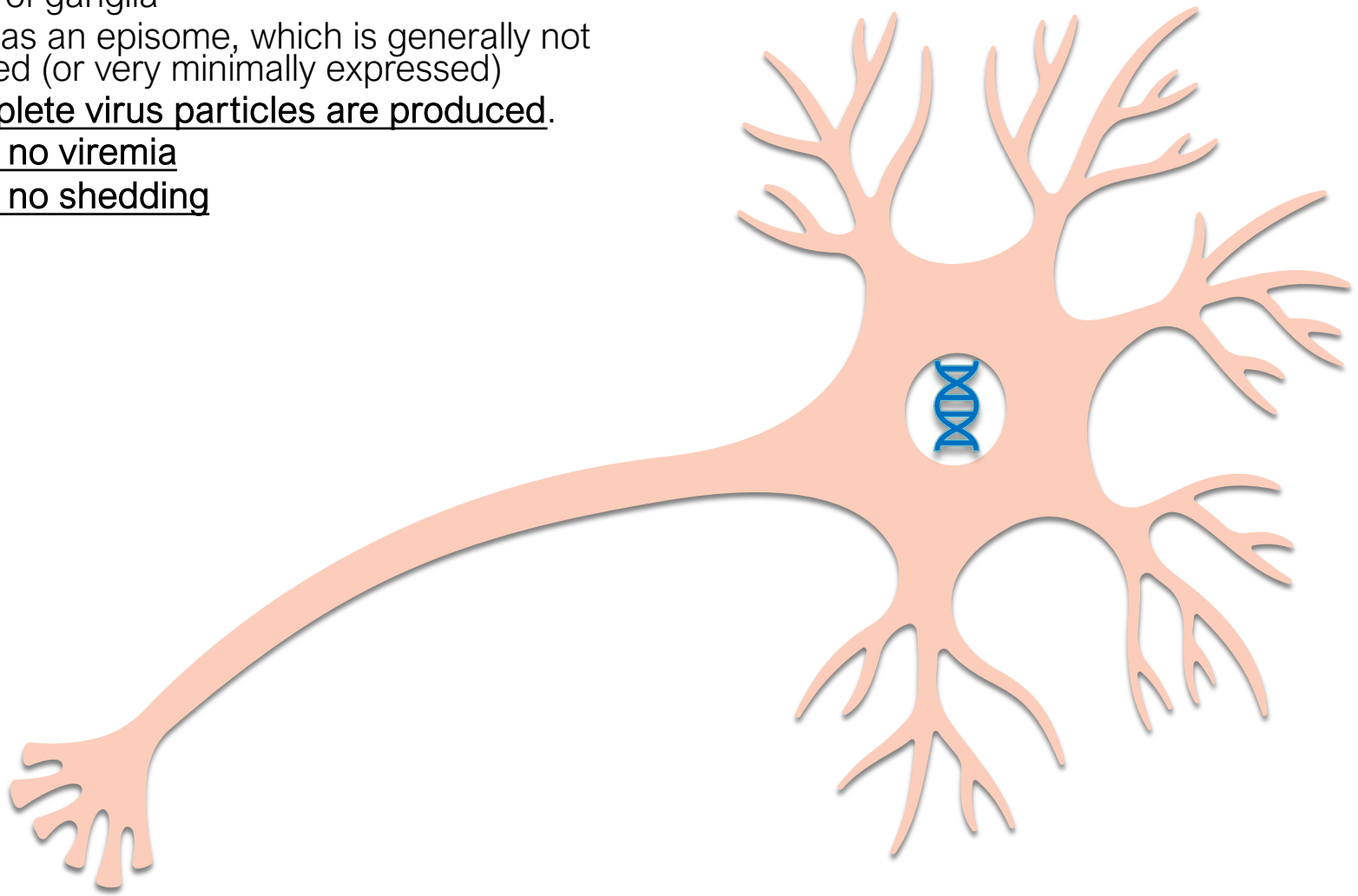


Herpesviridae: latency



Herpesviridae: latency

- Latency is the hallmark of herpesvirus infections:
  - Viral genome persists in nucleus of certain cells, e.g., neurons of ganglia
  - Persists as an episome, which is generally not expressed (or very minimally expressed)
  - No complete virus particles are produced.
  - There is no viremia
  - There is no shedding



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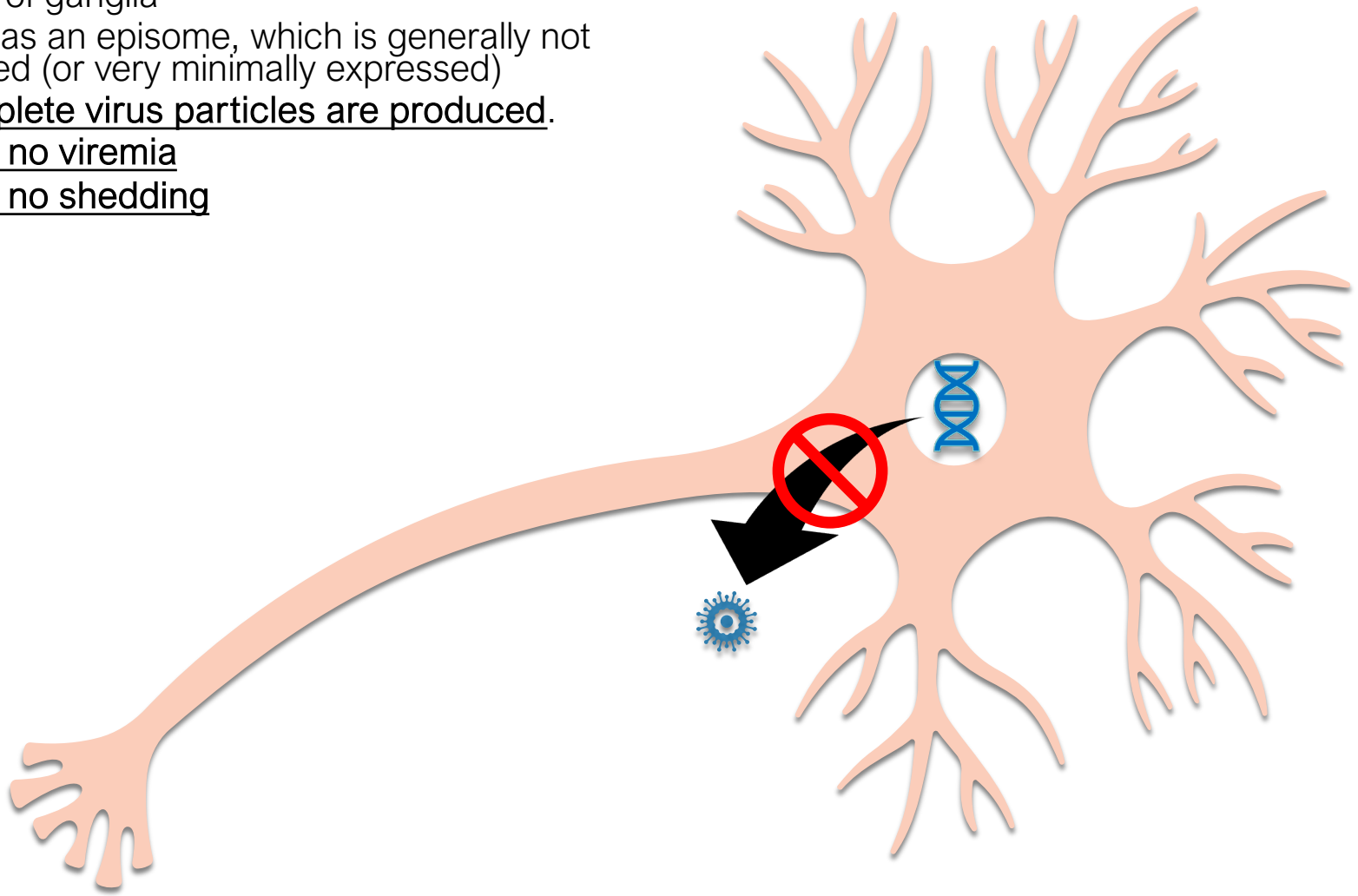
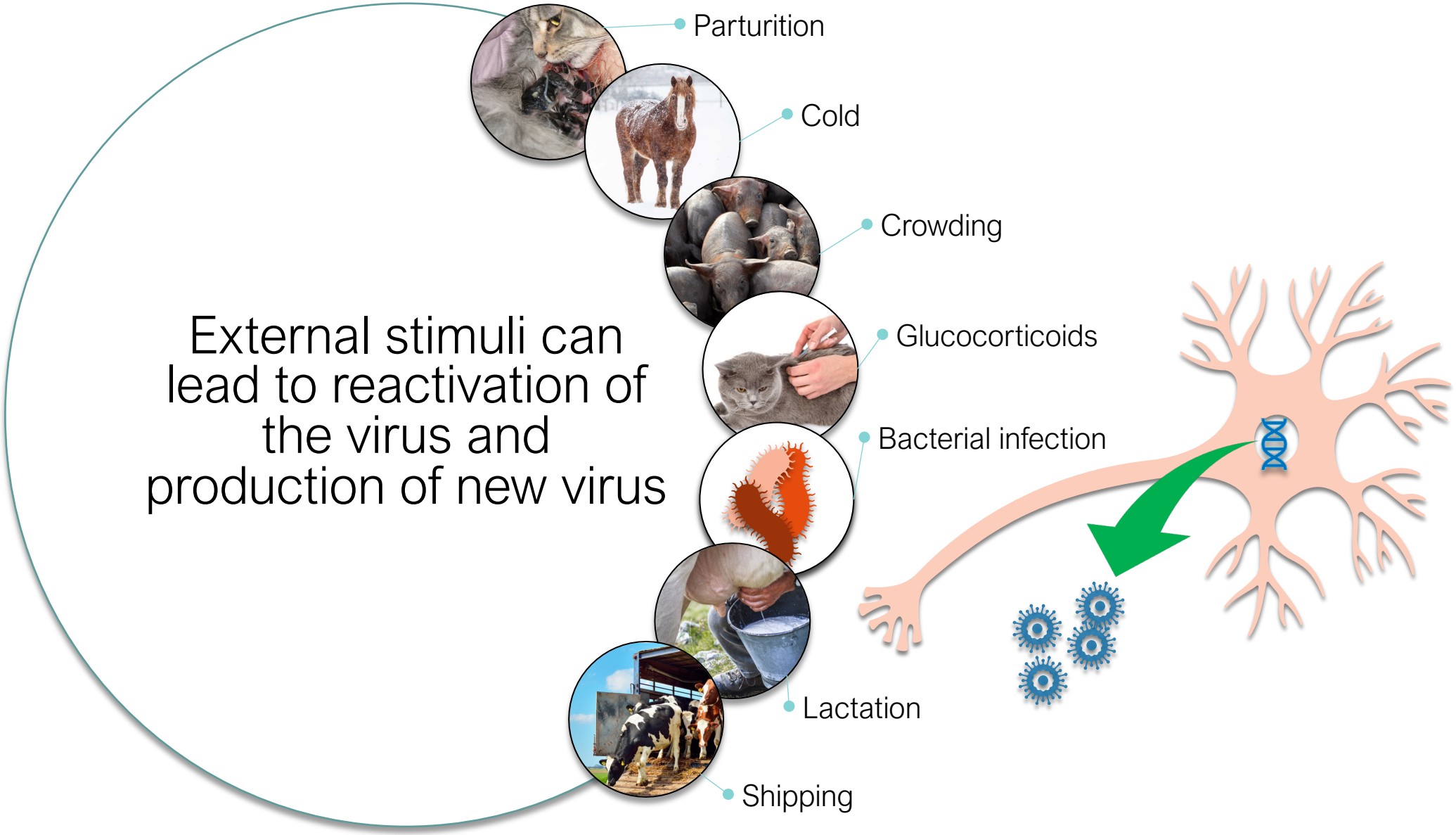
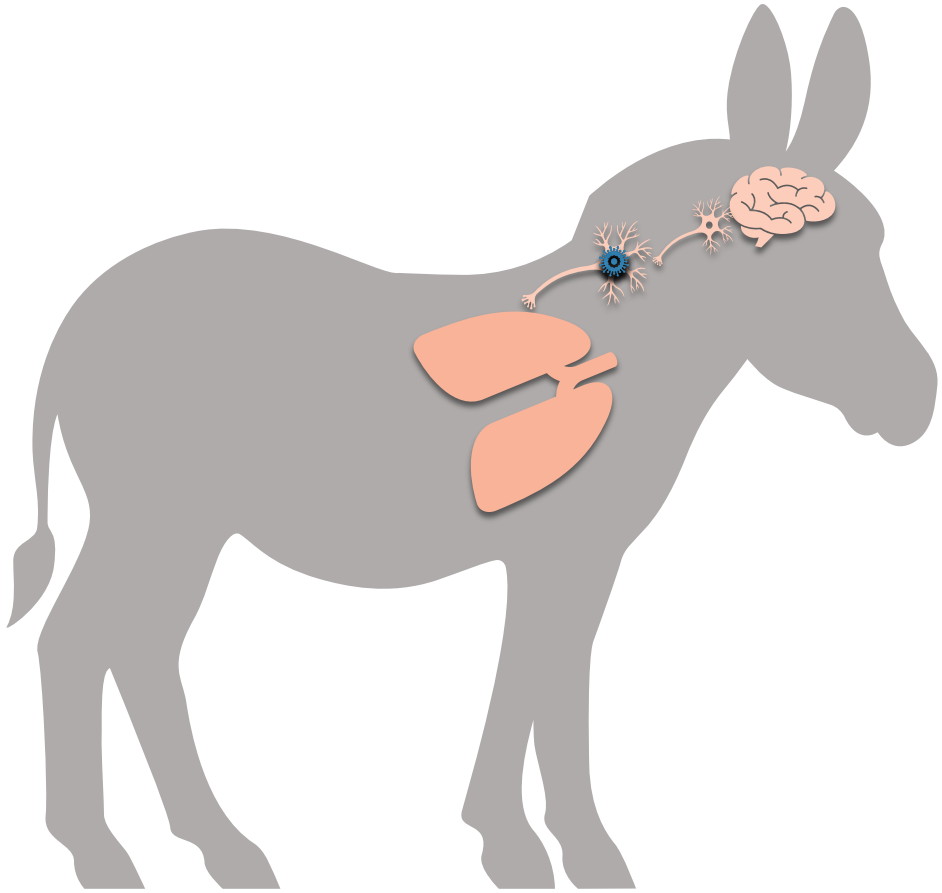


Herpesviridae: latency



Herpesviridae: latency



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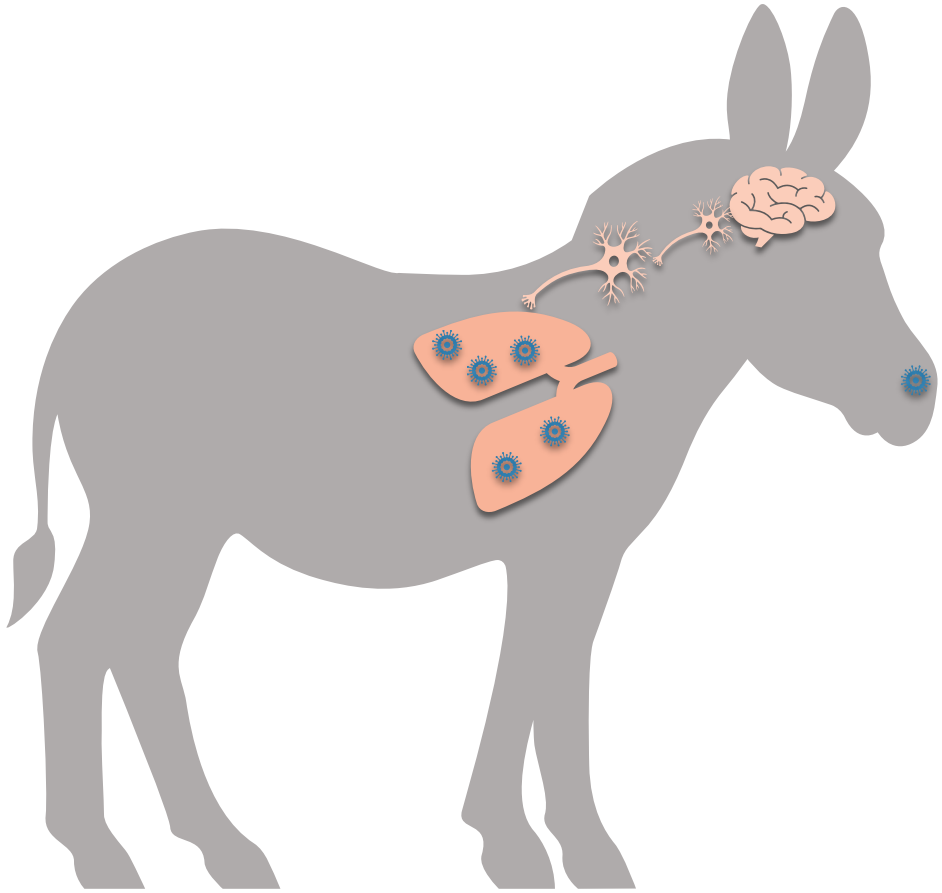
Herpesviridae: latency



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Herpesviridae: general

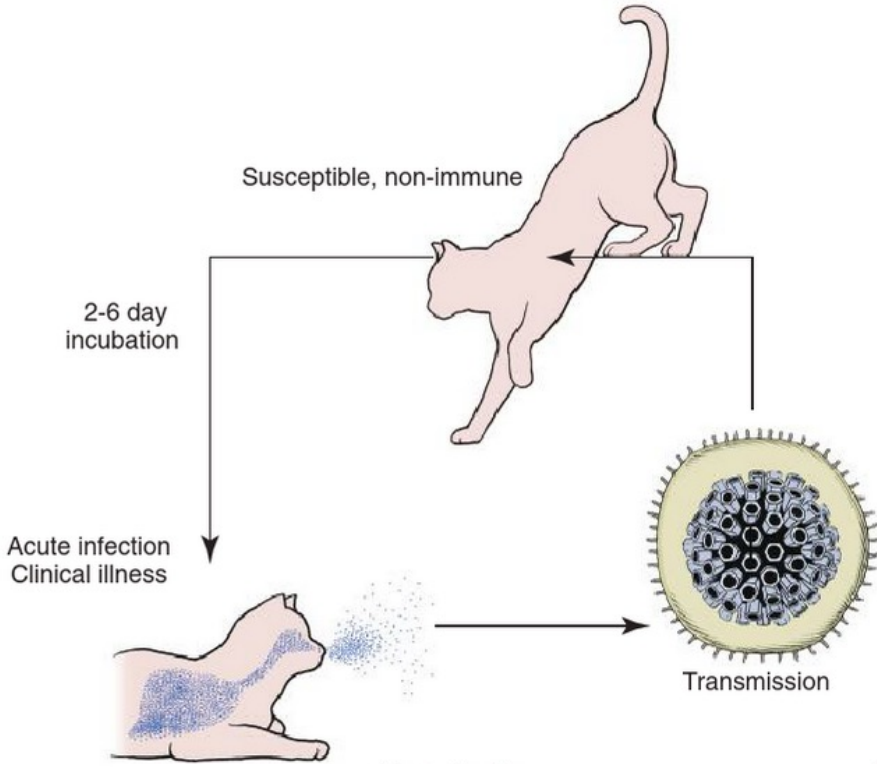


FIG. 14-1 FHV-1 carrier state: epidemiology. (Art by Brad Gilleland © 2010, University of Georgia Research Foundation Inc.)

Herpesviridae: general

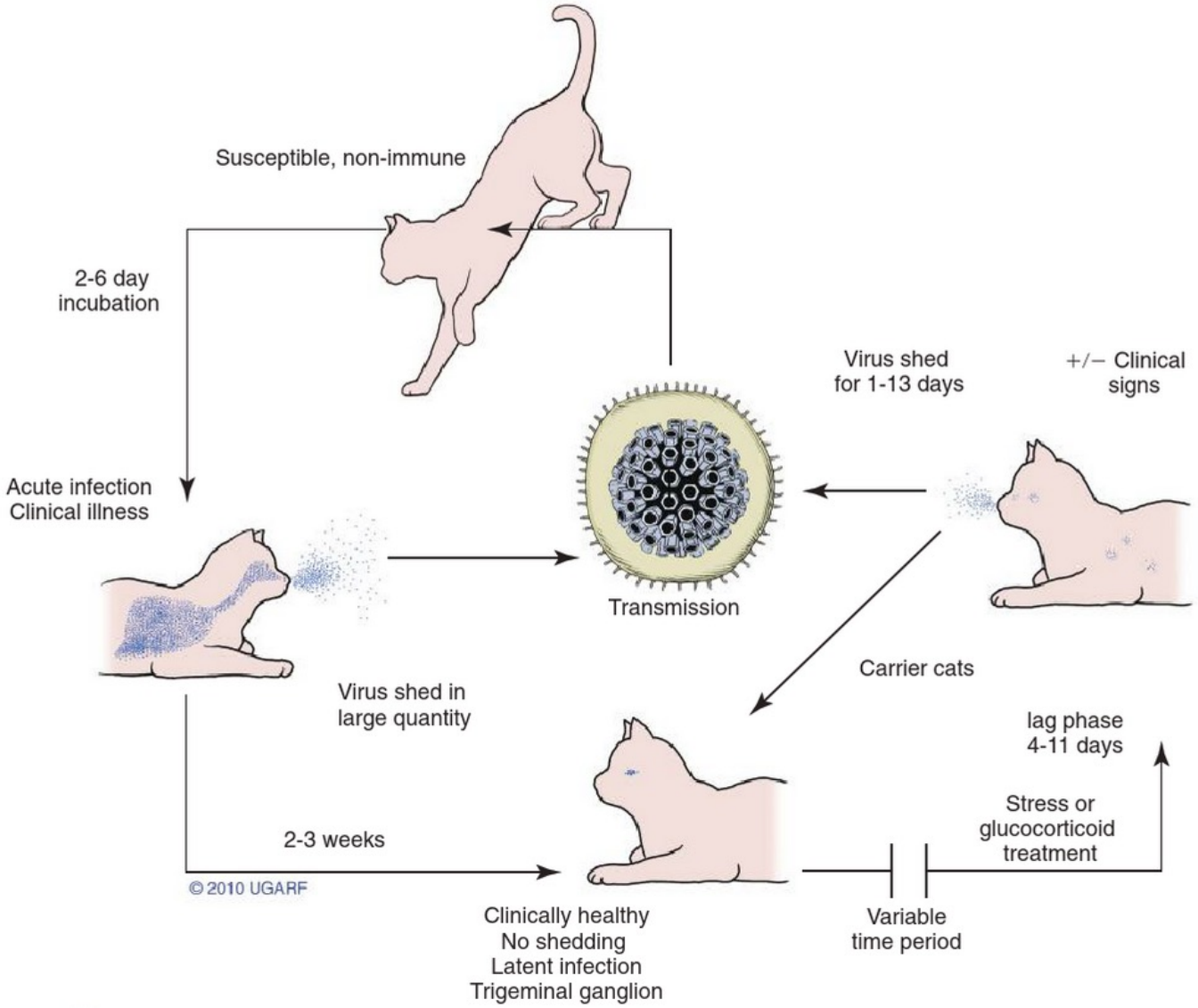


FIG. 14-1 FHV-1 carrier state: epidemiology. (Art by Brad Gilleland © 2010, University of Georgia Research Foundation Inc.)

Biological properties of the subfamilies in Family Herpesviridae

	Alphaherpesvirinae	*Betaherpesvirinae*	*Gammaherpesvirinae*
Host range	broad	narrow	narrow
Replication cycle	short	long	short
Cytopathicity in cell culture	rapid & efficient cell lysis	slow cytomegalia formation carrier cultures	rapid
Latent infections	nerve ganglia & CNS e.g., Trigeminal ganglia, Sciatic ganglia	lymphoreticular cells secretory glands kidneys & other tissues	lymphoid tissue (associated with tumors)
Examples	IBR virus Pseudorabies EHV-1 & EHV-4 FHV-1 ILT virus BHV-2 EHV-3, 6, 8 & 9	Cytomegaloviruses[a] Pachecco's disease virus	Epstein-Barr virus Malignant catarrhal fever virus EHV-2 EHV-5 EHV-7

[a]Cytomegaly refers to unique and marked enlargement of cells.

Herpesviridae: general pathogenesis

- Most herpesviruses are adapted to their hosts:

  - In most species, severity of disease is age-dependent:
    - Lethal in fetus or newborn
    - Severe in young animals without maternal antibodies & in immunosuppressed hosts
    - Inapparent or mild in adults

  OR

  - Disease is inapparent in adult natural host BUT lethal in other hosts, for example:
    - B virus of monkeys is lethal in humans
    - Herpes simplex virus-1 (HSV-1) of humans is lethal in monkeys, gibbons & tree shrews
    - Pseudorabies virus of adult pigs is lethal in other animals
    - Malignant catarrhal fever virus of wildebeest (African antelope) & sheep is lethal in cattle & farmed deer.

Herpesviridae: general transmission

- Enveloped viruses, susceptible to cleaning agents, etc.
- Transmission requires close contact between animals, such as:
  - Mucosal contact
    - Reproduction
    - Licking
    - Nuzzling between dam and offspring
    - “direct nose to nose”
    - etc
  - Droplet infection, as in sneezing (in closely confined populations such as feedlots, swine farrowing units, catteries, or broiler facilities).
  - Fomites & animal handlers
- Vaccination generally reduces disease, but not infection



Herpesviridae: important diseases

- There is a herpesvirus for every domestic animal species
- Most are common
- Most cause significant disease

Bovine herpesvirus 1	Infectious bovine rhinotracheitis
Ovine herpesvirus 2	Malignant catarrhal fever (in cattle)
Porcine herpesvirus 1	Pseudorabies
Porcine herpesvirus 2	Inclusion body rhinitis
Equine herpesvirus 1	Abortion, neurologic disease, respiratory disease
Equine herpesvirus 4	Rhinopneumonitis
Feline herpesvirus 1	Feline viral rhinotracheitis
Canine herpesvirus 1	Hemorrhagic disease in young dogs
Gallid herpesvirus 1	Infectious laryngotracheitis
Gallid herpesvirus 2	Marek's disease
Macacine herpesvirus 1	B virus



Macacine herpesvirus 1

Macacine herpesvirus 1

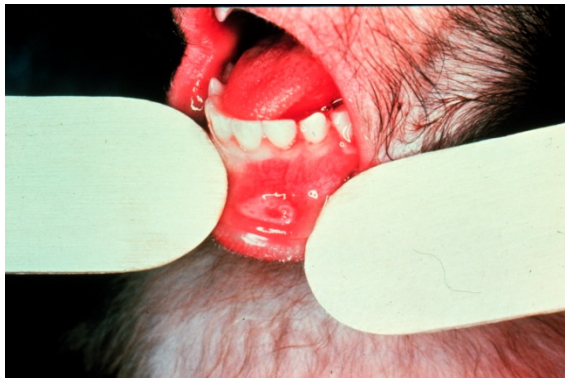
- “B virus” of macaques (formerly Cercopithecine herpesvirus 1)

- Inapparent infection in monkeys (usually), though may cause oral ulcers in macaques.
  - 75-100% of adult macaques in captivity are seropositive
  - Most are latently infected

- Virus is highly fatal in humans
  - Ascending paralysis and encephalitis
  - 79 % case fatality rate (but catching the virus is uncommon)
  - People who work with macaques are at ↑ risk
  - Virus is transmitted to humans by bite or scratch or exposure to saliva or fluids via contact with the eye









Avian herpesviruses

Image: Noah's Arkive

Avian herpesviruses

Gallid herpesvirus 1: ILT



Gallid herpesvirus 2: Marek's disease



Images: Noah's Arkive

Gallid herpesvirus 1 (ILT): general

- ILT = infectious laryngotracheitis

- Causes important respiratory disease in poultry
  - But can also infect pheasants & peafowl.

- Disease is most severe in mature birds (4-18 months old; i.e., egg layers and broiler breeders), particularly during winter when there is poor ventilation in poultry houses.
  - But can occur in birds of all ages

- Recovered birds & vaccinated birds are reservoirs of infection (because of latency).

Gallid herpesvirus 1 (ILT): transmission

- Introduction of new birds to a flock is the usual source
- Aerosolized droplets that are inhaled, or land on conjunctiva
  - Ingested also possible but less common
- Spread is rapid (2 – 8 weeks), but slower than Newcastle, HPAIV, and IB

Gallid herpesvirus 1 (ILT): clinical signs

- Rapid disease course in individual chickens (incubation period is 5 days)
- Low pathogenic strains only cause conjunctivitis, nasal discharge, & low egg production.
  - This is the most common form
- Highly pathogenic strains cause gasping, gurgling/rattling sounds, bloody mucus on beaks upon head shaking, & 50-70% mortality.



Image: Noah's Arkive

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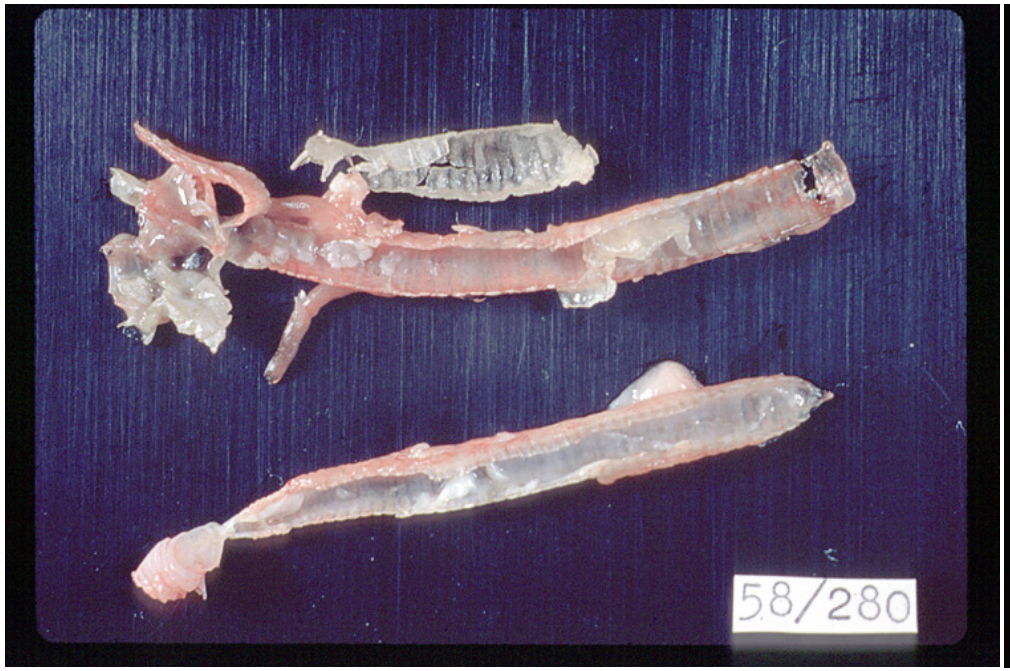
https://www.youtube.com/watch?v=-uvoDr8KWsQ

Gallid herpesvirus 1 (ILT): pathology





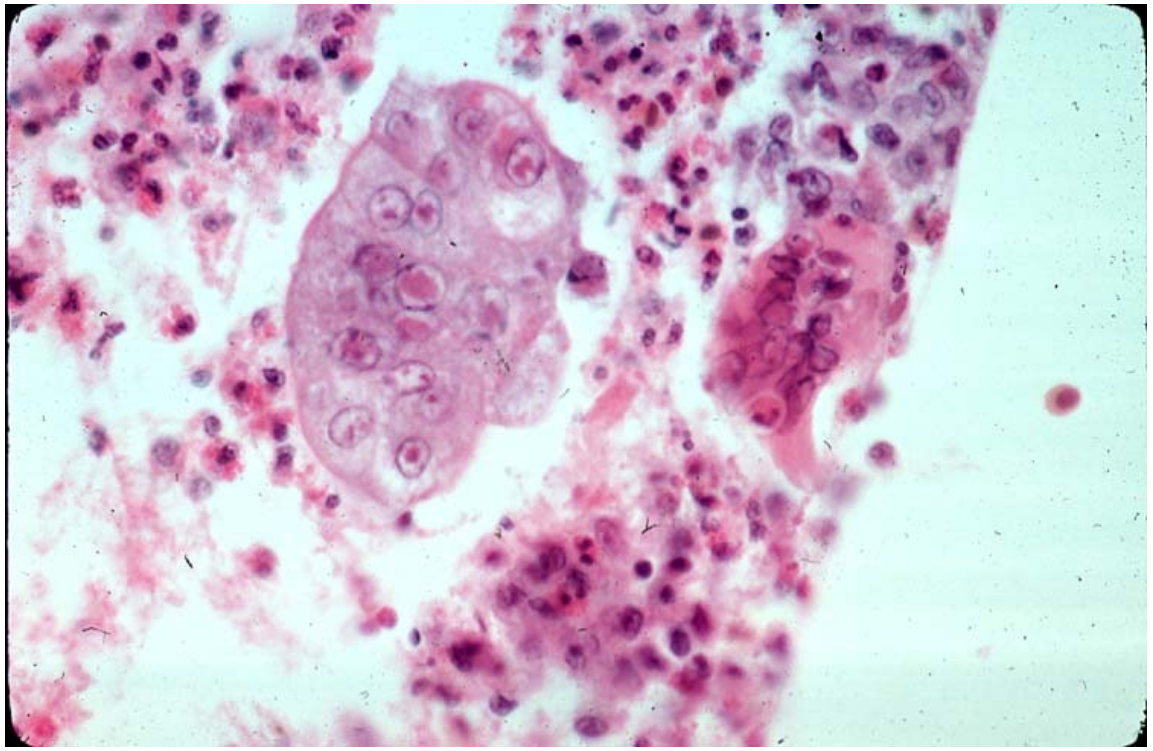
- Gross pathology:
  - Caseous plugs (diphtheritic membranes)
  - Hemorrhages in trachea
    - Bloody mucus on beaks upon heading shaking.

- Histopathology:
  - Ciliary disruption on tracheal mucosa, & intranuclear inclusion bodies (usually found in the detached epithelial cells).
  - Laryngotracheitis

Images: Noah's Arkive

Gallid herpesvirus 1 (ILT): diagnosis

- Differential diagnosis includes:
  - Newcastle disease, Avian influenza, Infectious bronchitis, & Fowlpox.
- Confirm diagnosis using:
  - Histopathology on trachea tissues (look for IN inclusions) + IHC
  - PCR
  - FA staining on trachea smears & tissues
  - Virus isolation from trachea
  - Seroconversion.



Gallid herpesvirus 1 (ILT): control

- Vaccination is done in endemic areas with use of attenuated vaccines in 4 week-old chickens.
  - Post-vaccinal disease is possible
  - Use of attenuated vaccines makes virus endemic (because of latency).
- All-in, all-out is a good option where feasible (e.g. broilers)
- ILT is an immediately notifiable disease – on-going issue in NB and NS
  - Infected premises are quarantined, depopulated, & disinfected (in Atlantic Canada); restock after 4-6 weeks.
- Recovered birds are immune but remain carriers for life

Avian herpesviruses

Gallid herpesvirus 1: ILT



Gallid herpesvirus 2: Marek's disease



Images: Noah's Arkive

Marek's Disease (MD) virus

- Very important neoplastic disease of both layer & broiler chickens
  - Results in immunosuppression, death, loss of egg production, & condemnation at slaughter.

- Every chick hatched commercially worldwide is vaccinated against MD either in ovo or at day-old.
  - 80 % of the 8 billion chickens farmed in the US are vaccinated in ovo

- Vaccination reduces losses (BUT there appears to be a relationship between introduction of new vaccines & development of more virulent strains of MD virus).

Gallid herpesvirus 2 (Marek's disease): pathogenesis

- Natural transmission is by inhalation of feather dust; virus does not spread vertically (via eggs)
  - Virus can replicate in the feather follicle epithelium

- Target cells for the virus are T-lymphocytes & feather follicular epithelium.
  - T-lymphocytes are transformed
  - Feather follicular epithelial cells are lysed & release cell-free virus

- MD lesions result from infiltration & in-situ proliferation of pleomorphic neoplastic T-lymphocytes in internal organs, skin, iris, & nerve trunks especially the sciatic nerve.

- Infection usually occurs at 3 weeks when maternal antibodies wane; disease is most common in 8-28 week-old chickens.

Gallid herpesvirus 2 (Marek's disease): clinical signs

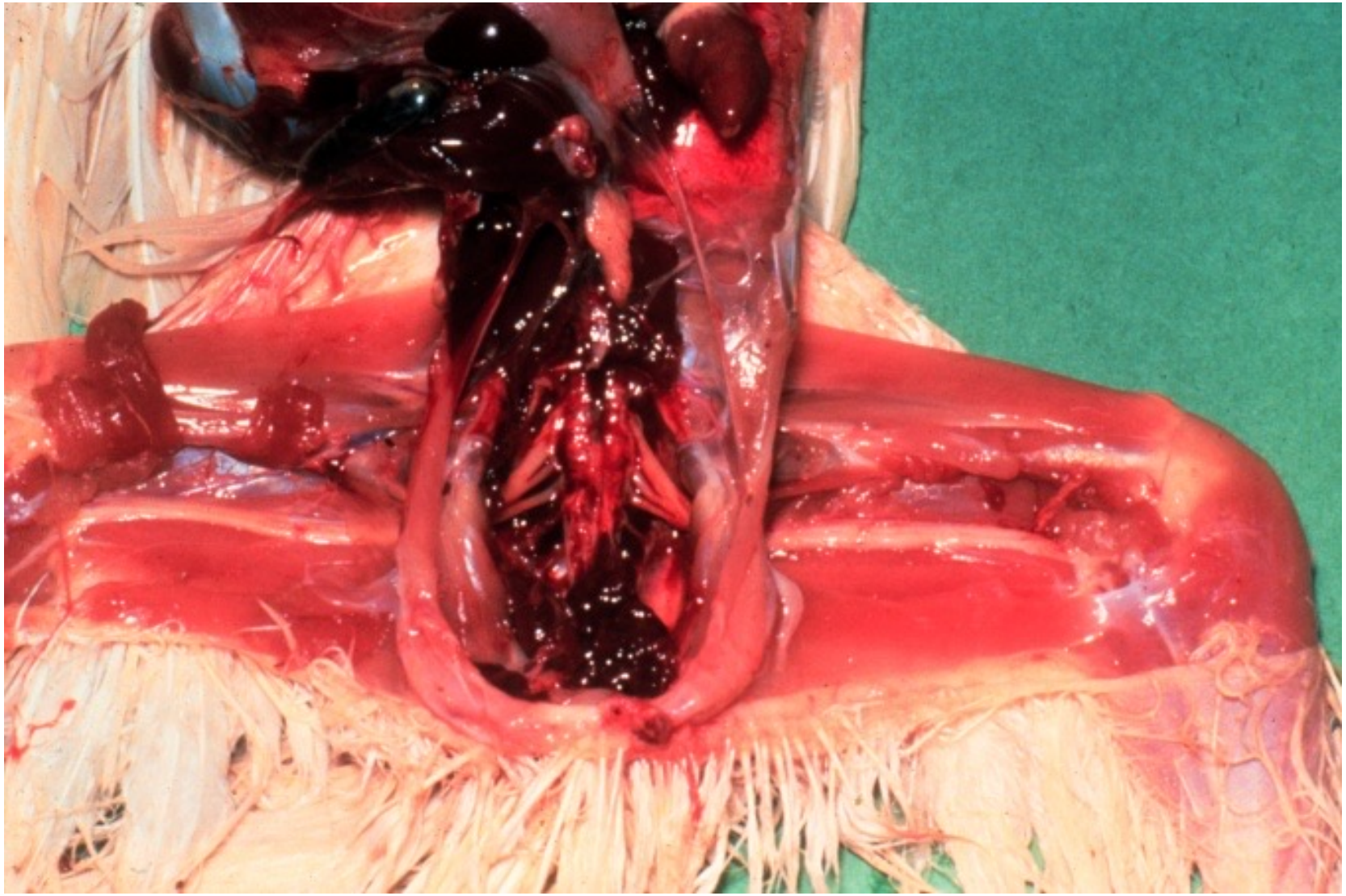
1. Acute
   - Affects nerves, presents with paralysis and neurological symptoms.
2. Classical
   - Tumours (lymphoma) in various organs
3. Ocular
   - Presents as iridal lymphoma
4. Cutaneous
   - Presents as follicular/cutaneous lymphoma

There is overlap of these 4 "syndromes"

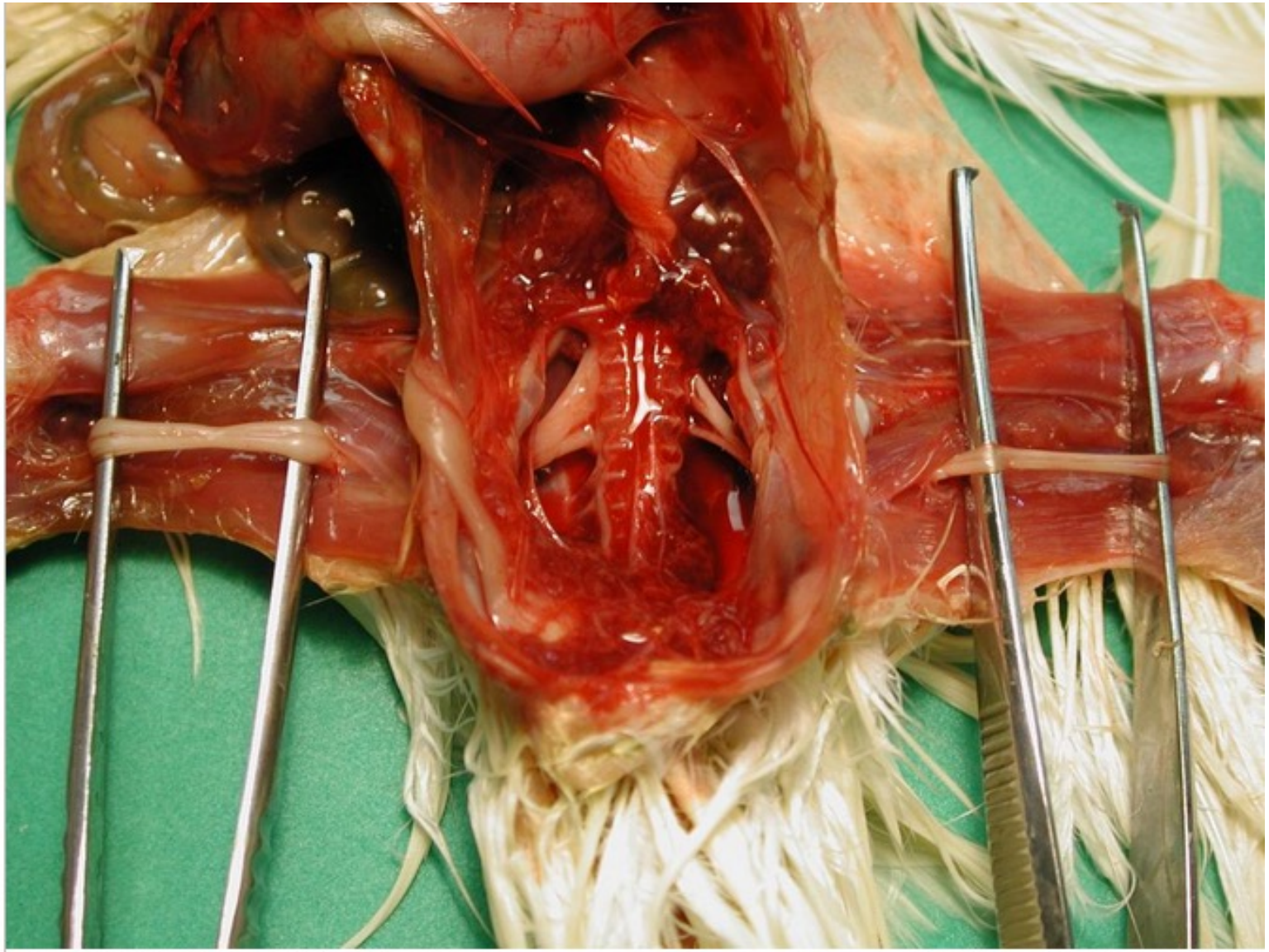
Acute Marek's disease



Acute Marek's disease



Acute Marek's Disease

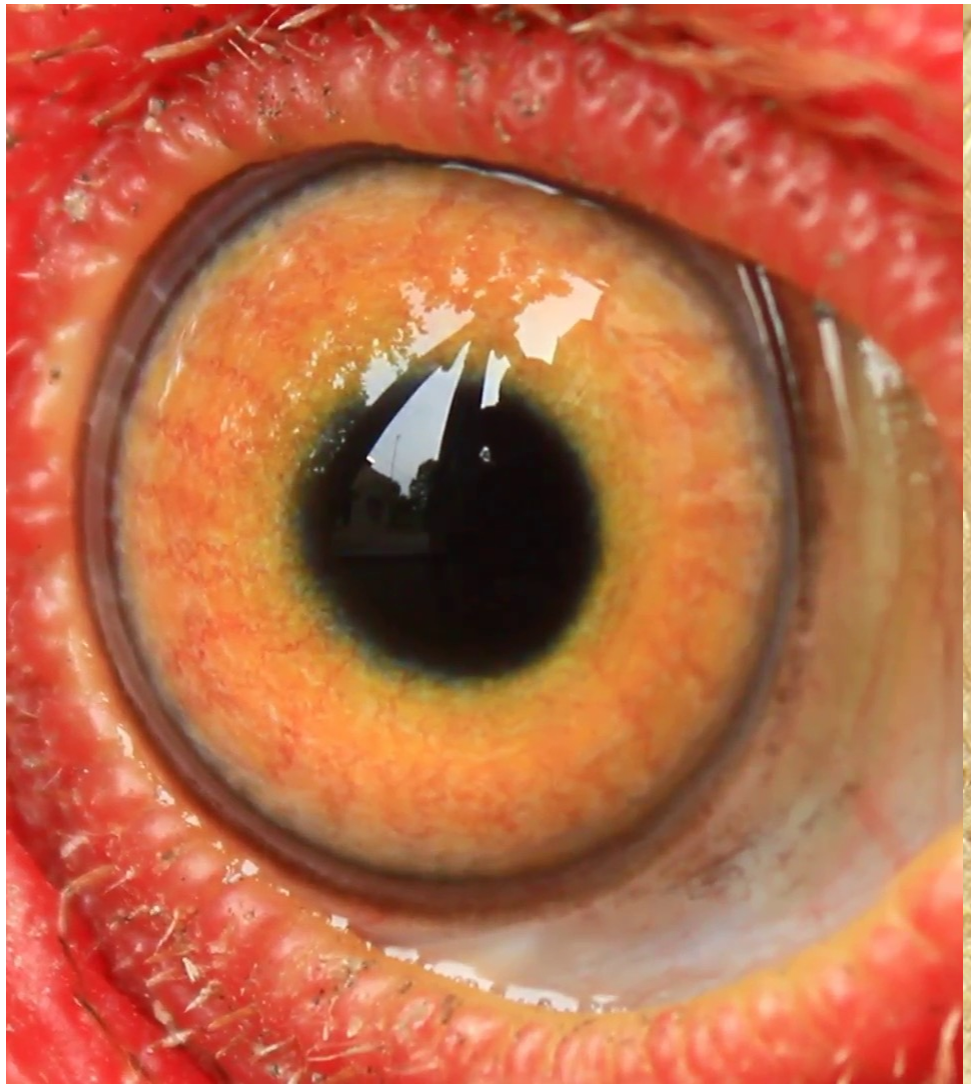


https://www.merckvetmanual.com/poultry/neoplasms/marek%E2%80%99s-disease-in-poultry

Classical Marek's disease



Ocular form



Normal



Marek's

Follicular/cutaneous form



Gallid herpesvirus 2 (Marek's disease): diagnosis

- MD must be differentiated from Avian leukosis

Criteria	ALV	Marek's Disease
Type of lymphoma	B cell	T cell
Bursa affected	Yes	No
Nerves affected	No	±
Age affected	> 14 weeks	> 4 weeks
Vaccine available	No	Yes

- Signalment, clinical signs, and gross findings are highly suggestive.
- Confirm with IHC or IF.
- Usual other tests are also available (e.g. PCR)

Gallid herpesvirus 2 (Marek's disease): control

- Vaccination in ovo at 18 days of incubation or at day of hatch, which results in lifelong protection against tumors.
- Vaccines prevent disease, but not infection.
- Biosecurity & good hygiene (age separation; "all-in, all-out" since there is no vertical transmission).
- Breeding programs to select genetically resistant strains of birds