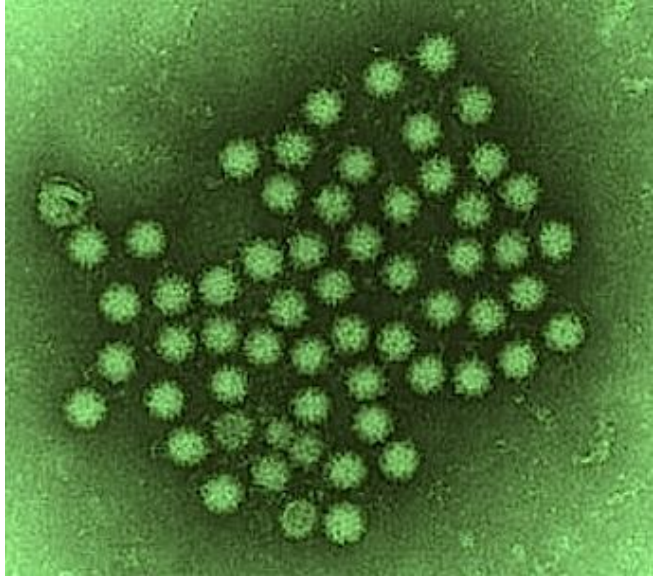
Feline Calicivirus Infection

- Feline calicivirus infection is a common respiratory disease in cats.
- The virus attacks the respiratory tract -- lungs and nasal passages -- the mouth, with ulceration of the tongue, the intestines, and the musculoskeletal system.
- It is highly communicable in unvaccinated cats, and is commonly seen in multicat facilities, shelters, poorly ventilated households, and breeding catteries.

Etiology



- *Small (35nm in diameter),*
- *non-enveloped spherical virion*
- Family name derived from the 32 cup-shaped (calix = cup) surface depressions which give a distinctive morphology in the electron microscope.
- *(+) sense, single-stranded (ss) RNA*.
- Reasonably resistant allowing survival in the environment.
- Antigenity: Considered to be a single serotype but strains form an antigenic mosaic reacting with other strains to different degrees. Some show lack of cross-protection.

http://www.abcdcatsvets.org/feline-calicivirus-infection-2012-edition/

Transmission

- Host range: Domestic cats & cheetahs. No zoonotic potential known or alternative hosts.
- Transmission occurs mainly by direct contact or via fomites.
- Aerosol transmission plays a minor role in spreading virus over distances of more than 1.3 m, probably because of the lack of viral aerosol production and the relatively small feline tidal volume.
- As a nonenveloped virus, FCV is highly tolerant to environmental stressors, as opposed to other respiratory pathogens (eg, FHV-1), and persists for at least 1 month in a dry environment at room temperature and perhaps longer at cooler temperatures.

- FCV is also more difficult to deactivate with disinfectants compared with most bacteria and enveloped viruses.
- Immunosuppressed cats and those living under environmental stress (eg, overcrowding, poor sanitation) are most at risk for infection.
- Young cats and kittens are most likely to show clinical signs of disease.

Pathogenesis

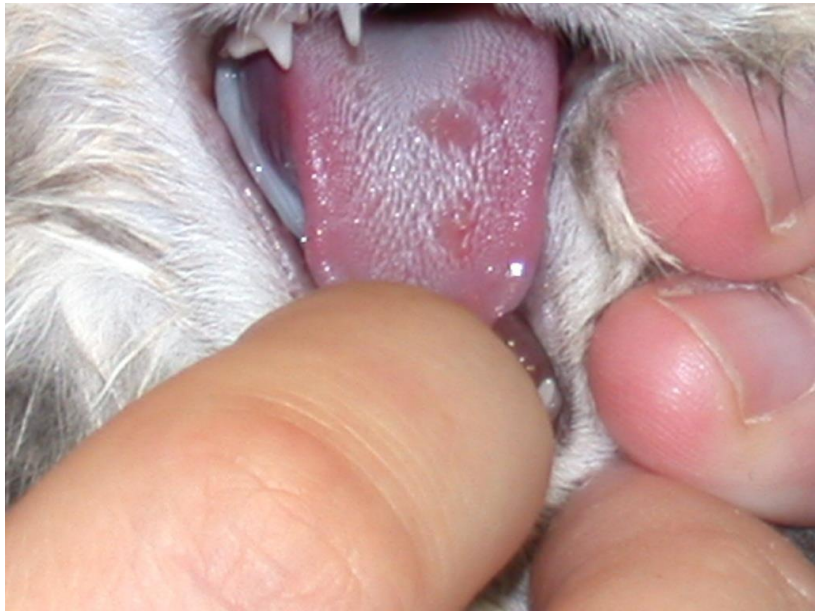
- The main routes of infection are ocular, nasal, and oral.
- The incubation period is 2 to 10 days.
- Viral replication occurs mainly in the oropharynx but can occur at other locations depending on biotype.
- This causes a variety of clinical presentations.
- A viremic phase is thought to occur a few days after the initial infection and before tissue infection causes epithelial necrosis and vesicle formation.
- The pathogenesis of virulent systemic feline calicivirus (VSFCV) could be enhanced by facilitated entrance into the circulation as either free or cell-associated virus.
- VSFCV appears to have a broader tissue tropism than non-VSFCV.

Clinical Signs

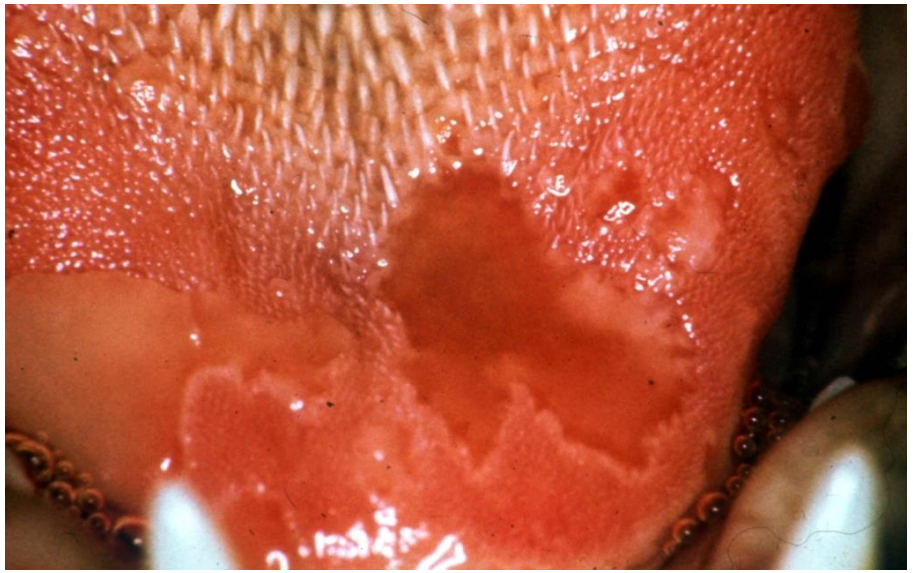
- FCV infection can cause acute oral and upper respiratory signs but also has been associated with chronic stomatitis, which may be immune-mediated.
- Recently, a new syndrome, the “virulent systemic feline calicivirus (VS-FCV) disease” has been described.

1- Acute oral and upper respiratory tract disease

- Clinical findings may differ, depending on the virulence of the FCV strain concerned, on the age of the affected cats and on husbandry factors.
- While in some cases infection is subclinical, in many others, there is a typical syndrome of lingual ulceration and a relatively mild acute respiratory disease.
- More severe signs can resemble the respiratory disease caused by FHV-1.



Mild epithelial defects after burst calicivirus aphthae ©Susann-Yvonne Mihaljevic



Characteristic tongue map-shaped lesions due to FCV infection ©Marian C. Horzinek

- Oral ulcerations,
- sneezing
- serious nasal discharge are the main signs.
- Fever
- Anorexia,
- hypersalivation due to oral erosions - located mainly on the tongue - They usually resolve after several days.

2- Chronic stomatitis

- FCV can be isolated from nearly all cats with the chronic lymphoplasmacytic gingivitis/stomatitis complex, and many cats test positive by PCR.

3- Limping syndrome

- An acute transient lameness with fever can be associated with FCV infection and vaccination.
- In natural infection, it occurs a few days or weeks after the acute oral or respiratory signs

4- Virulent systemic feline calicivirus (VS-FCV) infection

The causative virus strains are most commonly referred to as “virulent systemic feline calicivirus” (VS-FCV); however, this term is somewhat misleading as all FCV infections are systemic - but the disease caused by other FCV strains is usually local.

The disease appears to be more severe in adults than kittens.

In contrast to the common strains, VS-FCV causes systemic disease characterized by

- severe systemic inflammatory response syndrome,
- disseminated intravascular coagulation (DIC),
- multi-organ failure
- commonly death.

Mortality is up to 67%.

Eye lesions

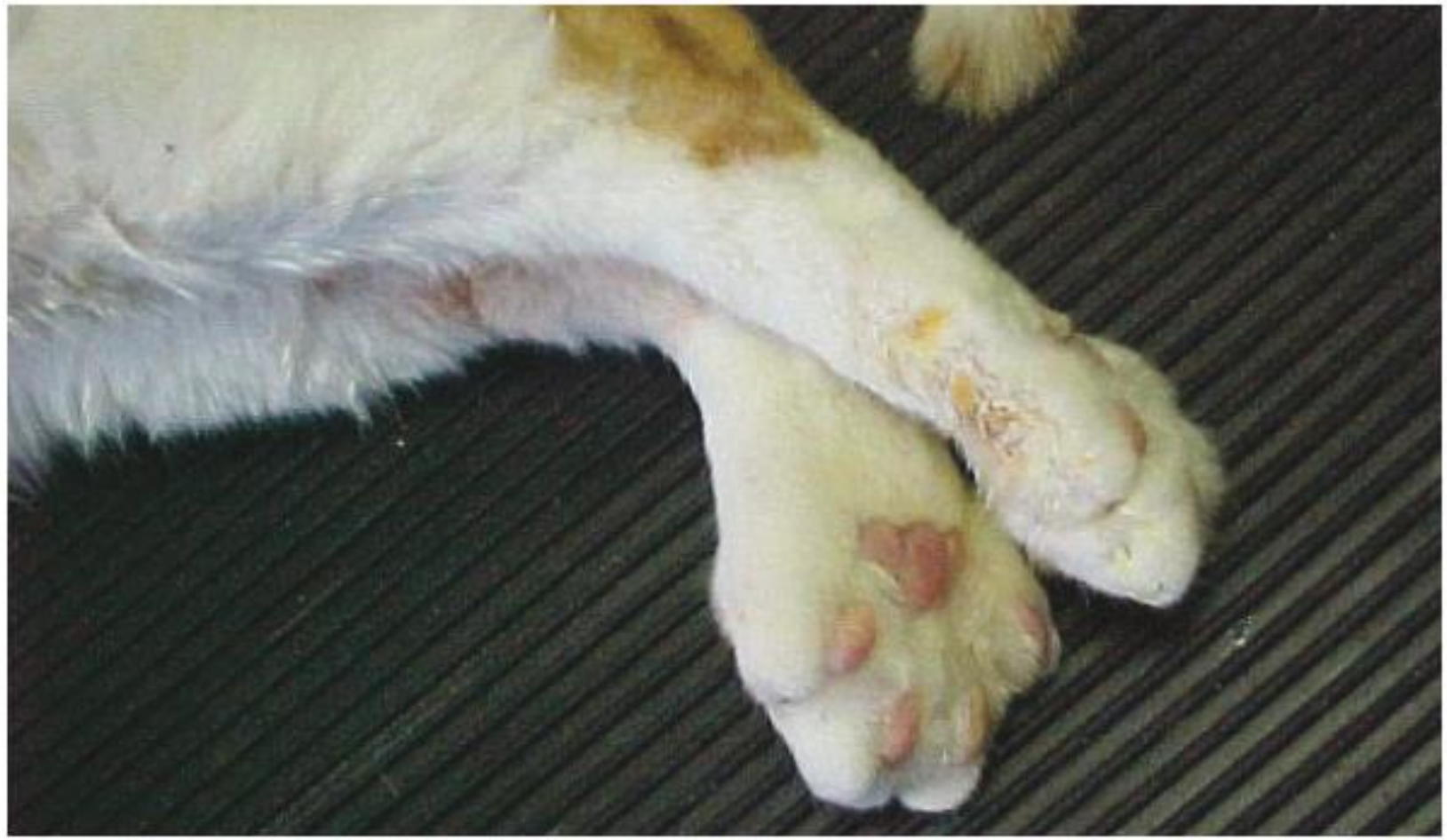
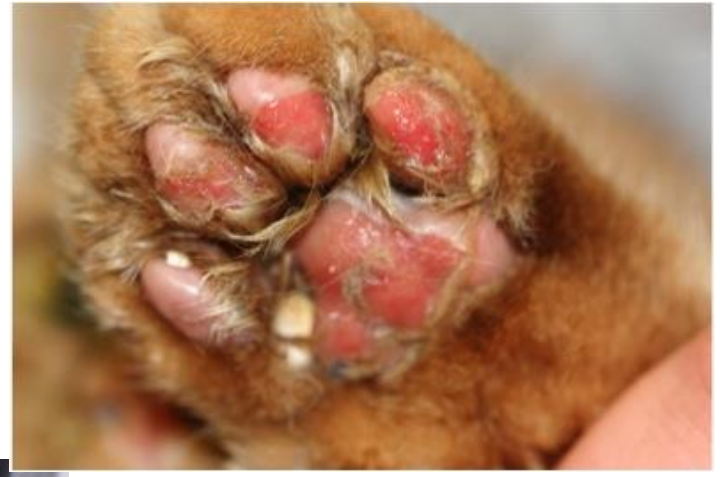
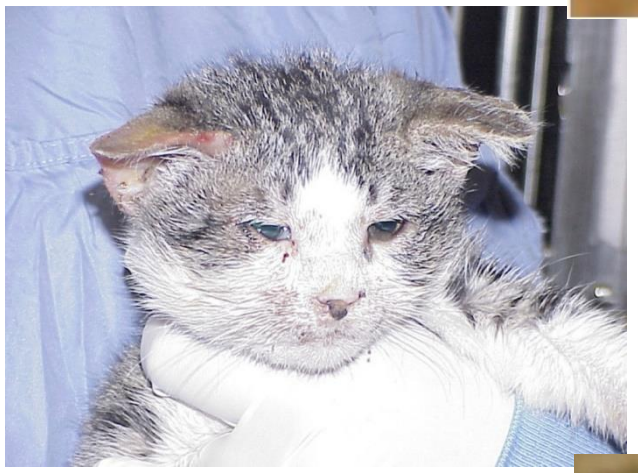


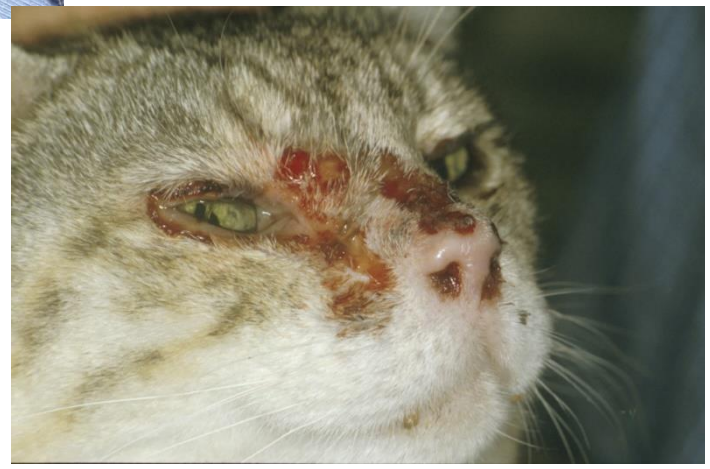
Figure 3 Hair loss, crusting and edema of the feet in a cat with VS-FCV. *Image courtesy of Dr Kate Hurley*

- The clinical signs of this form of disease are variable.
- The initial findings are frequently typical of a severe acute upper respiratory tract disease.
- Characteristic signs are cutaneous oedema and ulcerative lesions on the skin and paws.
- Oedema is located mainly on the head and limbs.
- Crusted lesions, ulcers and alopecia can be seen on the nose, lips, and ears, around the eyes and on the footpads.





Viirulent systemic calicivirus disease, excoriations of paws ©Uwe Truyen



Crusted lesions and ulcers due to VS-FCV infection ©Tim Gruffydd-Jones

Diagnosis

- The diagnosis of VS-FCV relies on clinical signs, high contagiousness and high mortality rate and isolation of the same strain from blood of several diseased cats, assessed by sequencing of hypervariable regions of the capsid gene.
- Because of the asymptomatic carrier phase, and the fact that viruses in live vaccines may occasionally be shed post-vaccination, caution should be taken when interpreting any FCV positive result because of the poor correlation between the presence of virus and clinical signs

- RT-PCR assays have been developed to detect FCV RNA in conjunctival and oral swabs, blood, cutaneous scrapings or lung tissue, depending on the clinical form and the outcome of the disease.
- Virus isolation; FCV replicates in cell lines of feline origin; its rapid growth in tissue culture may compromise identification of concurrent herpesvirus.
- Serology; FCV antibodies can be detected by virus neutralization or ELISA (Lappin et al., 2002). The seroprevalence is generally high in cat populations due to natural infection and vaccination.

Prevention and Control

- Management to limit or even prevent virus transmission is as important as vaccination in control.
- Vaccination of the queen will not prevent virus shedding, but may be beneficial in ensuring that the kittens benefit from higher levels of Abs through the colostrum and milk, providing protection for the first month or so of life.
- Shelter design and management should be aimed at avoiding cross infection of cats.

References

- http://www.petmd.com/cat/conditions/infectious-parasitic/c_ct_feline_calicivirus
- http://www.abcdcatsvets.org/feline-calicivirus-infection-2012-edition/

EQUINE VIRAL ARTERITIS

Equine Typhoid, Epizootic Cellulitis–Pinkeye,
Epizootic Lymphangitis Pinkeye

- Equine viral arteritis (EVA) is an economically important viral disease of equids.
- Stallions can become long term carriers of the virus, and transmit it during breeding.
- Acute illness also occurs in some horses. Although deaths are very rare in healthy adults, pregnant mares that become infected may abort, and very young foals may die of fulminating pneumonia and enteritis.

Conjunctivitis (“Pink-eye”)and Supraorbitalor periorbitaledema:

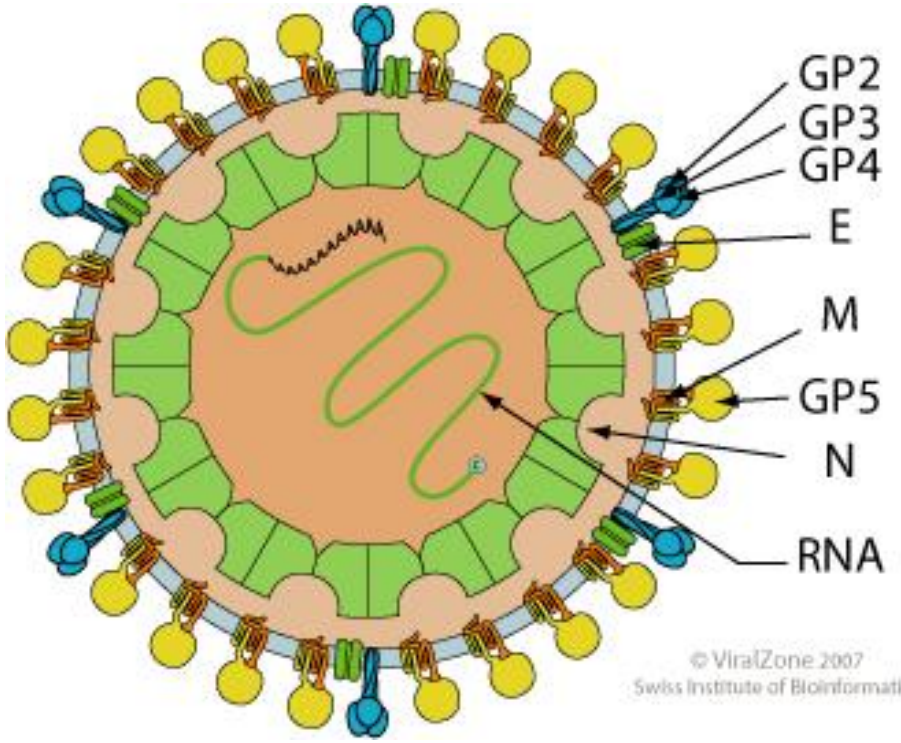
http://equine-reproduction.com/articles/EVA/Presentation/EVA_files/v3_slide0010.htm

Etiology

- Nidovirales order----Arteriviridae----Arterivirus----Equine arteritis Virus (EAV)
- RNA
- Enveloped
- Sensitive to ether and chloroform
- Isolates vary in their virulence and

potential to induce abortions.

- Only one serotype has been recognized.
- Equine arteritis virus is found in the Equidae.



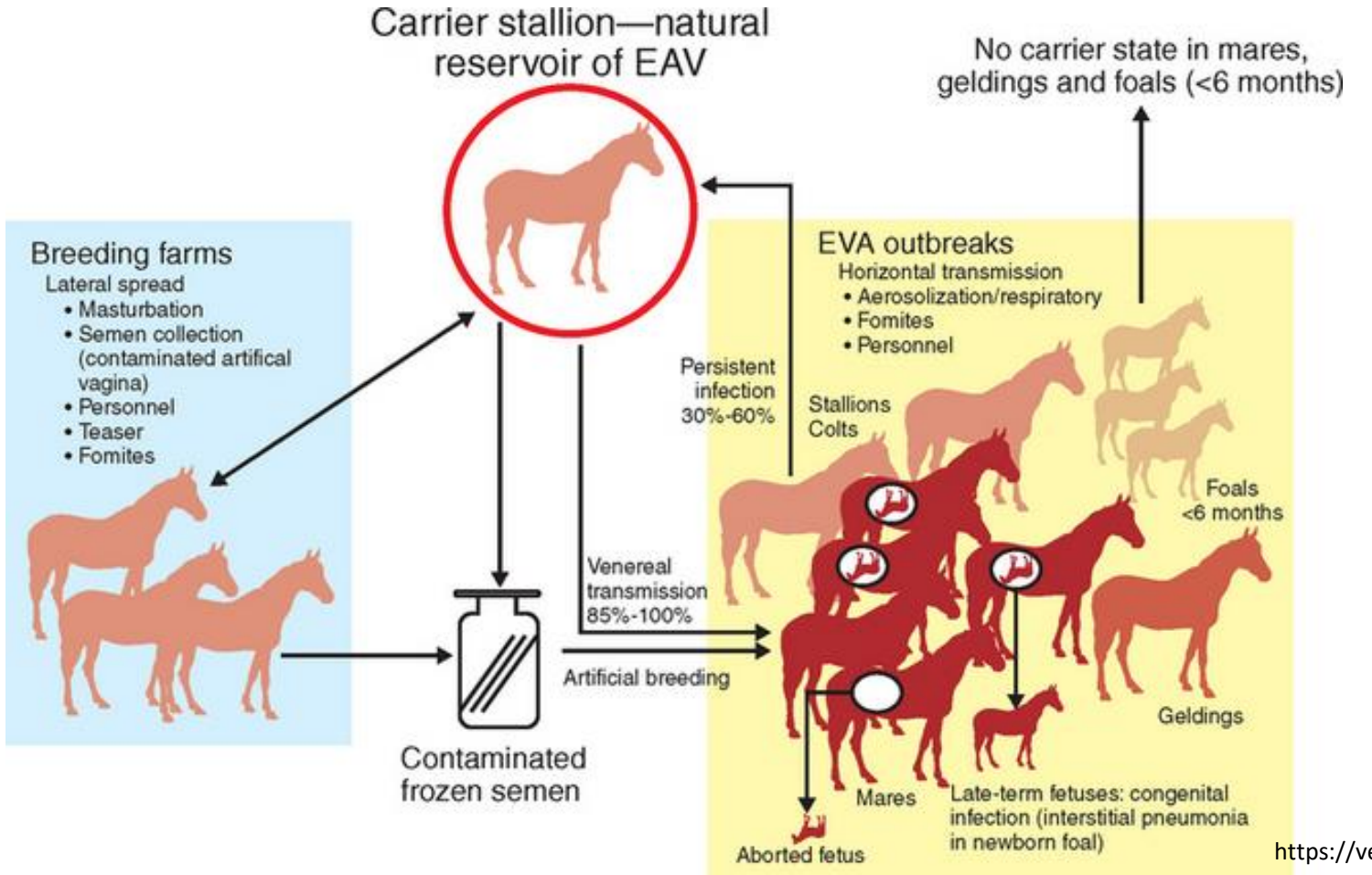
- Antibodies to this virus have been reported in horses, ponies, donkeys and zebras.

- Antibodies to EAV have been found in most countries where testing has been done.
- Seropositive horses have been reported in North and South America, Europe, Asia, Africa and Australia. Infections are common among horses in continental Europe, but rare in the United Kingdom.

Transmission

- Equine arteritis virus can be transmitted by the respiratory and the venereal routes.
- Acutely affected horses excrete the virus in respiratory secretions; aerosol transmission is common when horses are gathered at racetracks, sales, shows and other events.
- This virus has also been found in urine and feces during the acute stage.
- In mares, EAV can be found in vaginal and uterine secretions, as well as in the ovary and oviduct, for a short period after infection. Mares infected late in pregnancy may give birth to infected foals.
- Stallions shed EAV in semen, and can carry the virus for years.

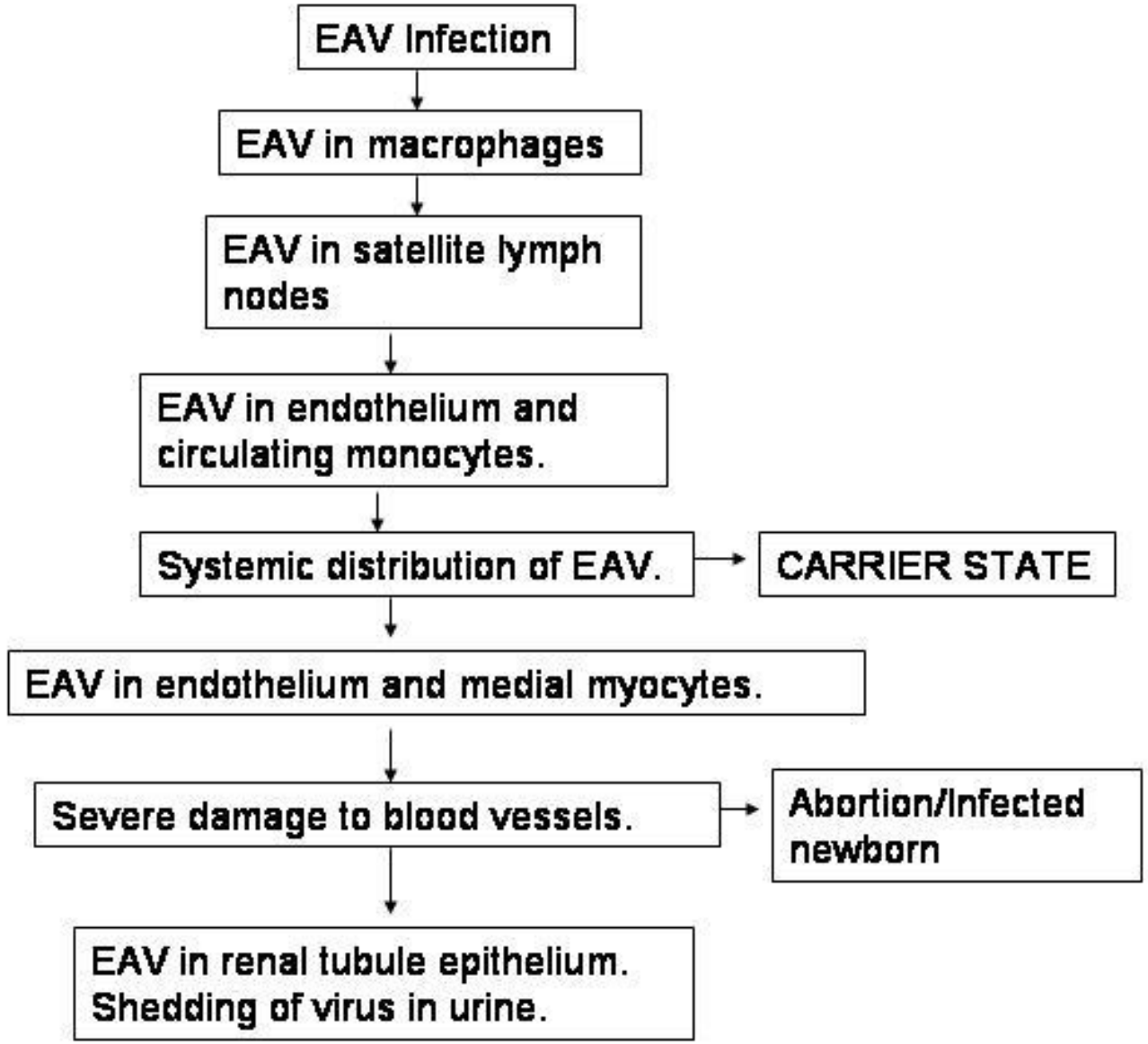
- Equine arteritis virus can be transmitted on fomites including equipment, and may be spread mechanically by humans or animals.
- This virus is inactivated in 20–30 minutes at 56-58ºC but can remain viable for 2 to 3 days at 37-38ºC and for up to 75 days at 4-8ºC.
- Semen remains infectious after freezing.



https://veteriankey.com/equine-viral-arteritis-2/

Pathogenesis and Pathology

- Infection of the lymphoid tissue of the nasopharynx then a leucopaenia and immunosuppresion.
- **Pathognomic medial necrosis of arteries**. This lesion is responsible for
  - oedema,
  - haemorrhage and
  - more rarely, thrombosis and infarction.
- Conjunctivitis and palpebral oedema give the name 'pink eye'.
- **Oedema** is also seen in the legs and lower abdomen.
- **Thoroughbred stallions have been shown to be intermittent or persistent shedders of virus, with the accessory sex glands (prostate and seminal vesicles) being the sites of persistence.**
- Virus infects the respiratory and alimentary tract resulting in nasal catarrh, coughing, dyspnoea (pleurisy), diarrhoea and colic.
- **Abortions** occur 10-30 days after infection in **50% of pregnant mares**. Congenital infection can also occur.



Through experimental and naturally infected models, the possible pathogenesis of this virus is understood.

1- The course of infection includes infection of the respiratory epithelium and alveolar macrophages first, and then onto the satellite lymph nodes.

2- The next stage of infection occurs at the bronchopulmonary lymph nodes, endothelium, and circulating monocytes; replication occurs here.

3- Systemic distribution of the virus follows and localization within the endothelium and medial myocytes of blood vessels and mesothelium occurs; severe damage occurs to blood vessels.

4- Apparently, the last site of invation is the renal tubular epithelium, where the virus may persist for an additional two weeks.

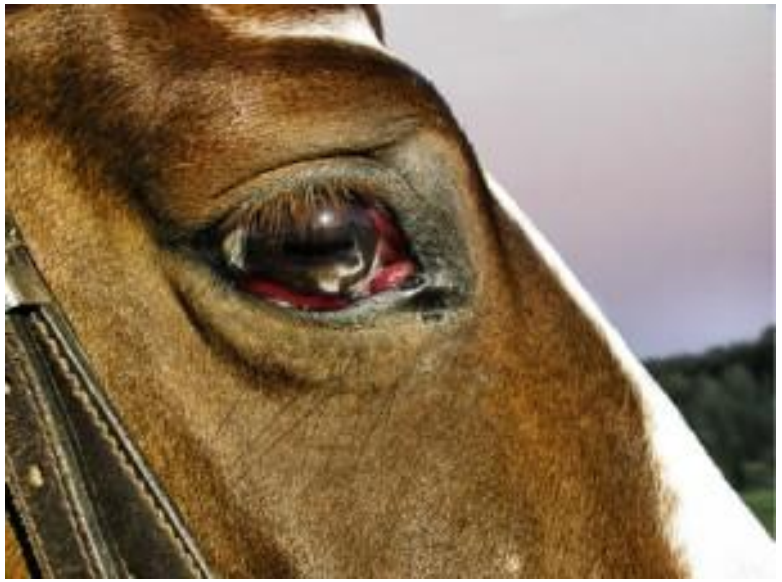
http://homepage.usask.ca/~vim458/virology/studpages2007/EVA/vet.html

Clinical Signs

- The incubation period varies from 2 days to 2 weeks. Infections transmitted venereally tend to become apparent in approximately one week.
- Infections transmitted venereally tend to become apparent in approximately one week.
- Fulminant infections with severe interstitial pneumonia and/ or enteritis can be seen in foals up to a few months of age.
- Systemic illness also occurs in some adults.

- In adult horses, the clinical signs may include
  - Fever
  - depression,
  - anorexia,
  - limb edema (particularly in the hindlimbs),
  - and dependent edema of the prepuce, scrotum, mammary gland and/or ventral body wall.
- Conjunctivitis,
- photophobia,
- periorbital or supraorbital edema and
- rhinitis can also be seen.
- Some horses develop urticaria; the hives may be localized to the head or neck, but are sometimes generalized.
- Abortions or stillbirths can occur in mares that are pregnant when they are exposed.
- Temporary decreases in fertility, including reduced quality sperm and decreased libido, may be seen in stallions during the acute stage of the disease

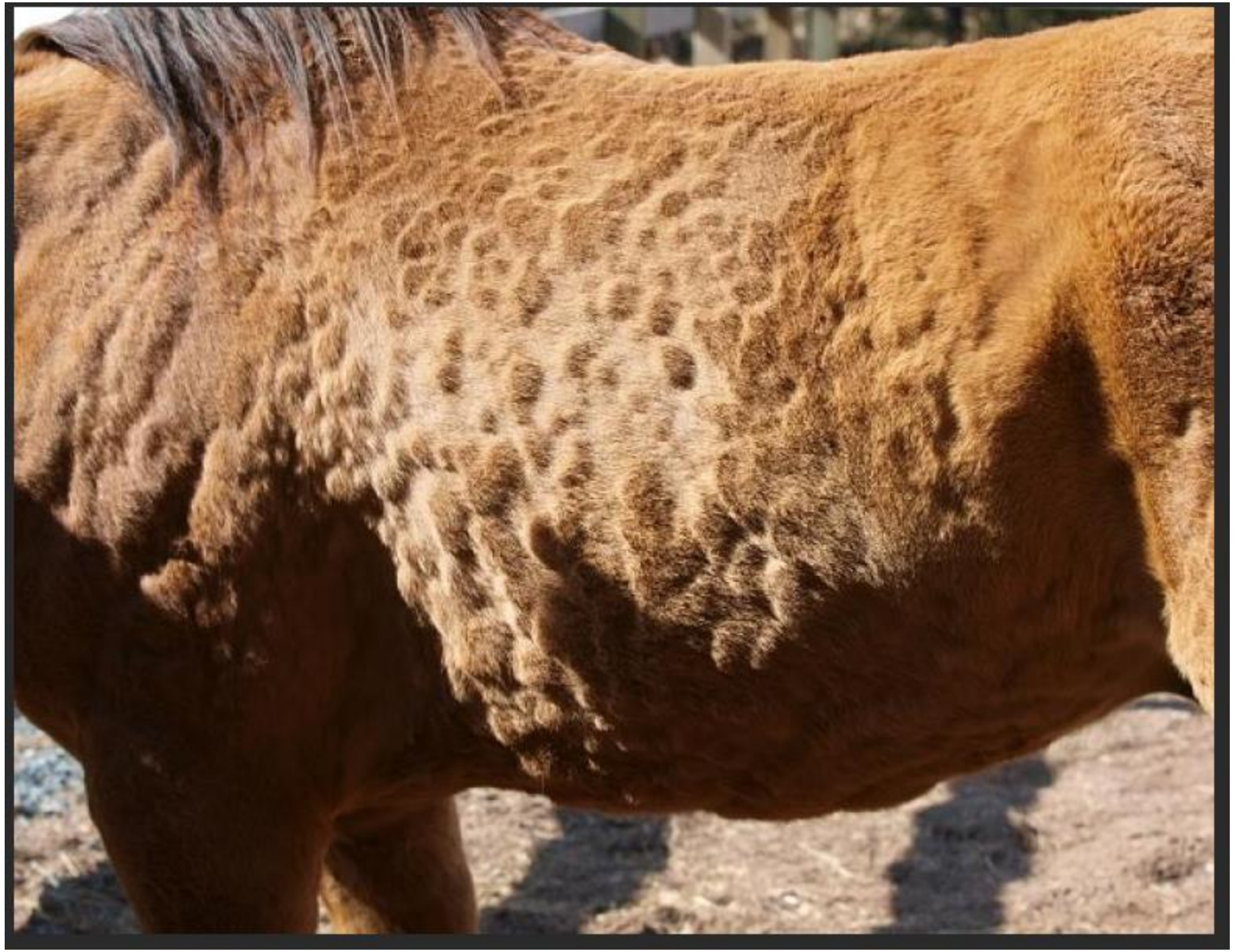
Horse, scrotum. Scrotal edema occurring in equine viral arteritis.

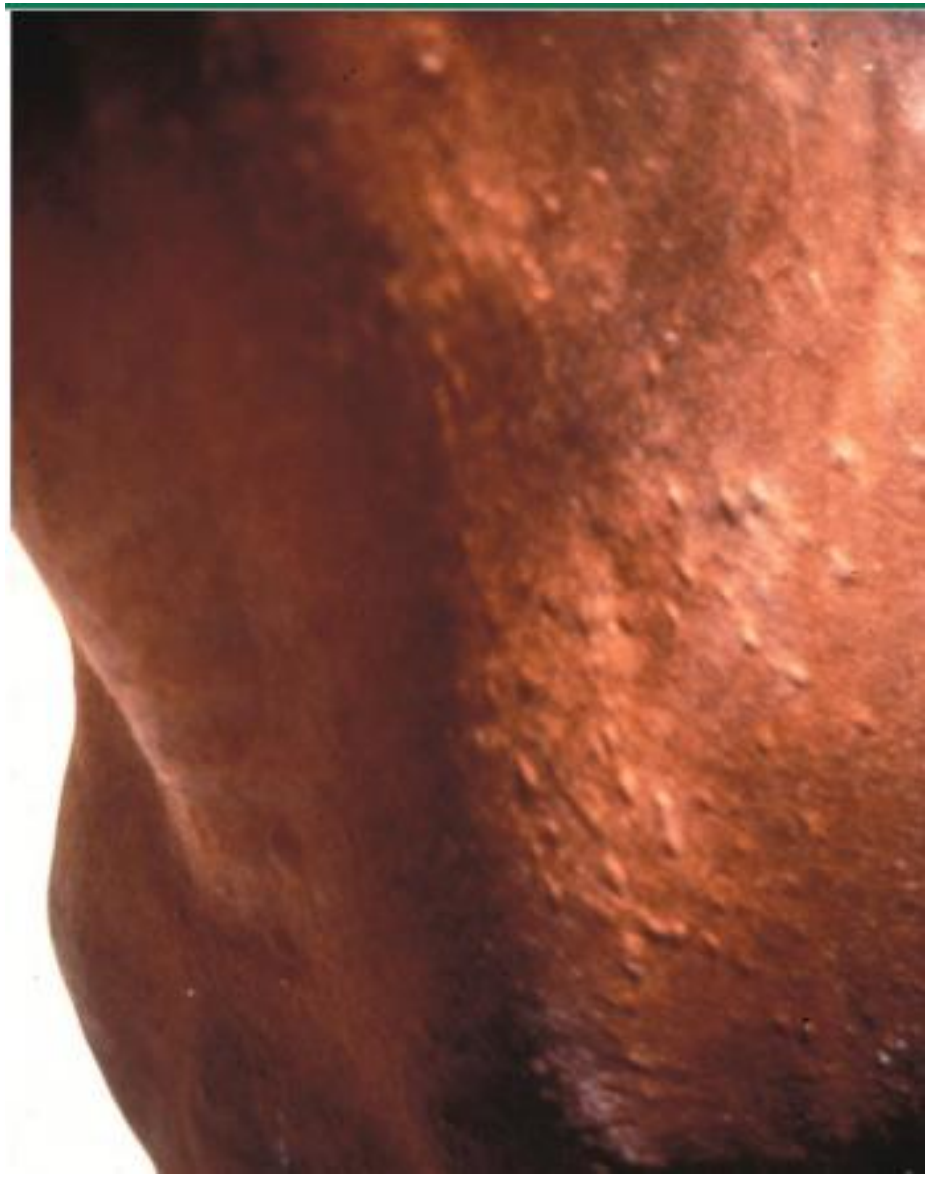


Depressed horses suffering from EVA
Picture courtesy J. Wood, University of Cambridge

https://vcahospitals.com/know-your-pet/equine-viral-arteritis-eva

http://www.brandonlakesanimalhospital.com/client-resources/breed-info/equine-viral-arteritis-eva/





Urticaria

Excessive lacrimation

Periorbital odema

Diagnosis

Clinical

- Equine viral arteritis should be considered when the clinical signs include fever, depression, edema, conjunctivitis, nasal discharges and abortions.
- This disease is difficult to differentiate from other systemic and respiratory illnesses of horses.

- virus isolation,
  - In recently infected animals, EAV may be recovered from nasal secretions, blood and semen as well as from a number of tissues and fluids at necropsy.
  - Carrier stallions can be identified by isolating the virus from semen; EAV is not found in the respiratory secretions, blood or urine of carriers.
  - This virus can be isolated in rabbit, equine and monkey kidney cells or cell lines. RK–13 (rabbit kidney) cells are the system of choice.
- the detection of viral antigens or nucleic acids,
  - RT-PCR
- Serology
  - virus neutralization, complement fixation (CFT), agar gel immunodiffusion (AGID), indirect fluorescent antibody, fluorescent microsphere immunoassay (MIA) and ELISA.

Differential diagnosis

- The differential diagnosis includes
- equine influenza,
- equine infectious anemia and
- African horse sickness,
- Getah virus,
- Hendra virus,
- equine rhinitis A and B viruses,
- equine adenoviruses,
- equine herpesviruses 1 and 4.
- purpura hemorrhagica and other streptococcal infections,
- poisoning from the toxic plant.

Prevention and Control

- Precautions should also be taken to avoid spreading the virus on fomites.
- EAV is readily inactivated by detergents, common disinfectants and lipid solvents.
- No specific treatment is available; however, most healthy horses other than young foals recover on their own.
- Good nursing and symptomatic treatment should be used in severe cases.
- Vaccination can also help contain outbreaks.

- Venereal transmission can be controlled by good management and vaccination.
- To protect pregnant mares from abortion, they should be separated from other horses and maintained in small groups according to their predicted foaling dates.

For example;

- Mandatory notification,
- annual testing,
- the identification of carrier stallions and
- control of transmission from these animals,
- and selective vaccination are being used in New Zealand to eradicate equine viral arteritis.

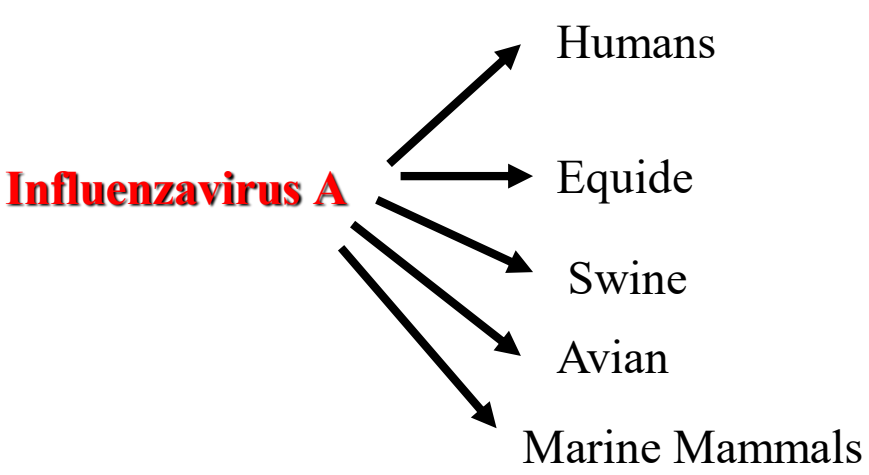
References

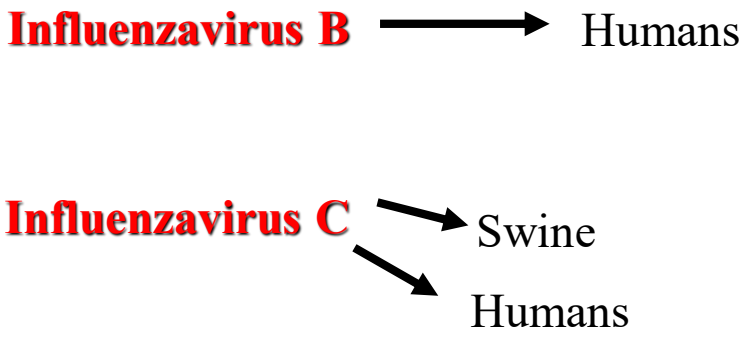
- http://www.cfsph.iastate.edu/Factsheets/pdfs/equine_viral_arteritis.pdf
- https://veteriankey.com/equine-viral-arteritis-2/

Equine Influenza

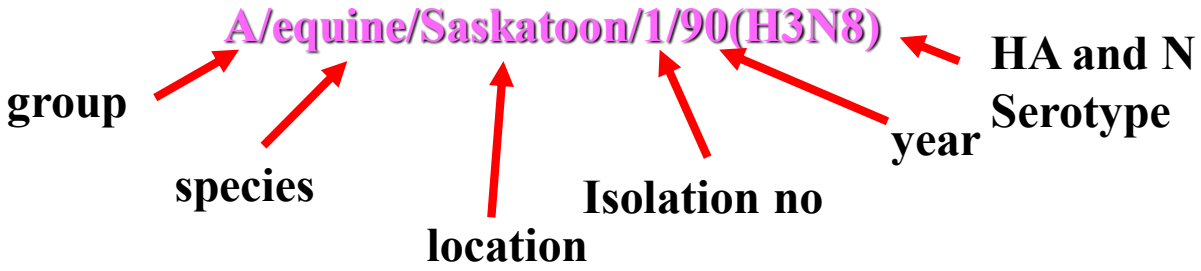
- Equine Influenza (EI) is a highly contagious though rarely fatal respiratory disease of horses, donkeys and mules and other equidae.
- The disease has been recorded throughout history, and when horses were the main draft animals, outbreaks of EI crippled the economy.
- Nowadays outbreaks still have a severe impact on the horse industry.

Orthomyxoviridae





Nomenclature



- A/equine/Prague/1/56(H7N7)
- A/fowl/Hong Kong/1/98(H5N1)
- A/swine/Lincoln/1/86(H1N1)

Distribution of HA serotypes in nature

HA serotype	Avian	Horse	Swine	Human
HA1	yes		yes	yes
HA2	yes			yes
HA3	yes	yes	yes	yes
HA4	yes			
HA5	yes			yes
HA6	yes			
HA7	yes	yes		
HA8-18	yes			

Distribution of N serotypes in nature

N serotype	Avian	Horse	Swine	Human
N1	yes		yes	yes
N2	yes		yes	yes
N3	yes			
N4	yes			
N5	yes			
N6	yes			
N7	yes	yes		
N8	yes	yes		
N9-11	yes			

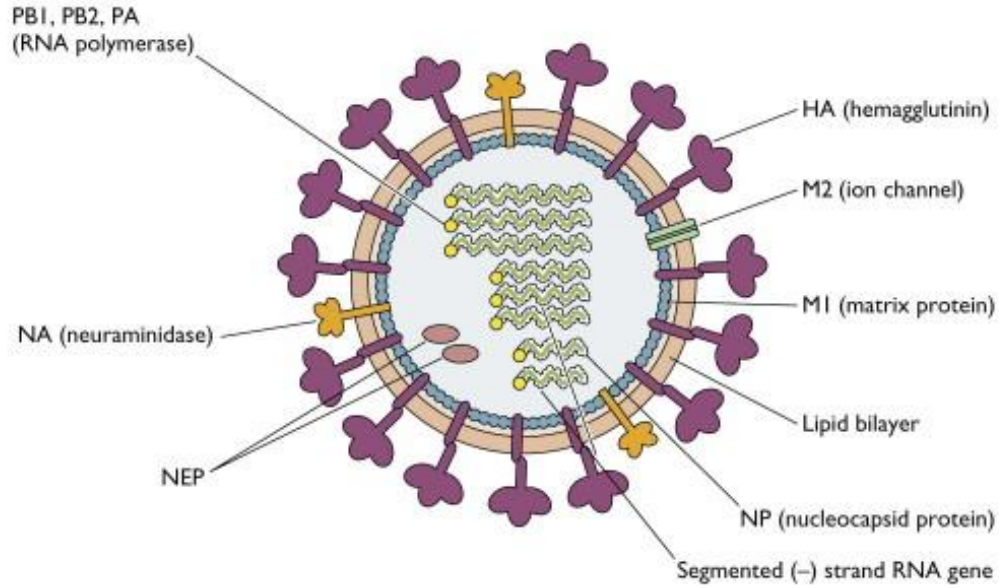
Significant A-type influenza epidemics

- H1N1, which caused Spanish Flu in 1918, and Swine Flu in 2009
- H2N2, which caused Asian Flu in 1957
- H3N2, which caused Hong Kong Flu in 1968
- H5N1, which caused Bird Flu in 2004
- H7N7, which has unusual zoonotic potential[24]
- H1N2, endemic in humans, pigs and birds
- H9N2
- H7N2
- H7N3
- H10N7

Etiology

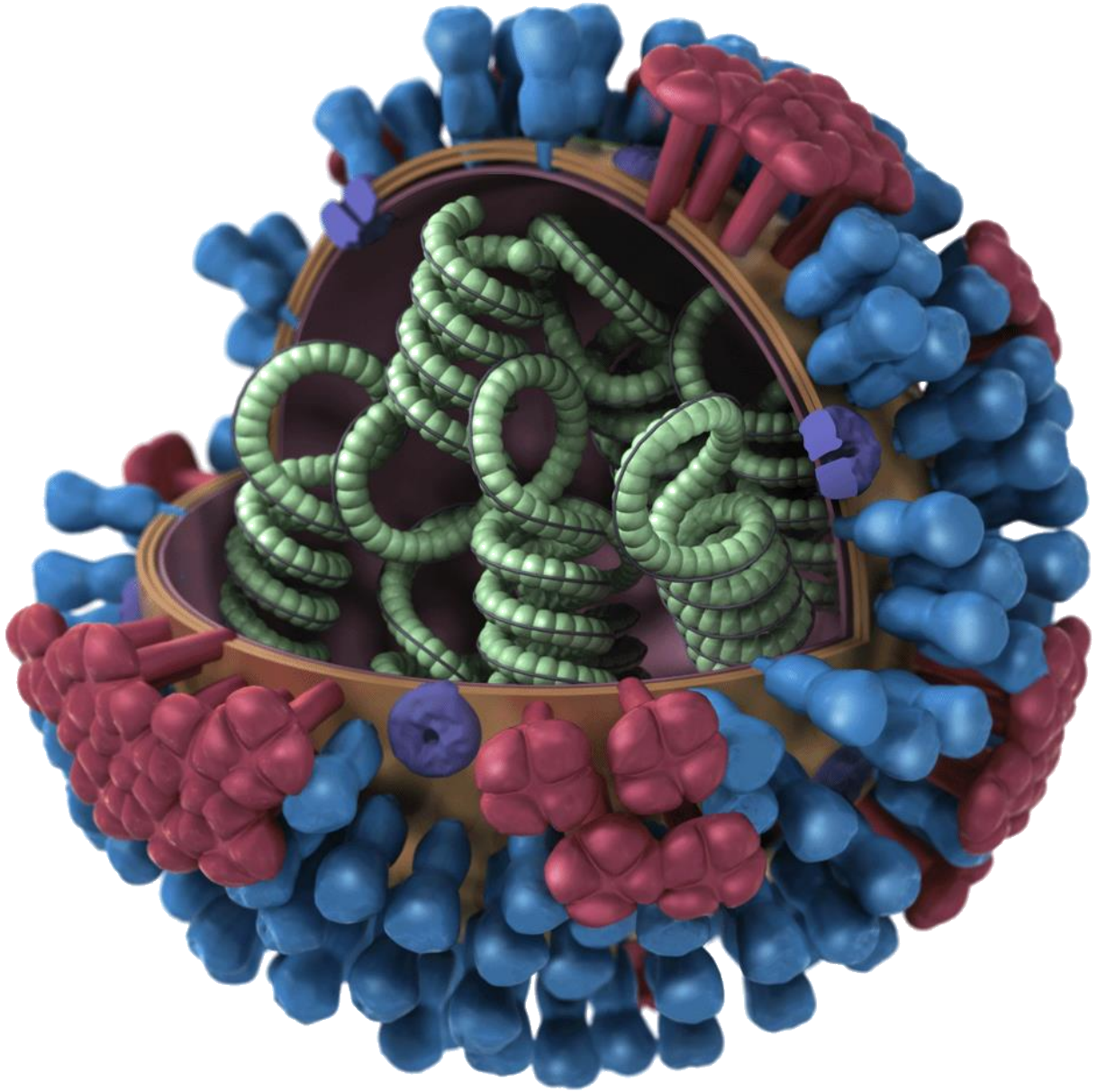
Orthomyxoviridae Influenzavirus

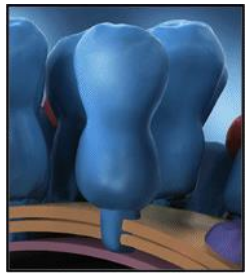
- Segmented, single stranded RNA
  - The single stranded RNA is negative sense, It has a different gene on each segment. The 8 segments are held together by the helical capsid comprised of nucleoprotein.
- enveloped
- Sensitive to Ether and Chloroform



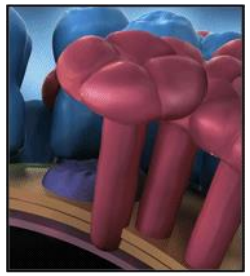
- HA and N
  - Each gene codes for one protein: **haemagglutinin** (H) spike, neuraminidase (N) spike, matrix (which lines the inside of the envelope and is like scaffolding), nucleoprotein, 3 viral polymerases and a large non-structural protein.
  - H enables the virus to attach to respiratory epithelial cells within seconds via sialic acid on the host cell. H also attaches to red blood cells in-vitro, hence its name.
  - Such haemagglutination is blocked when virus is pretreated with antibody (Haemagglutination inhibition (HI) test).
  - N is a sialidase enzyme which which prevents new virus simply reattaching to the same host cell and allows it to move to new cells

Two types are available, Type 1 (H7N7) and Type 2 (H3N8)

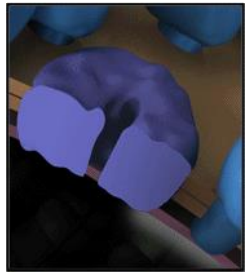




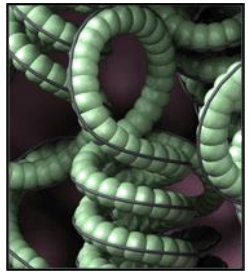
Hemagglutinin



Neuraminidase



M2 Ion Channel

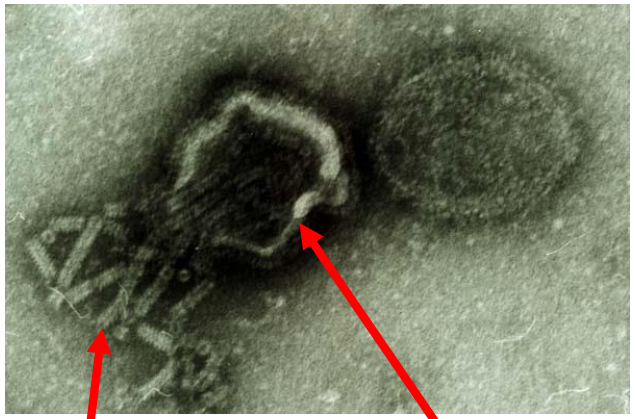


RNP

Etiology

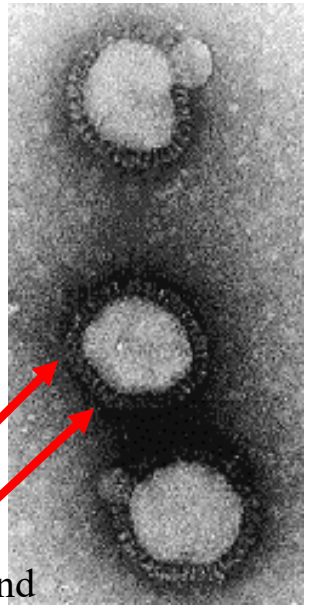
- Inoculates in the amniotic cavity of ECE.
  - **Cultivation and cytopathic effect:**
  - Influenza viruses are routinely grown to high titre in the allantoic cavity of 10-day-old fertile bird eggs (chickens and ducks) or more rarely in kidney cells for vaccines and diagnosis. Virus is detected by its ability to haemmagglutinate red blood cells.
- virus cause cpe in cell culture
- Under natural conditions it is only seen on equids.
- They are related to but distinct from the viruses that cause human and avian influenza.

Etiology



Nucleocapsid
(RNA surrounded with protein)

envelope



haemagglutinin and neuraminidase “spikes” on envelope

100 nm

Antigens

1. Type specific.

A, contains the veterinary isolates. B and C are human. The A antigens are on the nucleoprotein and can be identified by ELISA in certain diagnostic tests eg on nasal swabs.

2. Subtype specific antigens on H and N.

detected by HI and NI tests.

- The external H and N envelope glycoproteins carry the subtype antigens H1 to H18 and N1 to N11. Vaccinal immunity involves neutralisation of the subtype specific antigens on H.
- H1 to H15 viruses are in ducks which are the source of new mammalian subtypes.
- Equine influenza type 1 and type 2 carry H7 N7 and H3 N8 respectively ie their vaccines do not cross protect.

3. Antigenic drift - variation of H within a subtype within a host species

4. Antigenic shift - change of subtype of H within a host species

Transmission

- Virus is highly contagious.
- EI is spread by contact with infected animals, which in coughing excrete the virus.
- In fact animals can begin to excrete the virus as they develop a fever before showing clinical signs.
- It can also be spread by mechanical transmission of the virus on clothing, equipment, brushes etc carried by people working with horses.

- Once introduced into an area with a susceptible population, the disease, with an incubation period of only one to three days, spreads quickly and is capable of causing explosive outbreaks. Crowding and transportation are factors that favour the spread of EI.

Factors Strengthening Epizootics / Epidemics

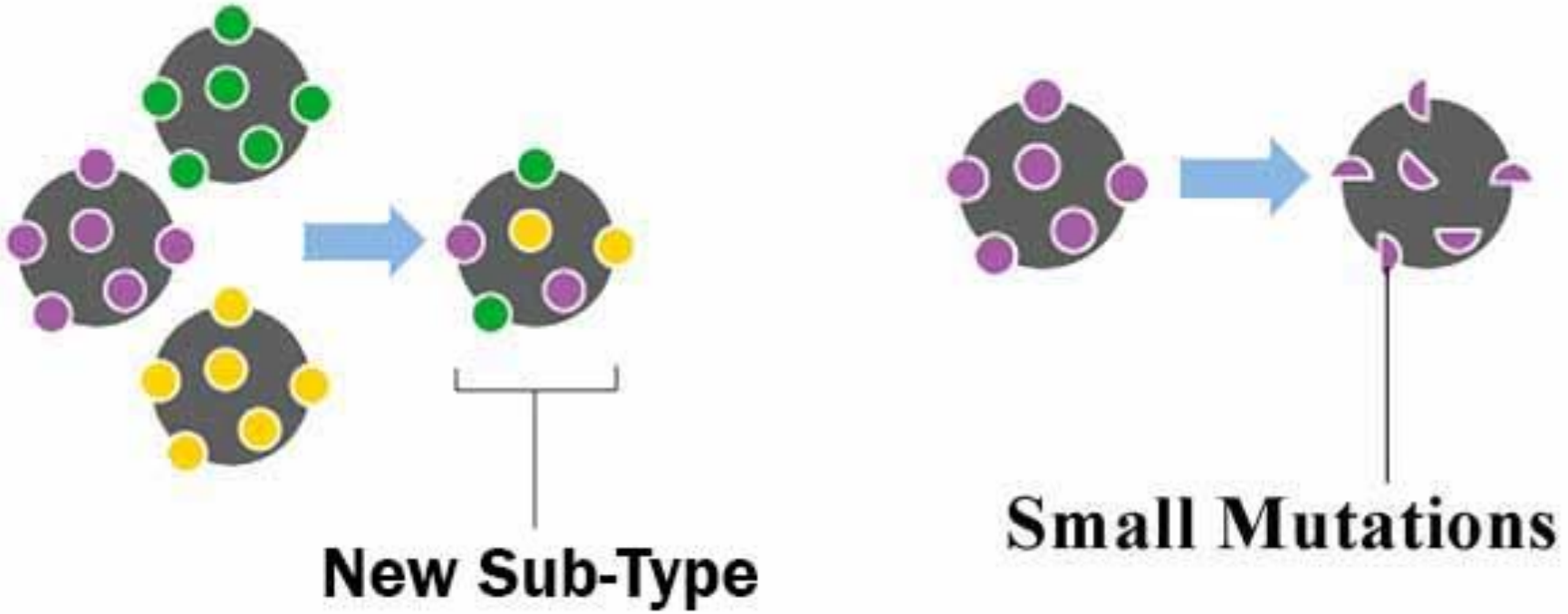
- Antigenic drift
- Reassortment and antigenic shift
- Short-term immunity
- Transfer between species
  - It is known to pass through dogs.

Antigenic drift

- evolution of a variant within a subtype, meaning imperfect protection by old vaccines
- *Why?* Each H molecule carries 5 antigenic regions via which antibodies can HI, neutralize and block attachment to host cells. A change in any region results in antigenic drift. The RNA genes of influenza are constantly mutating, during error-prone replication. If the mutation involves escape from neutralisation the variant is selected in infected animals.
- Drift is detected by 2-4-fold alterations in HI titres between one isolate and another isolate recovered several years later. Drift is now best assessed by panels of mAb in HI tests and nucleotide sequencing of the neutralisation sites on H.
- These **mutations accumulate with time**. The human viruses appear to accumulate more mutations than the equine, which may relate to the presence of more people than horses in the world.

Differences Between

Antigenic shift & Antigenic drift



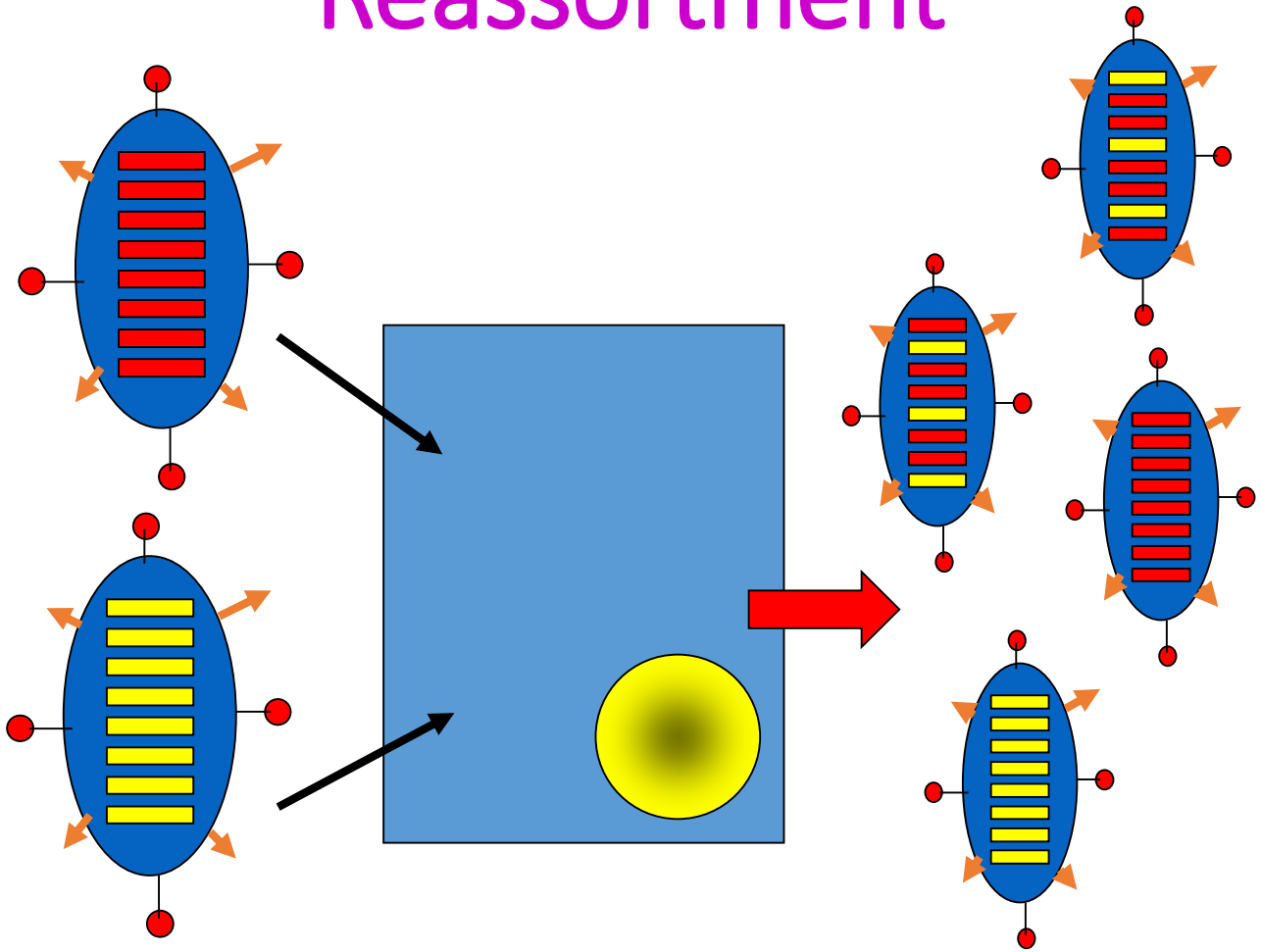
https://microbiologyinfo.com/differences-between-antigenic-shift-and-antigenic-drift/

Reassortment and antigenic shift

- Complete change of H molecule meaning no protection by old vaccines. Shift occurs by a) gene reassortment, b) change of species specificity

a) Gene reassortment Pigs become infected with duck virus and human virus at the same time, eg on a chinese commune where all 3 species live close together. Some virus reassorts its RNA segments in the pig respiratory epithelial cells to produce a new virus with a duck H gene for attachment and a 7 human genes for virus growth. This new virus will infect vaccinated humans because it has a brand new subtype of H.

Reassortment



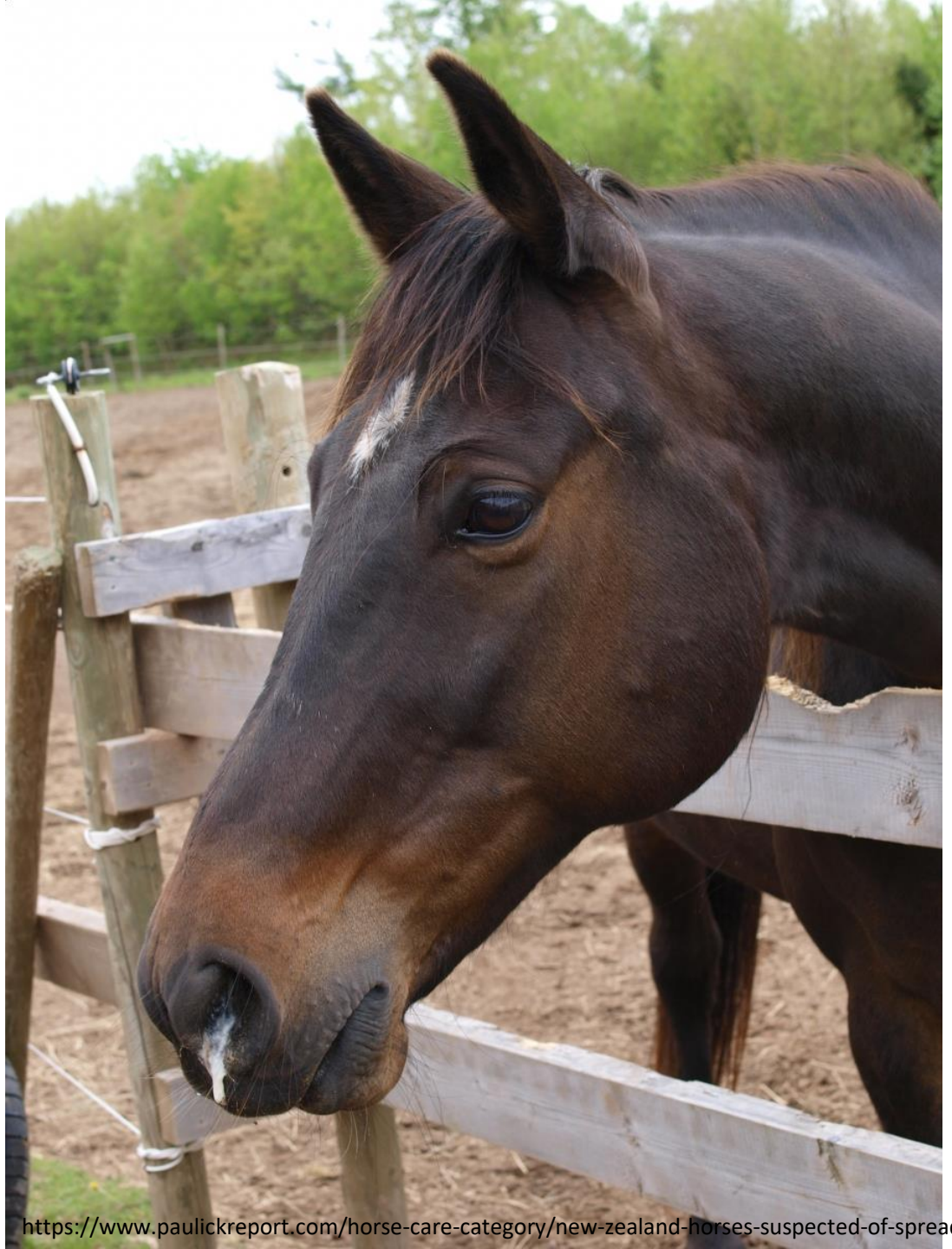
b) Change of species specificity. A 1997 virus which killed at least 8 Hong Kong children was related in all 8 gene segments to an H5 chicken fowl plague virus. This HK virus could have originated from migratory ducks, spread to chickens, undergone mutations to become more virulent in chickens and thereby become infectious to man. For this reason a million chickens were slaughtered in HK in 1998 although the human cases had already stopped.

Pathogenesis

- Once the virus enters the organism, Aerosol virus infects the ciliated epithelium of the nasal mucosa and then may extend to the bronchioles with resulting epithelial cell necrosis, which manifests as bronchiolitis and serous exudation
- The virus spreads to the respiratory tract in 2-4 days. Rhinitis occurs.
- Histopathologically, cell infiltration in bronchial regions and thickening in alveolar walls are seen.

Clinical Signs

- A harsh dry cough follows an incubation period of 1-3 days when the horse also develops pyrexia, depression, loss of appetite, enlarged submandibular lymph nodes, muscle pain and weakness.
- Secondary bacterial infection follows defective muco-ciliary transport.
- While most animals recover in two weeks, the cough may continue longer and it may take as much as six months for some horses to regain their full ability. If animals are not rested adequately, the clinical course is prolonged.



https://www.paulickreport.com/horse-care-category/new-zealand-horses-suspected-of-spreading-equ

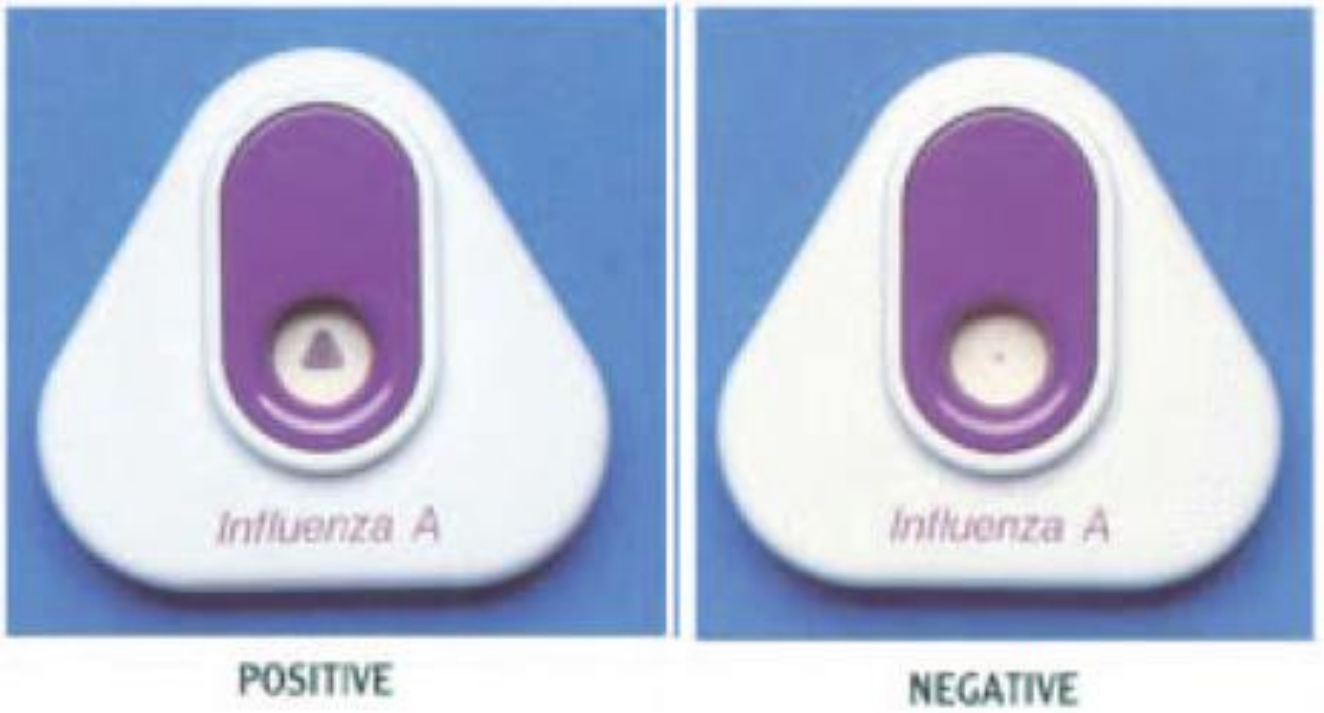
http://www.debenvalleyvet.co.uk/Event.aspx?informationid=27

- A fatal bronchopneumonia is more likely if horses continue to be exercised.
- Type 2 cause more severe infections.
- In some cases, there is a cough that does not heal (due to the viral presistence) (two-year-old-caugh).

Diagnosis

- Virus isolation:
  - Samples are taken from several horses because only a low proportion may be excreting virus. Deep nasal swabs are collected by inserting a long swab 12 inches into each nostril -
  - THE SWAB IS deposited INTO 10 ML TRANSPORT MEDIUM (sterile basic salts solution containing antibiotics), transported at 4 C and frozen at -70 C.
- Antigen detection:
  - Directigen Flu A is a commercial antibody capture ELISA for type A antigens of nucleoprotein in swabs. It does not tell the lab which subtype is involved

- Serology:
  - Following clinical disease a 4 fold increase in serum antibody to H7 of equine 1 or H3 of equine 2 will occur between bleeds taken during the acute and convalescent phase (2 weeks later). This antibody can be detected by haemagglutination inhibition (HI) and will say whether virus is equine 1 or 2.
- Directigen Flu-A



Immunity and epidemiology:

- As with most viruses the period of virus excretion from nasal secretions is during the first 10 days following infection before spec-immunity kicks in.
- Secreted IgA antibodies in horses are important for protection.
- Vaccinated animals can excrete virus without disease and have carried the virus between countries eg to South Africa from USA.
- As with other resp viruses spread is by personnel and instruments (which most vets do not realise) as well as by aerosol eg at race meetings.
- No zoonotic risk.

Chemotherapy

- Those who block the membrane fusion
  - Amantidine (Symmetrel)
  - Remantidine (Flumadine)

- Neuraminidase inhibitors
  - Zanamivir (Relenza)
  - Oseltamivir (Tamiflu)

Prevention and Control

- Isolate coughing horses to minimise spread and use disposable syringes when treating them.
- *Prophylaxis* is by vaccination.
- Vaccines combination of A/Equine 1 (H7N7) ve A/Equine 2 (H3N8)
- Vaccination is practiced in most countries. However, due to the variability of the strains of virus in circulation, and the difficulty in matching the vaccine strain to the strains of virus in circulation, vaccination does not always prevent infection although it can reduce the severity of the disease and speed recovery times.

Single vaccination provides protection for 2-3 months. The second vaccination should be done again after 6-9 months.

- When the disease appears, efforts are placed on movement control and isolation of infected horses.
- The virus is easily killed by common disinfectants, so thorough cleaning and disinfection is part of biosecurity measures in responding to the disease.
- Since the disease is most often introduced by an infected animal, isolation of new entries to a farm or stable is paramount to preventing the introduction of disease to a premise.

- http://www.oie.int/doc/ged/D14001.PDF
- **PETER H. RUSSELL, BVSc, PhD, FRCPath, MRCVS**, Department of Pathology and Infectious Diseases, The Royal Veterinary College, http://www.pitt.edu/~super1/Virology/virology.htm