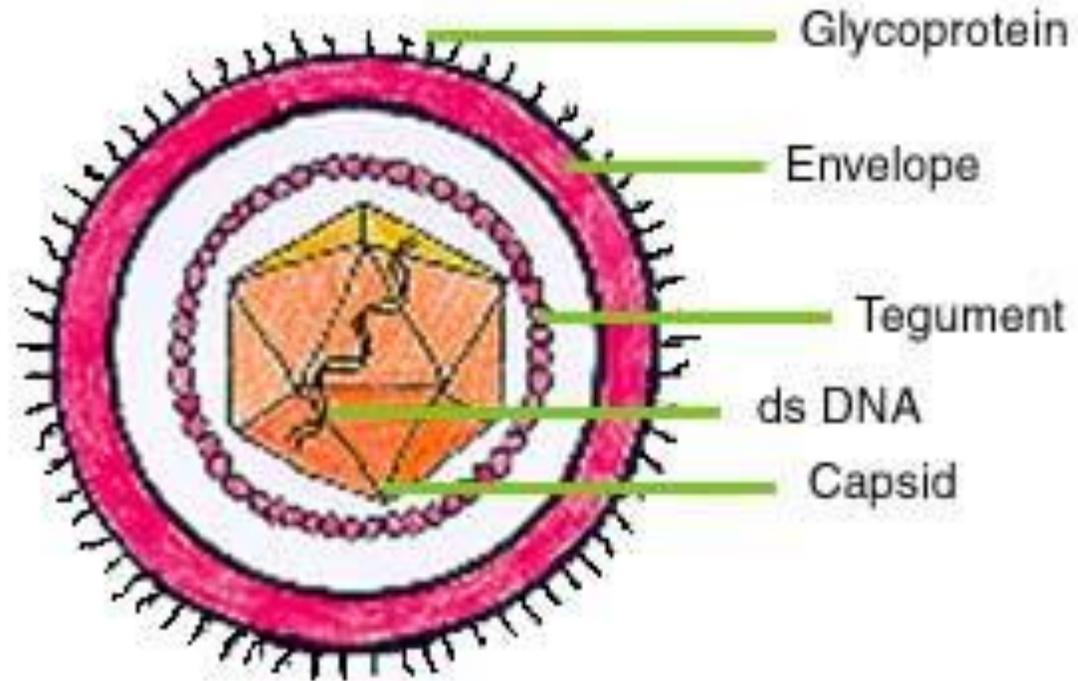


HERPESVIRIDAE



- These large viruses cause many diseases which involve erosions/necrotic lesions of the the respiratory tract, brain, blood vessels, placenta and urinogenital tract
 - eg infectious bovine/feline rhinotrachietis, pseudorabies, equine abortion.
- **Structure**
- Herpesviruses have double stranded DNA enclosed in an icosahedral capsid to a diameter of 100-150 nm.
- The envelope glycoproteins are the most important vaccine antigens.
- Nucleus replication
- ★ • **Latency following primer infection**
- There are 3 subgroups.

Herpesviridae

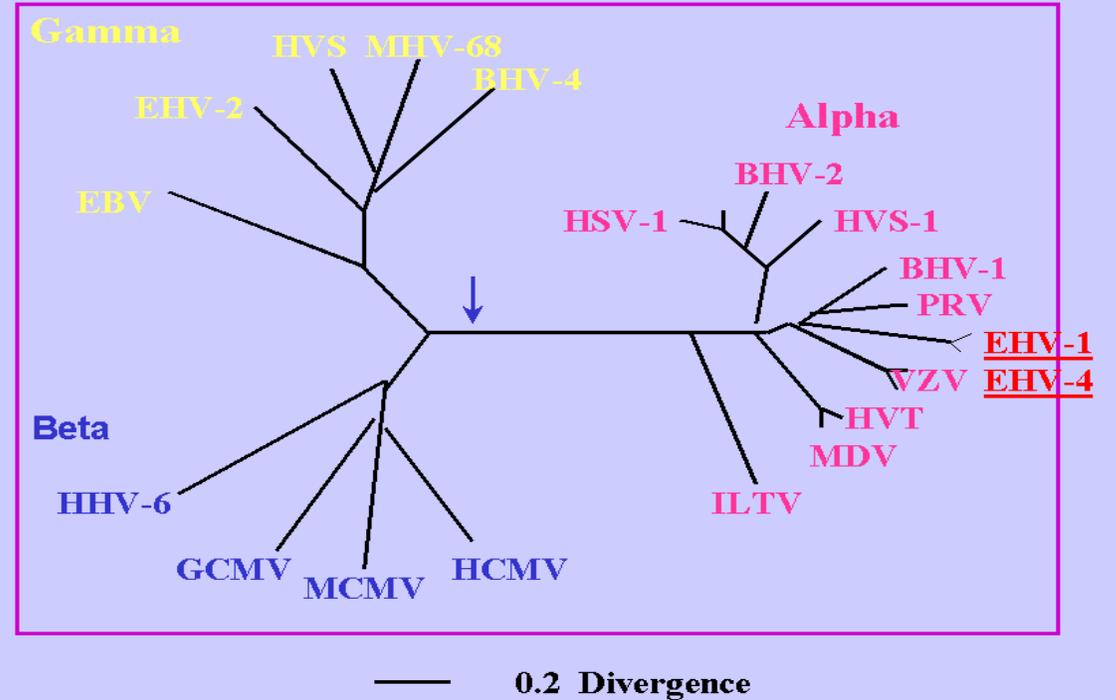
Sub Family

Alphaherpesvirinae

Betaherpesvirinae

Gammaherpesvirinae

Evolutionary relatedness of herpesviruses and their subfamilies



(Based on McGeoch et al. 1995 J. Mol. Biol. 247 443-458)

Alphaherpesvirinae

Bovine Herpes Virus
Type 1,2,5



Equine Herpes Virus
Type 1,3,4



Caprine Herpes Virus
Type 1



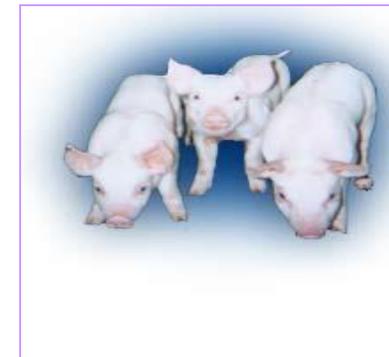
Canine Herpes Virus
Type 1



Feline Herpes Virus
Type 1



Porcine Herpes Virus
Type 1



- Betaherpesvirinae
- In this subgroup, there are viruses that cause **infection in humans**. Only SHV2, which affects rhinitis in pigs, is present in this group.

Gammaherpesvirinae

Cattle;

Bovine Herpes Virus Tip 4 ve Alcelaphine herpesvirus (BHV-3)

Horses;

Equine Herpes Virus Tip 2 ve Tip 5

Sheep;

Ovine Herpes Virus Tip 1 ve Tip 2

Goats;

Caprine Herpes Virus Tip 2

Herpesviruses are bad news for 4 reasons

1. Some of them infect crucial target tissues e.g. the **brain and maternal placenta**.
2. All become latent of recovered animals. Subsequent **reactivation during stress** causes disease or tumours.
3. All **are cell-associated** and **can spread between cells by cell fusion**. Inactivated vaccines which induce circulating antibody therefore do not work well and safe strong live **vaccines** which stimulate long term cytotoxic T cells are **difficult to make**. (DNA vaccines, with Th1 cytokine genes as adjuvants, are the answer if ever licensed)
4. **Virulence** is associated with presence of a thymidine kinase (TK) gene, so this is deleted from genetically engineered vaccines eg to Aujeszky's virus. TK accelerates new DNA synthesis by salvaging thymidine from degraded DNA into TTP.

Infectious Bovine Rhinotracheitis (IBR),
Infectious Pustular Vulvovaginitis (IBV),
Infectious balanoposthitis (IPV)

- Infectious bovine rhinotracheitis/infectious pustular vulvovaginitis, caused by **bovine alphaherpesvirus 1 (BHV-1)**, is a disease of domestic and wild cattle.
- The virus is distributed **worldwide**.
- BHV-1 virus causes two diseases in cattle:
 - **infectious bovine rhinotracheitis (IBR)**
 - **infectious pustular vulvovaginitis (IPV)**.
- The clinical signs are characterized by fever and involvement of the upper respiratory tract, including conjunctivitis, rhinitis and tracheitis.
- Secondary bacterial infections may lead to pneumonia, especially in intensively managed livestock, such as beef cattle in feedlots.

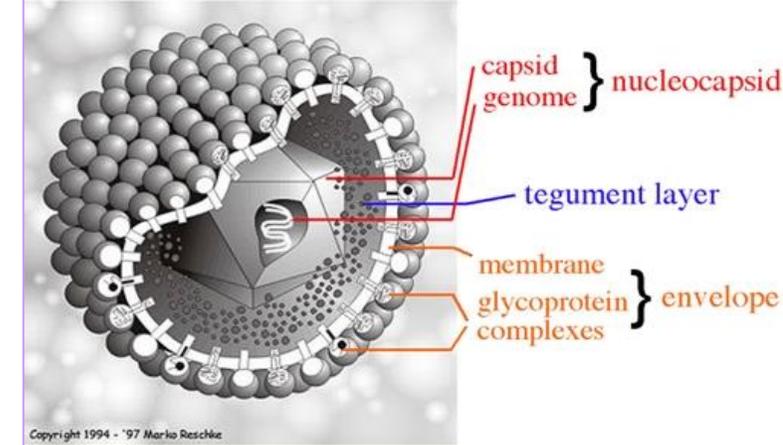
Etiology

- Family Herpesviridae subfamily Alphaherpesvirinae
- Enveloped
- DNA
- Icosahedral symmetries
- Only a single serotype of BHV-1 is recognized; however, three subtypes of BHV-1 have been described on the basis of endonuclease cleavage patterns of viral DNA:

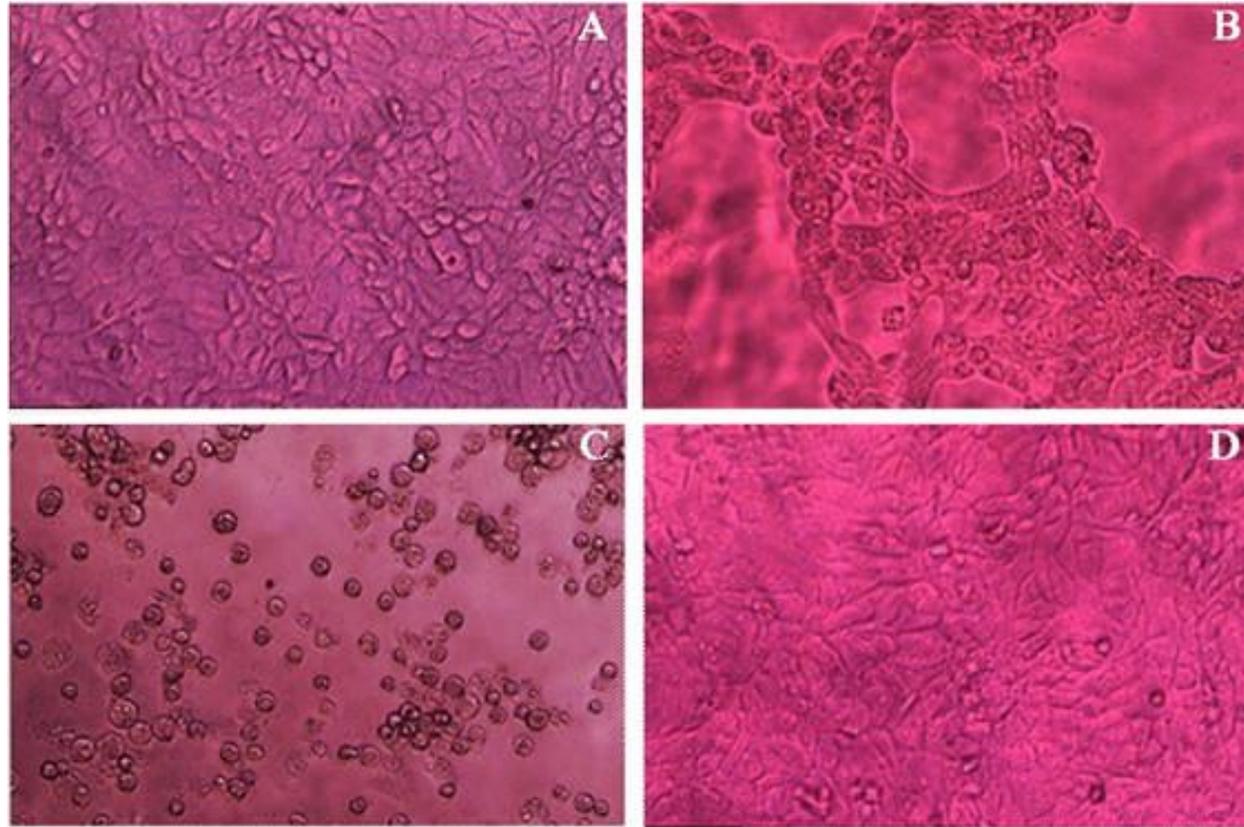


- BHV-1.1 } respiratory disease, abortus
- BHV-1.2a }
- BHV-1.2b → genital disease
- BHV-5 (previously known as BHV-1.3 (encephalitic subtype))

Three major glycoproteins, gB, gC, and gD induce neutralizing antibody responses



- Virus could be isolated Bovine tissue cultures; MDBK.



Boubaker–Elandalousi, Ramzi, et al. "Non-cytotoxic *Thymus capitata* extracts prevent Bovine herpesvirus-1 infection in cell cultures." *BMC veterinary research* 10.1 (2014): 231.

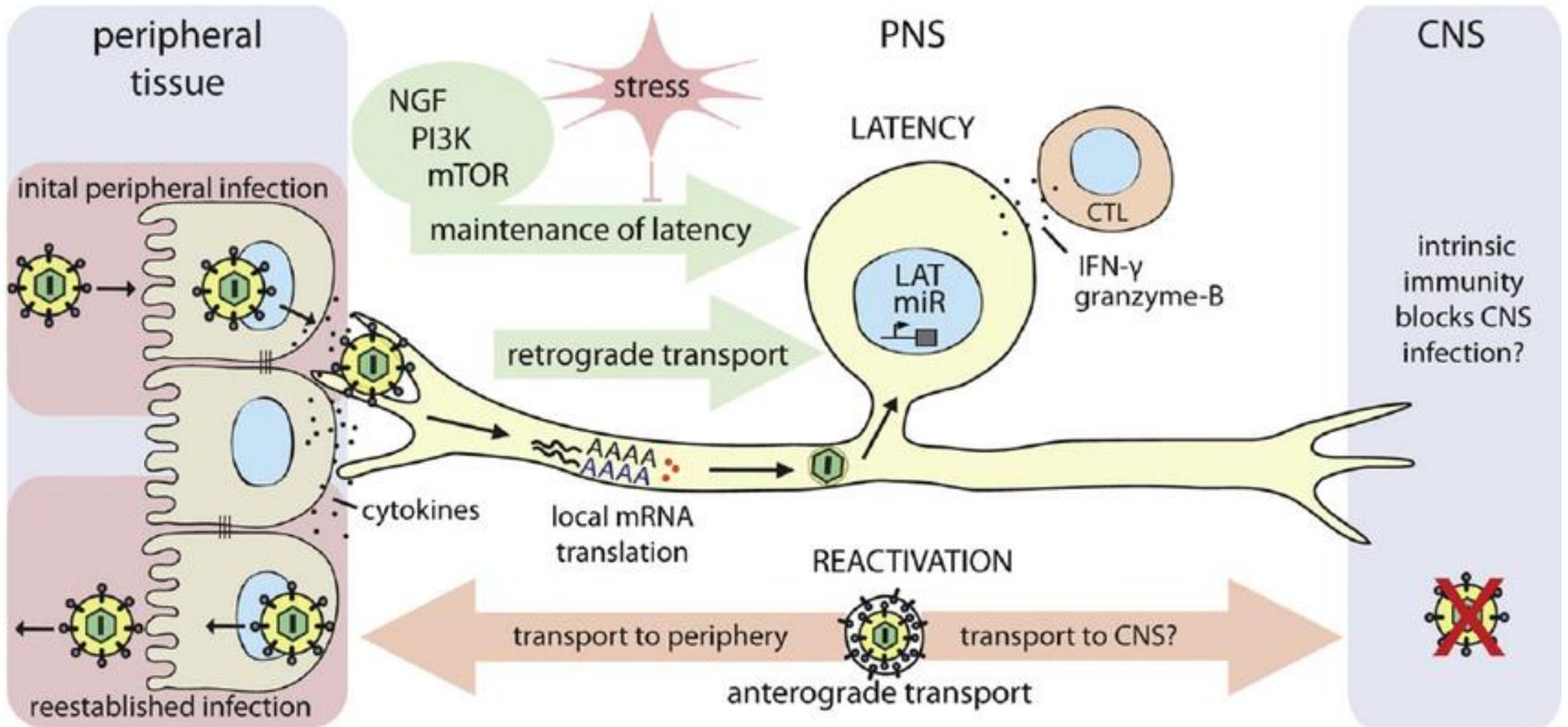
Transmission

- BHV-1 infections are widespread in the cattle population. IBR is a highly contagious and infectious viral disease that affects cattle of all ages.
- Infection occurs by **inhalation** and **requires contact** between animals spreading quickly through the group.
- Transmission can occur in the absence of visible lesions and through artificial insemination with **semen** from subclinically infected bulls.
- Milk
- Cattle with latent BHV-1 infections generally show no clinical signs when the virus is reactivated, but they serve as a source of infection for other susceptible animals.

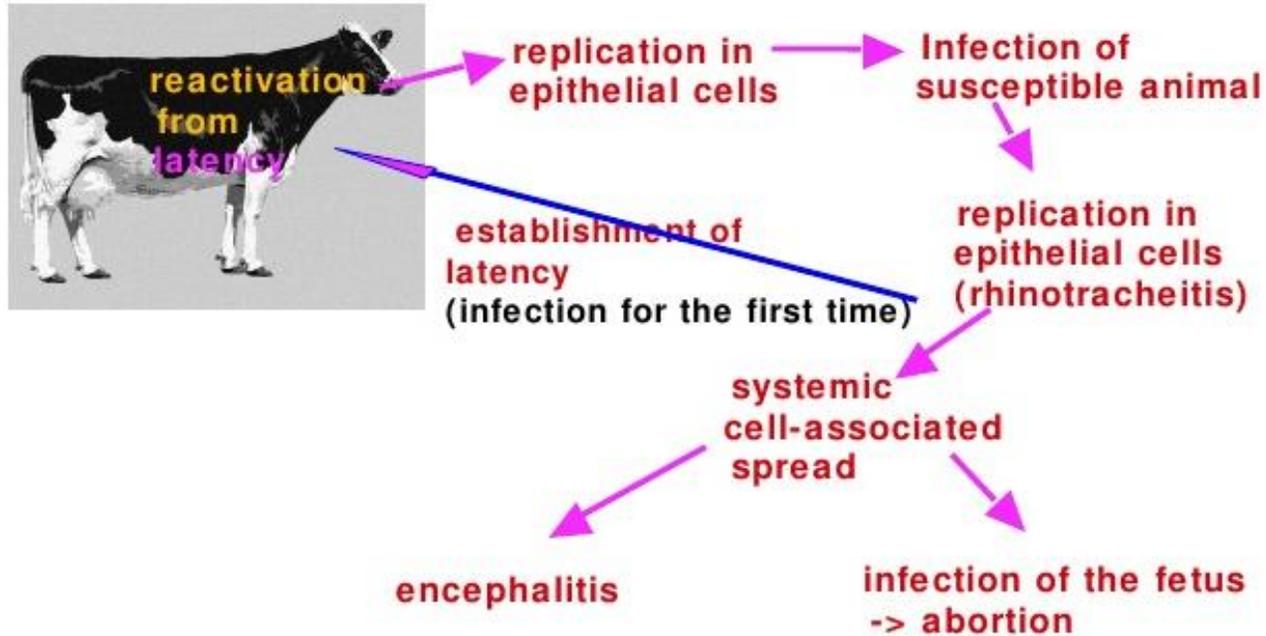
- In feedlot cattle, **the respiratory form is most common.**
- The viral infection alone is not life-threatening but predisposes to secondary bacterial pneumonia, which may result in death.
- In breeding cattle, **abortion or genital infections are more common.**
- Genital infections can occur in bulls (infectious pustular balanoposthitis) and cows (IPV) within 1–3 days of mating or close contact with an infected animal.

★ Pathogenesis

- The virus enters the animal **via the respiratory route** and replicates at high titers in mucous membranes of the upper respiratory tract and in the tonsils.
- It then spreads to the conjunctiva and **reaches the trigeminal ganglion** via neuronal axonal transport.
- **After genital infection**, BHV-1 replicates in the mucous membranes of the vagina or prepuce and becomes **latent in sacral ganglia**.
- **The viral DNA remains in the neurons of the ganglia for the entire life of the host.**
- Stress, such as transport and parturition, can induce reactivation of the latent infection. Consequently, the virus can spread intermittently into the environment.

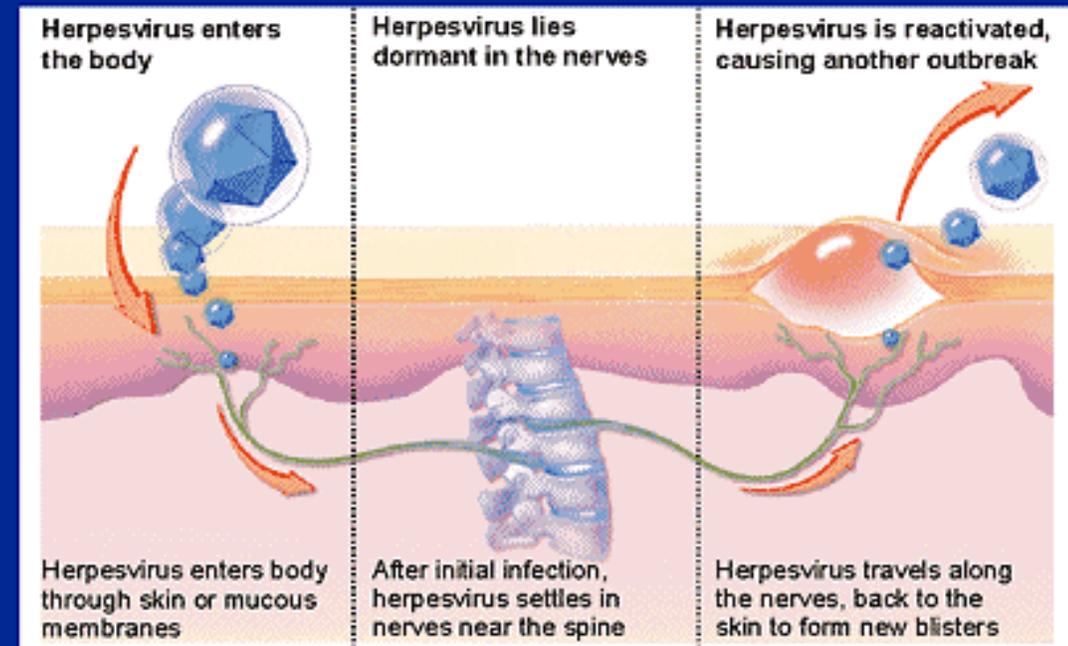


Infection in the animal



Once infected, animals become lifelong carriers of the virus.

Pathway of a Herpes Infection



Clinical Signs

A. Respiratory infection

- Fever (40°–42°C),
- depression,
- decreased feed intake,
- increased respiratory rate,
- cough,
- nasal and lacrimal discharge are common.
- Dyspnea, possibly with open-mouthed breathing, may become pronounced in the later stages of the disease.
- Subcutaneous emphysema may occur.
- Secondary bacterial pneumonia is a frequent occurrence.
- **Abortion** as a complication of the respiratory form of BHV-1 infection has been frequently reported in North America and Europe.



Suspected IBR in a recently purchased Charolais bull. The bull was febrile (41.5°C). The lungs were also scanned to check for chronic suppurative pneumonia.





B. Genital infection

- Genital infection with BHV-1 occurs in both sexes and is a more frequent manifestation of this herpesvirus infection in cattle on pasture.
- The infection may result in the development of vesicles, pustules and erosions or ulcers in the mucosa of the vulva and vagina or on the penis and prepuce.

1. Vulvovaginitis

This painful condition, which is known as infectious pustular vulvovaginitis (IPV), may be observed within a few days of mating.

- Frequent urination and tail lifting are the first clinical signs.
- There may be hyperaemia or oedema of the vulva and the posterior third of the vagina.
- Small red to white ulcers develop into pustules (0.5–3 mm in diameter).
- There may be a thick yellow or white mucopurulent exudate, especially in cases complicated by secondary bacterial infection.



2. Balanoposthitis

The disease in bulls is known as infectious pustular balanoposthitis (IPB).

After a 2–3 days incubation period, pustules appear on the mucosal surface of the penis and prepuce.

These pustules can progress to ulcers with a mucopurulent discharge and may prevent a bull from serving.

A proportion of infected bulls will also excrete virus in their **semen**. In turn, infected semen can infect susceptible females, **by natural or artificial insemination**.



C. Conjunctivitis

- The conjunctival form of BHV-1 infection, which resembles 'pink eye', is relatively uncommon.
- There can be occasional involvement of the cornea, and a panophthalmitis.
- In some cases, the only sign of infection is conjunctivitis.



IBR with severe palpebral congestion

Immunology

- An infection normally elicits an antibody response and a cell-mediated immune response within 7–10 days.
- The immune response is presumed to persist for life, although it may fall below the detection limit of some tests.
- Maternal antibodies are transferred via colostrum to the young calf, which is consequently protected against BHV-1-induced disease.
- Maternal antibodies have a biological half-life of about 3 weeks but may be detected occasionally in animals up to 9 months old, and rarely in animals over this age.

Diagnosis

- Uncomplicated BHV-1 infections can be diagnosed based on the characteristic signs and lesions.
- Samples should be taken early in the disease, and a diagnosis should be possible in 2–3 days.
- A rise in serum antibody titer also can be used to confirm a diagnosis. It is not possible to detect a rising antibody titer in abortions, because infection generally occurs a considerable length of time before the abortion, and titers are already maximal.
- BHV-1 abortion can be diagnosed by identifying characteristic lesions and demonstrating the virus in fetal tissues by
 - PCR,
 - virus isolation,
 - Immunoperoxidase
 - fluorescent antibody staining.

Prevention and Control

- Immunization with **modified-live or inactivated** virus vaccines generally provides adequate protection against clinical disease.
- Both IM and intranasal modified-live vaccines are available, but the IM types may cause abortion in pregnant cattle.
- The intranasal vaccines can be used in pregnant cattle.
- Only inactive vaccines are used in our country.





- There are a variety of effective IBR vaccines available, including **MARKER VACCINES** that allow vaccinated animals to be distinguished from naturally infected ones (**DIVA**) on serology tests.
- To aid in eradication, **deletion mutant vaccines** have been developed that permit discrimination between antibody produced in response to the vaccine and antibody produced in response to natural exposure.

Differential test for marker vaccinated and IBR positive cow

1. IBR infected cow



Test: Y=anti gB
Y=anti gE

2. Traditional vaccine



Test: Y=anti gB
Y=anti gE

3. Bovilis IBR marker



Test: Y=anti gB

Y= Antibodies • gB and gE= Proteins on surface of virus

DIVA

means differentiating
infected from vaccinated
animals

gE(-) marker vaccine

This vaccine is obtained by deletion mutant of the glycoprotein E-encoding gene.

This gene is responsible for pathogenicity and is not essential for virus replication.



virus



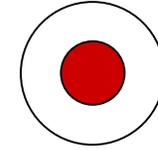
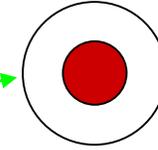
Vaccine virus

Marker aşı ile aşılama;

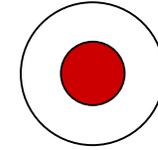
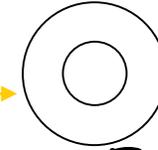
gE(-) marker aşı ile aşılama sonrasında serumda gE dışında tüm glikoproteinlere karşı antikor tespiti mümkündür.



Antikor ELISA



enfekte

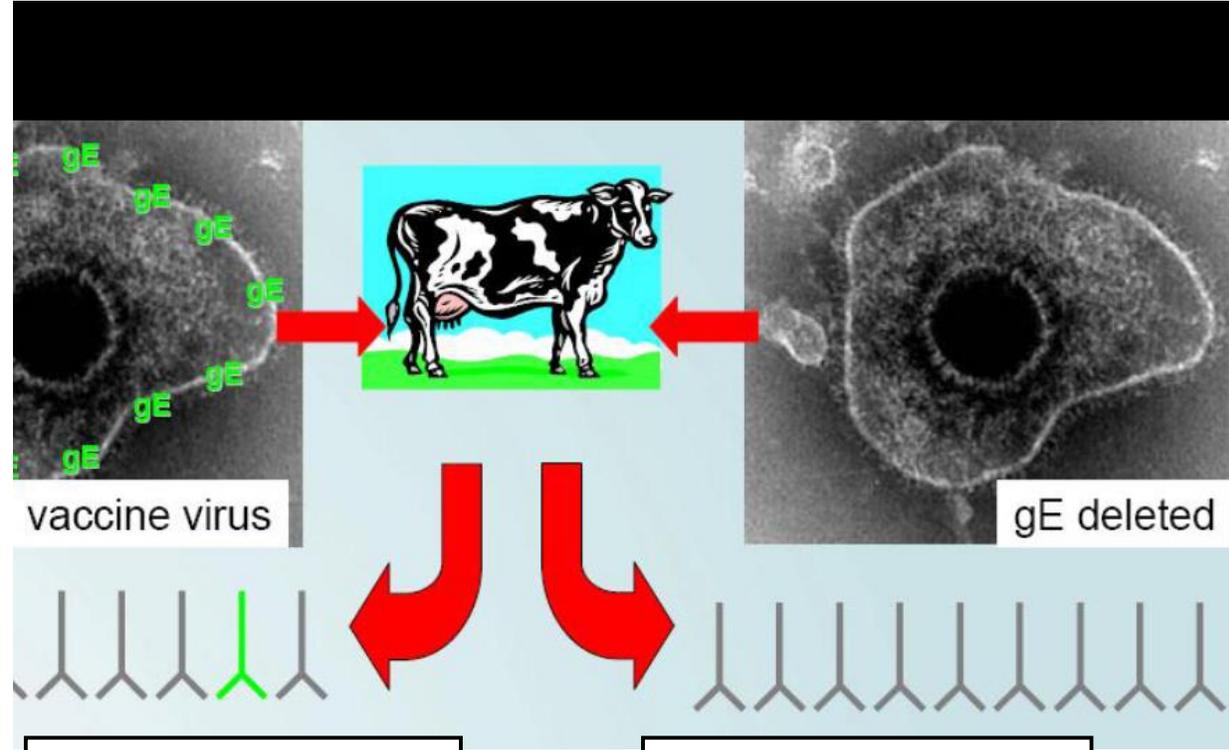


aşılı

gE

gB

Antikor pozitif hayvanlar



gE'ye karşı ab pozitif

gE'ye karşı ab negatif

Konvansiyonel aşılı ya da enfekte

marker aşısı ile aşılı

- IBR vaccination is inexpensive, either by single intranasal or intramuscular injection and is incorporated into veterinary herd plans.
- Elimination of the virus from closed herds is possible with testing and vaccination.
- Eradication of the virus is possible by a combination of
 - serologic surveillance,
 - culling of reactors,
 - biosecurity,
 - vaccination.
- Some European countries have eradicated IBR and exports to these countries require a negative test for the virus.

References

- <http://www.msdkvetmanual.com/respiratory-system/respiratory-diseases-of-cattle/viral-respiratory-tract-infections-in-cattle#v3293459>
- CHAPTER 2.4.13. INFECTIOUS BOVINE RHINOTRACHEITIS/
INFECTIOUS PUSTULAR VULVOVAGINITIS OIE Terrestrial
Manual 2008
- <http://www.nadis.org.uk/bulletins/ibr.aspx>

Bovine Herpesvirus 4

- Gammaherpesvirinae
- dsDNA
- Bovine herpesvirus 4 (BHV-4) has been called 'passenger' virus by some authors, because it causes mainly subclinical disease.
- BHV-4 infection is associated with cattle diseases of the genital tract, such as vulvovaginitis, post-partum metritis and abortion.

- The range of species susceptible to BHV-4 is quite broad. Among ruminants, American bison, African buffalo, sheep and goats support natural or experimental infection with BHV-4.
- BHV-4 has also been isolated from lions and from cats.

Systems Affected;

BHV-4 is transmitted directly and indirectly through infected material, including **genital secretions**, especially **respiratory secretions** of infected animals.

- **mammary gland diseases of large ruminants**
 - **reproductive diseases of large ruminants**
 - **reproductive diseases of small ruminants**
-
- BHV-4 infection is worldwide distributed, but the seroprevalence varies from 4 % in Switzerland to 50 % in northern Italy.

Pathology

- Except for the defined role of BHV-4 in genital diseases,
 - It may be speculated about its contribution to other pathologies. BHV-4 was designated as 'passenger' virus when it was isolated from ethmoidal tumours in Indian cattle.
- The virus replicates within mucosal cells and then invades the mononuclear cells, causing generalized infection and crossing the placenta to infect the unborn fetus.
- Indeed, the virus infects mononuclear blood cells and this feature allows it to be distributed in the whole body.
- In primary infection and during reactivation phases of the latent state, BHV-4 can be re-isolated from virtually all bovine tissues and organs. It is therefore very hard to discriminate between a 'by chance' isolation and a direct role of the virus in the observed lesions.

Clinical Signs

- BHV-4 can cause **abortion and births of weak or dead lambs, calves and kids**. It can also increase the incidence of **retained fetal membranes**.
- In dairy cattle, BHV-4 can cause **mastitis** and associated udder lesions and milk changes.
- The virus has also been isolated from cases of **conjunctivitis and respiratory disease** in calves, but it is unclear and somewhat doubtful whether it was the responsible pathogen in these cases. **The respiratory route is however the main route of transmission of the virus.**
- As with all **herpesviruses**, BHV-4 can **undergo latency, often residing in the trigeminal ganglia** similar to BHV-1 (IBR) and **re-emerging with stress** and/or immunosuppression.
- **Recovered cattle often become latent carriers.** In endemic BHV-4 areas, both acute and latent infections are quite common.

Diagnosis

- BHV-4 can be **isolated from nasal or vaginal secretions** or from organs from cows at necropsy.
- Viral DNA can be detected by **PCR**.
- Antibodies to BHV-4 can be detected using **ELISA and Indirect Immunofluorescence**. Immunoperoxidase assays are also available.
- It must always be considered that presence and positive identification of BHV-4 does not mean that it is responsible for the observed disease.

Control

- **Exclusive use of hygienic measures** can gain control of BHV-4. Seropositive animals should be removed wherever possible due to the high likelihood that they are latent carriers of disease. Infected cows that calve should be isolated approaching and following parturition, as **huge quantities of virus are shed in uterine exudates**.
- **Vaccines were developed in the USA** but are not widely used.

References

- <https://www.cabi.org/isc/datasheet/91709>
- https://en.wikivet.net/Bovine_Herpesvirus_4
- Fabricant CG; Gillespie JH; Krook L, 1971. Intracellular and extracellular mineral crystal formation induced by viral infection of cell cultures. *Infection and Immunity*, 3:416-419.
- [Kruger JM; Osborne CA; Goyal SM; Pomeroy KA; O'Brien TD, 1990. Clinicopathologic and pathologic findings of herpesvirus- induced urinary tract infection in conventionally reared cats. *American Journal of Veterinary Research*, 51\(10\):1649-1655; 27 ref.](#)
- Thiry E; Bublot M; Dubuisson J; Pastoret PP, 1989. Bovine herpesvirus 4 (BHV-4) infections of cattle. In: G. Wittmann, ed. *Herpesvirus diseases of cattle, horses, and pigs*. Kluwer Academic Publishers, Norwell, 96-115.

Equine Herpesvirus Infection

(Equine viral rhinopneumonitis, Equine abortion virus)

Etiology

- Equine herpesviruses (EHV) Alphaherpesviridae
- enveloped
- double stranded DNA viruses
- There are 5 alpha herpesviruses that infect horses
 - EHV-1, 2, 3, 4, and 5.
- we will focus on EHV-1 and EHV-4, which are the two that result in serious clinical disease in the horse.

- Equine herpesvirus 1 (EHV-1) and equine herpesvirus 4 (EHV-4) comprise two antigenically distinct groups.
- The two most significant are
 - EHV-1, which causes respiratory disease, abortion, and neurologic disease
 - EHV-4, which primarily causes respiratory disease and only occasionally can cause abortion or neurologic disease.

- Both viruses are ubiquitous in horse populations worldwide and produce an **acute febrile respiratory disease** upon primary infection, characterized **by rhinopharyngitis and tracheobronchitis**.
- Outbreaks of respiratory disease occur annually among foals in areas with concentrated horse populations.
- The age, seasonal, and geographic distributions vary and are determined by immune status and horse population.
- In individual horses, the outcome of exposure is determined by viral strain, immune status, pregnancy status, and possibly age.
- **Infection of pregnant mares with EHV-4 rarely results in abortion.**

- Mares may abort several weeks to months after clinical or subclinical infection with EHV-1.
- The neurologic form of EHV-1 has demonstrated increasing morbidity and mortality and appears to be evolving in virulence and behavior.
- The natural reservoir of both EHV-1 and EHV-4 is the horse.
- Latent infections and carrier states are seen with both virus types. Transmission occurs by direct or indirect contact with infectious nasal secretions, aborted fetuses, placentas, or placental fluids.

Transmission

Respiratory transmission (most common route of exposure)

- Inhalation of droplets from coughing and snorting.
- Mares which have aborted, or whose foals have died, can transmit infection via the respiratory route.
- Shedding by the respiratory route typically lasts for 7-10 days, but can be much longer.
- Therefore, based on a thorough risk analysis of the particular outbreak or case, a period of 14 to 28 days after resolution of clinical signs may be necessary before release from movement restrictions/isolation.

Direct transmission

- Aborted fetuses, fetal membranes and/or fluids are significant sources of the virus.
- Infected foals are highly contagious and can transmit infection to other horses via the respiratory route through shedding virus into the environment.

Indirect transmission

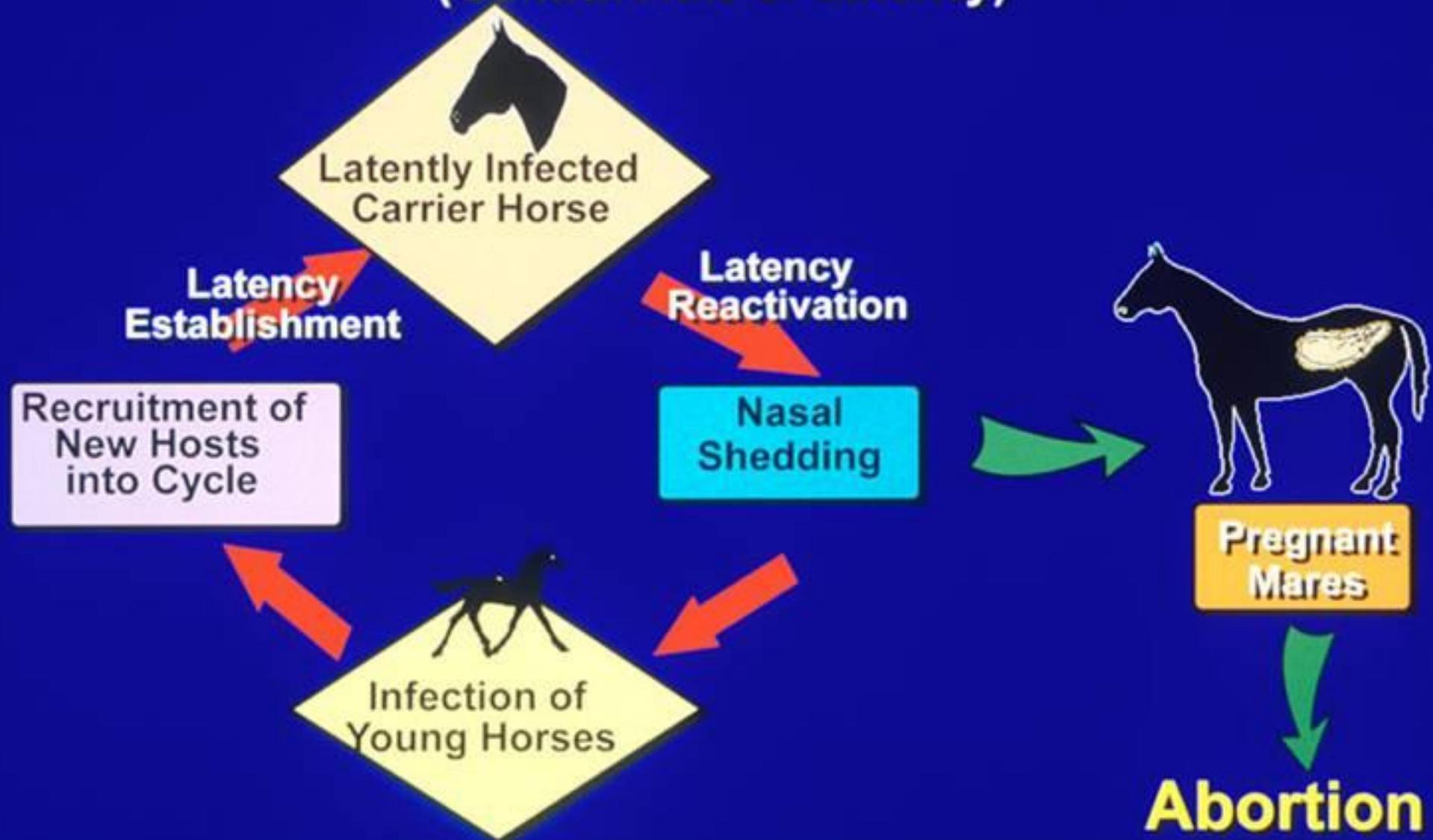
- Virus can be viable for several weeks in the environment once it has been shed by the horse.
- Virus contaminated fomites are a significant factor in transmission.

Also, following infection, horses may become latent carriers of EHV; virus may be reactivated after stress or high doses of corticosteroids.

Pathogenesis

- The pathogenetic mechanisms of EHV-1 and EHV-4 differ significantly.
- **EHV-4 infection** is restricted to respiratory tract epithelium and associated lymph nodes;
- **EHV-1** strains develop cell-associated viremia and have a predilection for vascular endothelium, **especially the nasal mucosa, lungs, placenta, adrenal, thyroid, and CNS.**
 - The neuropathic strain of EHV-1 produces a viremic load 10- to 100-fold higher than that of non-neuropathic strains.

Life Cycle of EHV-1 (Central Role of Latency)

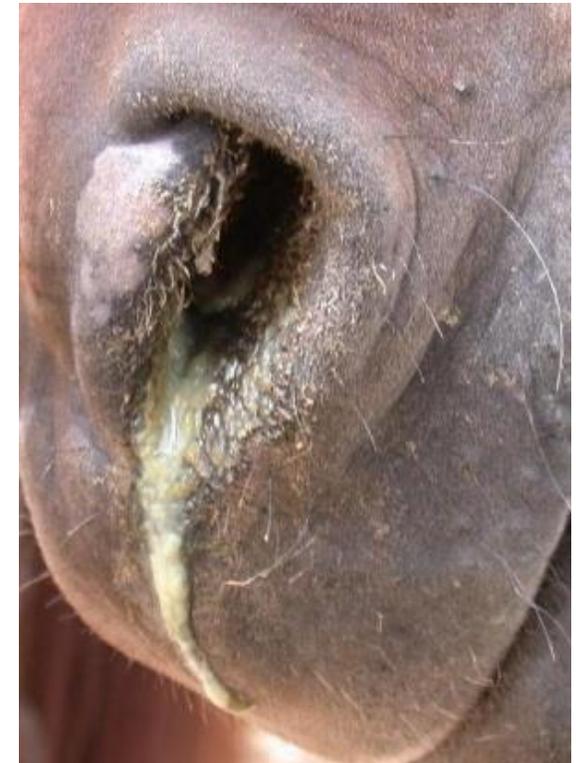


Clinical Signs

- The incubation period (period of time from exposure to development of first clinical signs) ranges from 2 to 10 days.
- **Fever** is often biphasic and can be transient.
 - The initial febrile phase precedes infection of the upper respiratory tract. The second febrile phase (6-7 days) often precedes a systemic viremia. Fever may go undetected and may be the only clinical sign noted in an infected horse. Temperature monitoring twice a day is recommended.

Respiratory disease

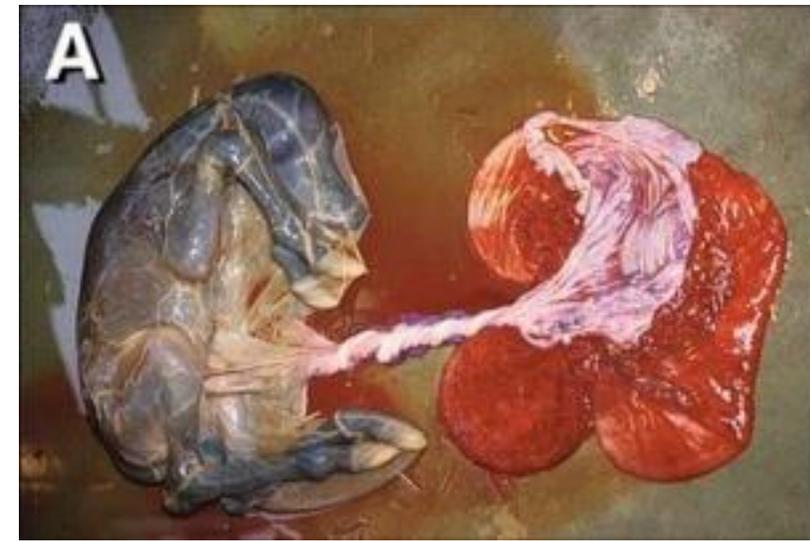
- Fever (38.9-41.7°C)
- Coughing
- Nasal discharge
- Variable enlargement of the mandibular and/or retropharyngeal lymph nodes
- Lethargy, anorexia
- Conjunctivitis
- Ocular disease including uveitis and keratitis
- **Neonatal foals** infected in utero are usually abnormal from birth and exhibit any combination or all of the following:
 - o Fever
 - o Lethargy
 - o Weakness
 - o Jaundice
 - o Respiratory distress/stridor/pneumonia
 - o CNS signs (occasionally)
 - o Death commonly occurs within 3 days.
- **Older foals:** nasal discharge is the most common sign of disease.



Abortion

- Most often, no warning signs of impending abortion in the mare.

Typically occurs in late pregnancy (7+ months); very occasionally as early as 4 months.



Neurologic disease

- Incoordination of the hind (and occasionally fore) limbs :
- Ataxia or wobbly gait
- Urine retention/dribbling
- Bladder atony
- Recumbency with inability to rise
- Neurologic signs are often preceded by fever and/or respiratory signs

Sponsored by Pfizer

Neurologic EHV-1

BY KIMBERLY S. HERBERT

Continuing research offers hope that soon we'll understand how the terrifying neurologic EHV-1 disease occurs, and what to do to prevent it

Equine herpesvirus-1 (EHV-1) causes many problems, including abortion, respiratory disease, neurologic disease, death in newborn foals, and a newly recognized syndrome described as peracute pulmonary vasculitis of adult horses (which strikes adult horses in their lungs and kills them almost overnight).

Neurologic disease caused by EHV-1 has been recognized for many years. However, in recent years there has been an increase in the number of EHV-1 neurologic cases worldwide. No one knows why.

This particular disease is one that's especially of concern because it has the potential for causing devastating outbreaks and

for shutting down much of the industry, especially the racing industry.

In April 2005, an unusual press announcement was released by George Allen, PhD, head of the Office International des Epistasies (OIE) reference laboratory for equine herpesvirus located at the University of Kentucky's Gluck Equine Research Center, and his British research colleagues. They bypassed the long wait for a scientific journal publication to let the horse industry know that the neurologic form of EHV-1 was caused by a mutation in the virus strain, and the mutation could be detected by laboratory tests.

Allen and Nicholas Davis Pevsner, PhD,



This horse is showing classic hind end neurologic signs ("flag sitting") with EHV-1.

head of equine infectious diseases at the Animal Health Trust in Newmarket, England, stated, "We have developed methods to identify genetic differences between strains of EHV-1 circulating in the field. Isolates of EHV-1 recovered from over 100 outbreaks of abortigenic (abortion-causing) or neurologic disease in several countries around the world over the past 40 years have been examined. Some of the strains are unique to North America and others to the European continent."

The strain-typing method was used to verify transmission of infection between outbreaks of EHV-1 neurologic disease in different locales. An important observation from the studies was the discovery that a mutation within a single EHV-1 gene is associated with strains of the virus recovered from neurological cases.

Current research is directed at determining the effects of the mutation in this gene (viral DNA polymerase gene) on the biological and pathological properties of the virus. Alteration of the viral enzyme's replicative efficiency would explain many of the properties unique to paralytic strains of EHV-1, such as their increased replicative vigor (they multiply faster), ability to cause a log (tenfold) greater magnitude of post-infection viremia in the horse (much more virus circulates in the horse's body and can be shed), enhanced capacity to infect cells of the central nervous system, and

A neurologic case (as seen here) can reveal variable signs, with the most common being hind limb weakness and incoordination that can progress to recumbency (ability to rise).



Equine Herpes Virus (EHV): Viral abortion can occur from 4 months to full term pregnancy, but most commonly from the eight-month stage onwards

EHV 1 and 4

real time PCR (qPCR) is more sensitive than conventional PCR.

A commercial ELISA test kit, suitable for use in practice, is available for detection and differentiation of EHV-1 and EHV-4 specific antibodies directed against viral glycoprotein gG

Sample	Test	Shipping	Handling
Nasopharyngeal Swab and EDTA or citrated blood Both blood and NP swab should be tested together	EHV 1 or 4 PCR; Viral Isolation	PCR testing send swab in plain red top tube; for viral isolation place swab in viral transport media or red top tube with a few drops of sterile saline	Chilled overnight
Sera	EHV 1 and 4 Serum neutralization (SN)	Leak proof container	Chilled overnight
Sera	CF	Not available in US	Chilled overnight
Sera	ELISA* Differentiation of EHV 1 from 4	Leak proof container	Chilled overnight
	* specific antibodies directed against viral glycoprotein gG (Svanovir™)		

Immunology

Immunity after natural infection with either EHV-1 or EHV-4 involves a combination of humoral and cellular immunity.

- Whereas **little cross-protection** occurs between virus types after primary infection of immunologically naive foals, **significant cross-protection** develops in horses after repeated infections with a particular virus type.
- Most adult horses are latently infected with EHV-1 and EHV-4.
- The infection remains dormant for most of the horse's life, although stress or immunosuppression can lead to re-emergence of the disease and shedding of infectious virus.
- Immunity to reinfection of the respiratory tract may persist for as long as 3 mo, but multiple infections result in a level of immunity that prevents clinical signs of respiratory disease.
- Decreased resistance in pregnant mares allows cell-associated viremia, which can result in transplacental infection of the foetus.

Prevention and Control

For prevention and control of EHV-4– and EHV-1–related diseases, management practices that reduce viral spread are recommended.

- New horses (or those returning from other premises) should be isolated for 21 days before commingling with resident horses, especially pregnant mares.
- Management-related, stress-inducing circumstances should be avoided to prevent recrudescence of latent virus.
- Pregnant mares should be maintained in a group away from the weanlings, yearlings, and horses out of training.
- In an outbreak of respiratory disease or abortion, affected horses should be isolated and appropriate measures taken for disinfection of contaminated premises.
- No horse should leave the premises for 3 wk after recovery of the last clinical case.

- **Vaccination** (EHV-4 and EHV-1) should begin when foals are 4–6 mo old.
- A second dose is given 4–6 wk later, and a third dose at 10–12 mo of age. Booster vaccinations may be indicated as often as every 6 mo through maturity (5 yr of age).



- Vaccination programs against herpesviruses should include all horses that travel to high-risk destinations (racetrack, show grounds) and all other horses on the premises.
- A high-antigen load, inactivated EHV-1 vaccine is recommended to prevent EHV-1 abortion.
- Vaccine should be administered during months 3, 5, 7, and 9 of pregnancy.
- Mares are often vaccinated with inactivated EHV-1/EHV-4 at an interval 4–6 wk before foaling.
- A modified-live EHV-1 vaccine is available to help prevent respiratory disease caused by EHV-1.

References

- <https://ahdc.vet.cornell.edu/docs/EquineHerpesvirusFinal030513.pdf>
- <http://animalscience.uconn.edu/extension/publications/herpesvirus.htm>
- <http://www.msdivetmanual.com/respiratory-system/respiratory-diseases-of-horses/equine-herpesvirus-infection>

BOVINE MAMILLITIS
BOVINE ULSERATIF MAMILLITIS
PSEUDO LUMPYSKIN DISEASE

Bovine herpesvirus 2 (BHV-2) is the causative agent of two diseases.

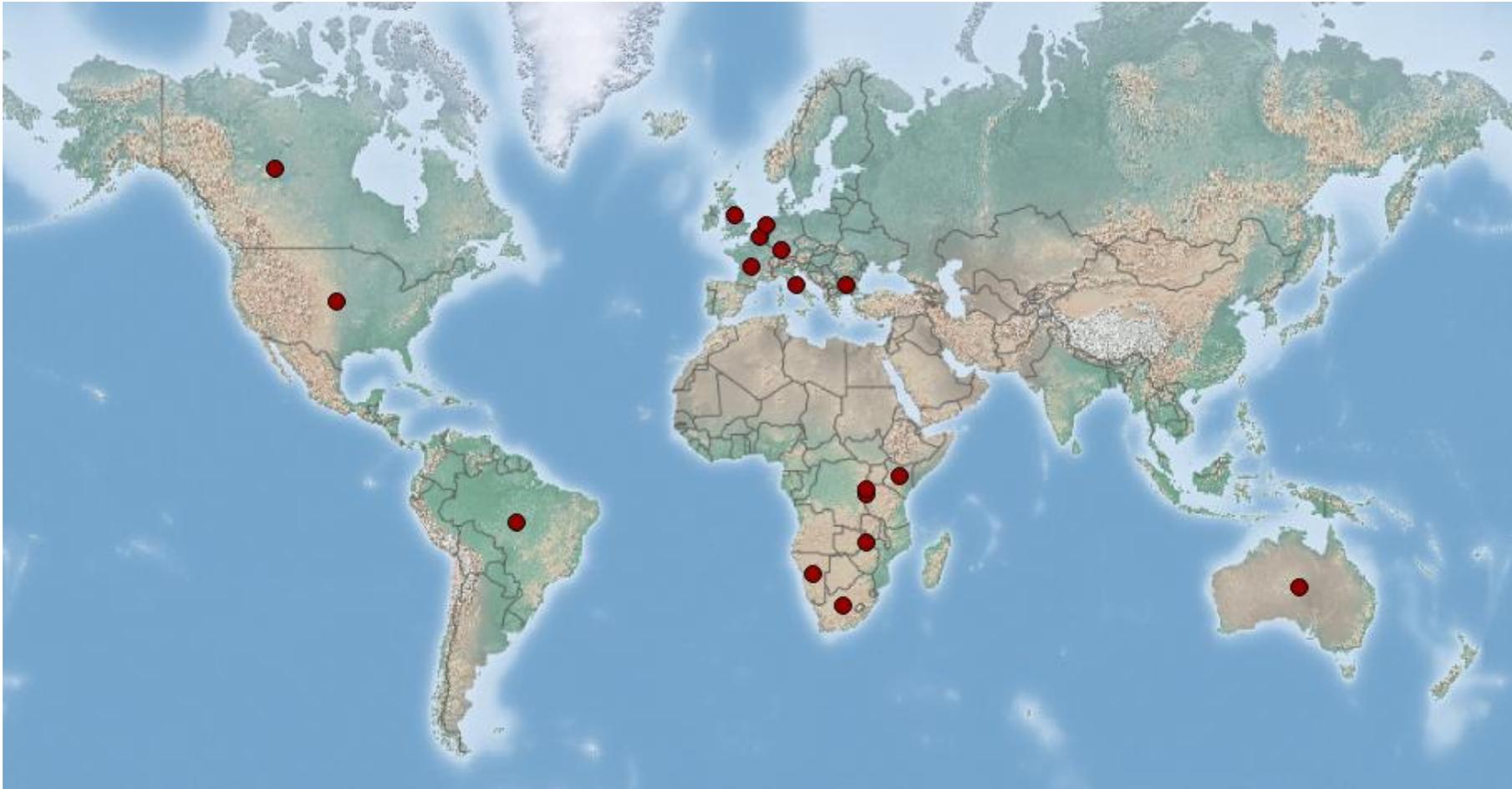
I. The first is localized in the udder and called **bovine herpes mammillitis**.

II. The second is a **generalized cutaneous form** named Allerton disease or **pseudo-lumpy skin disease**, due to its similarity with the capripoxvirus infection causing lumpy skin disease.

Etiology

- Alphaherpesvirinae
- BHV-2
- It is serologically one type
- Antigenically close with human herpes viruses (herpes simplex 1 and 2).
- Virus forms roundness, lysis, and intranuclear inclusions in bovine cells.

- Cattle and buffalo are natural hosts of BHV-2. Sheep and goats can be experimentally infected and develop local lesions



- BHV-2 can occur sporadically or in outbreaks that often have a seasonal association with cold weather and may result in reduced milk production and increased susceptibility to bacterial mastitis.
- The generalized form is often seen in South Africa, summer and autumn. Arthropods are also thought to transmit the virus. However, vector identification was not performed.
- Mamillitis form, milking machines is the most important reason.
- Arthropods have also been reported to be transmitted.
- Outbreaks are associated with the introduction of subclinically infected animals into the herd.

Clinical Signs

➤ Bovine herpes mammillitis

- The incubation period is 4 to 10 days.
- This disease is usually observed in dairy cows during the second part of the year and usually heifers in 2 to 10 days after calving. It can also be observed in bulls.
- The virus is transmitted directly from animal to animal and indirectly by contaminated material.
- Biting flies could also play a role in virus transmission.
- The lesions are localized on the teats, and rarely on the udder and perineum.
- The skin is swollen and translucent and some vesicles may be visible. The lesions appear blue or purple.
- Teats are generally painful, and affected cows often resist milking, leading to development of mastitis.
- They evolve as ulcers and resolve without complications within 4 weeks.
- Suckling calves may become affected, showing the same lesions on the lips, the nose and in the mouth.



➤ Pseudo-lumpy skin disease

- Pseudo-lumpy skin disease is a generalized and febrile disease.
- Circumscribed nodules suddenly appear on the skin of the whole body.
- These nodules are hard, palpable and circular.
- A slight depression is visible in their centre.
- After a few days, necrosis follows, the nodules evolve as ulcers and are covered by scabs.
- After 2 weeks, the lesions are resolved but leave areas provisionally devoid of hair.



<http://www.fao.org/docrep/003/t0756e/T0756E03.htm>

Diagnosis

Clinical diagnosis

Bovine herpes mammillitis is suspected when the characteristic lesions appear on the teats, especially in late summer and early winter.

The disease must be differentiated from pseudo-cowpox.

Pseudo-lumpy skin disease produces lesions very close to those induced by lumpy skin disease. However, the slight depression observed in the centre of the nodules is characteristic of pseudo-lumpy skin disease.

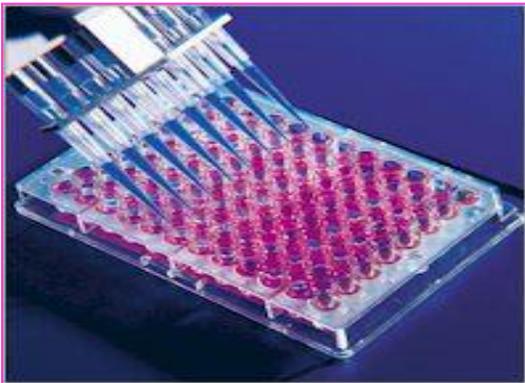
Laboratory

The virus can be isolated from the lesions, especially from vesicles when they are present.

The virus grows in most bovine cell lines, such as bovine embryonic kidney or testicle cells.

Serological diagnosis is achieved by seroneutralization.

Alternatively an ELISA can be performed for the detection of specific BHV-2 antibodies.



Prevention and Control

- No commercial vaccine against BHV-2 is available.
- Control is only performed during BHV-2 outbreaks, no preventative controls are used.
- Affected cows should be isolated from the herd and milked separately.
- The milking machine should be disinfected with iodophores, and insecticides should be used to eliminate biting flies.

References

- <https://www.cabi.org/isc/datasheet/91712>
- [Gourreau JM; Moussa A; Dubois A; Hermitte P; Delmache P; Fedida M; Guerrin R, 1989. Epidemic of ulcerative thelitis due to mammillitis herpesvirus in Haute-Marne. Point Vétérinaire, 21\(123\):633-635.](#)
- [Gourreau JM; Pauluzzi L, 1988. Bovine ulcerative mammillitis. Point Vétérinaire, 20\(114\):507-520; 143 ref.](#)
- Scott FMM, 1989. Bovine herpesvirus 2 infections. In: Wittmann G, ed. Herpesvirus Diseases of Cattle, Horse and Pigs. Massachusetts, USA:Kluwer Academic Publishers, 73-95.