PATHOGENESIS IN VIRAL INFECTIONS

- Viral pathogenesis covers the events that occur in the organism from the introduction of the virus into the organism until the disease occurs.
- Viral pathogenesis is the process by which a viral infection leads to disease.
- The outcome of viral infections depends on the interaction of a number of viral and host factors.

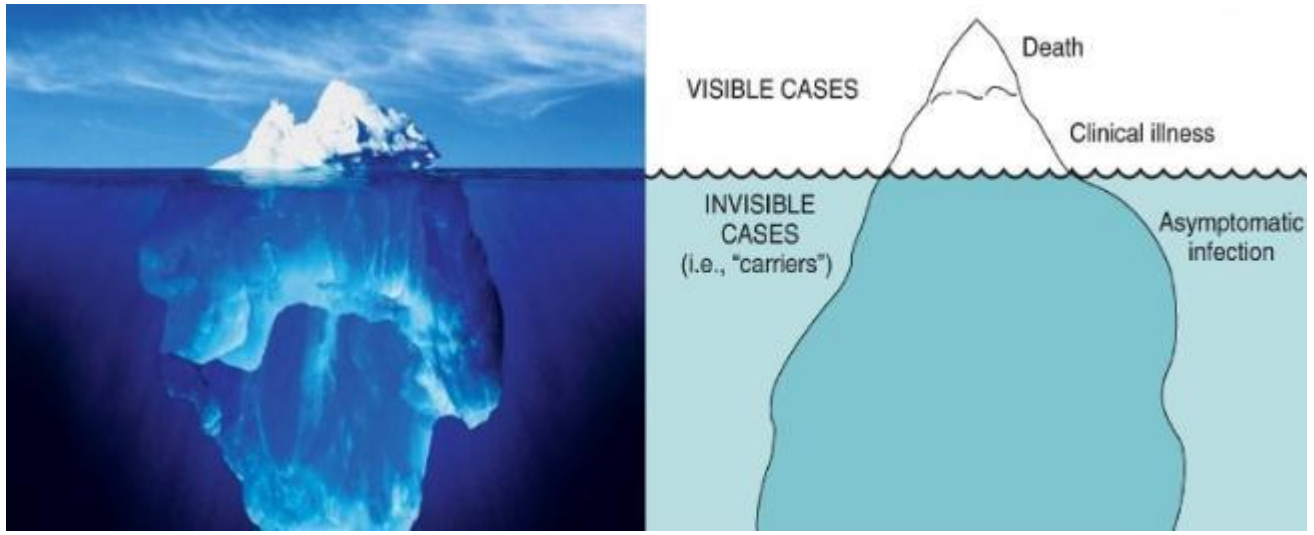
- Viral pathogenesis describes the processes by which viral infections cause disease and involves virus-host interactions at the cellular and systemic levels that determine whether a virus will cause disease, what form that disease will occur, and how severe the disease will be.

What's involved?

- How the pathogen enters the organism
- First site of replication
- The way it is disseminated in the organism
- Development of pathological changes and clinical symptoms (disease development)
- Shedding of the pathogen

Heise MT. Viral Pathogenesis. Reference Module in Biomedical Sciences. 2014:B978-0-12-801238-3.00079-9. doi: 10.1016/B978-0-12-801238-3.00079-9. Epub 2014 Nov 28. PMCID: PMC7157475.

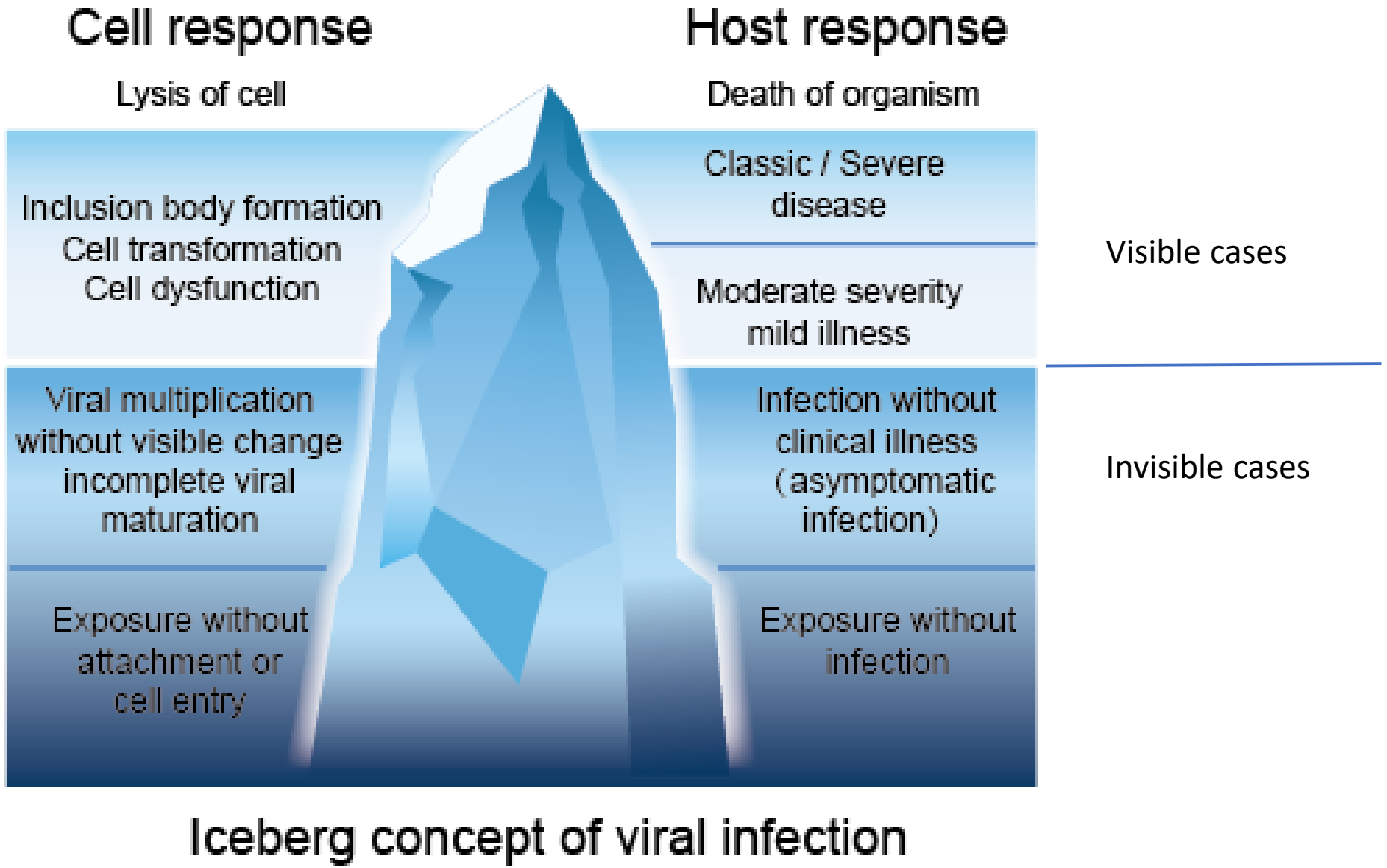
Iceberg concept of infection



- Not every disease is caused by an infectious agent and not every infection may have symptoms.
- Infection is necessarily caused by an agent (such as virus, bacteria, parasite).
- Disease can be explained as a condition that causes local or general condition disorder in the body.
  - The majority of interactions with virus do not result in infection.
    - Most infections are asymptomatic or sub-clinical.
  - Infections that cause mild symptoms may not be recognized.
    - Moderate symptoms may be classified as a disease.
  - Only severe symptoms are clearly recognized as a disease.

https://www.docplexus.com/posts/iceberg-phenomenon-of-disease

Eccles, Ronald. (2002). Acute Cooling of the Body Surface and the Common Cold. Rhinology. 40. 109-14.



Iceberg concept of viral infection

https://www.creative-diagnostics.com/Viral-Antigens.htm

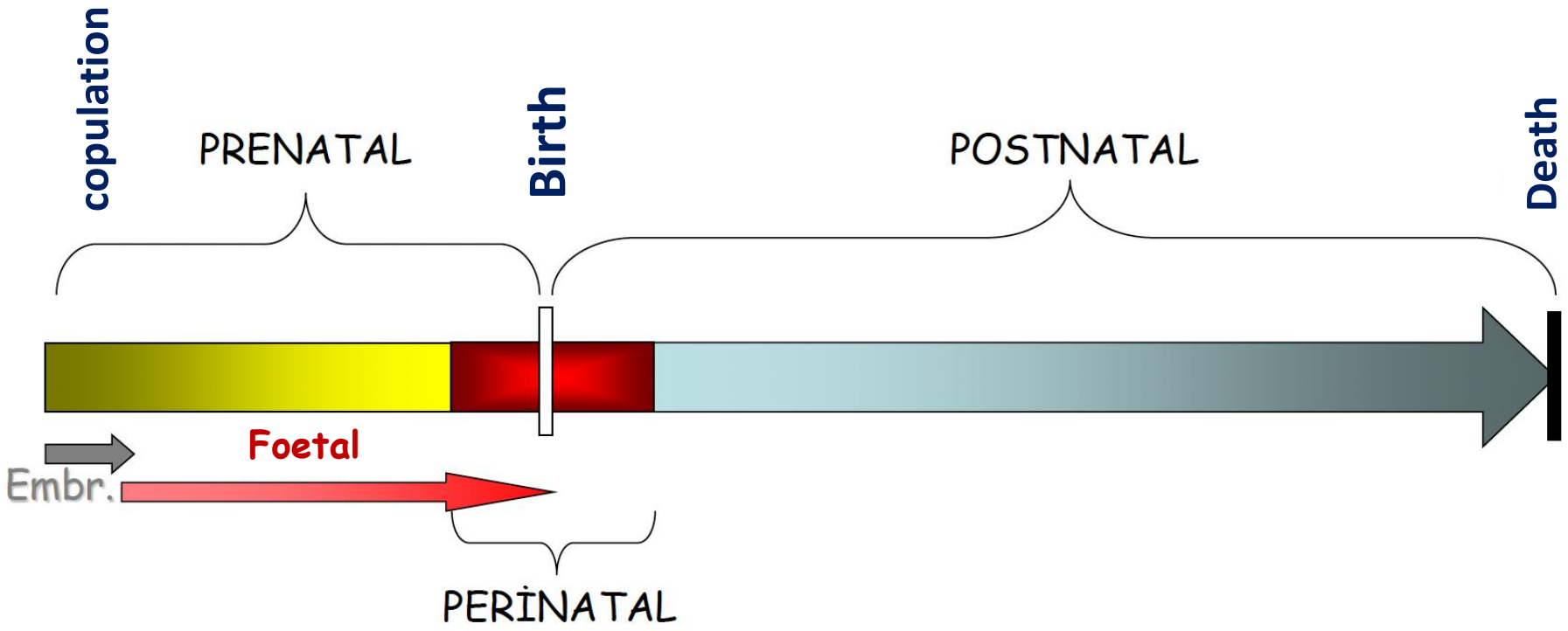
Several factors, both viral and host-related, play an important role in the development of disease. These factors can be summarised as follows:

- For disease to occur, a virus with sufficient amount and sufficient virulence (the ability of the microorganism to cause disease) must enter the body. Viruses that do not have sufficient quantity and virulence cannot cause disease because they cannot overcome the host's defence systems.
- If there are cells carrying their own receptors in the area they enter, viruses can only infect by binding to these cells. Otherwise, they are eliminated in a short time.
- Viruses may not cause disease when they enter the organism through routes other than their natural route of entry where they cause disease. For example, Influenzaviruses that enter the organism through the respiratory system do not cause disease when they enter through the blood.

- If the organism has already been exposed to the virus and has formed antibodies against the virus, it is resistant to infection with the same virus. In such animals, specific antibodies block the effect of the virus.
- Various genetic factors affect the development of virus infections. For example, some cat breeds are more susceptible to FIP infection. The factor that is effective in this is the difference of Major Histocompatibility (MHC) genes.
- Nutrition is very important in the occurrence of viral infections. Good nutrition is a factor that has a direct effect on the strengthening of the immune system.
- During the development of a viral infection, the patient's disease or the host's health affects the course of the infection. As immunosuppression develops in infected individuals, they become susceptible to infection. The incidence and severity of infection is greatly increased.

Periods of Exposure to An Infection

1. PRENATAL PERIOD (BEFORE BIRTH)
2. PERINATAL PERIOD (DURING BIRTH)
3. POSTNATAL PERIOD (AFTER BIRTH)



1. Prenatal Period Infections

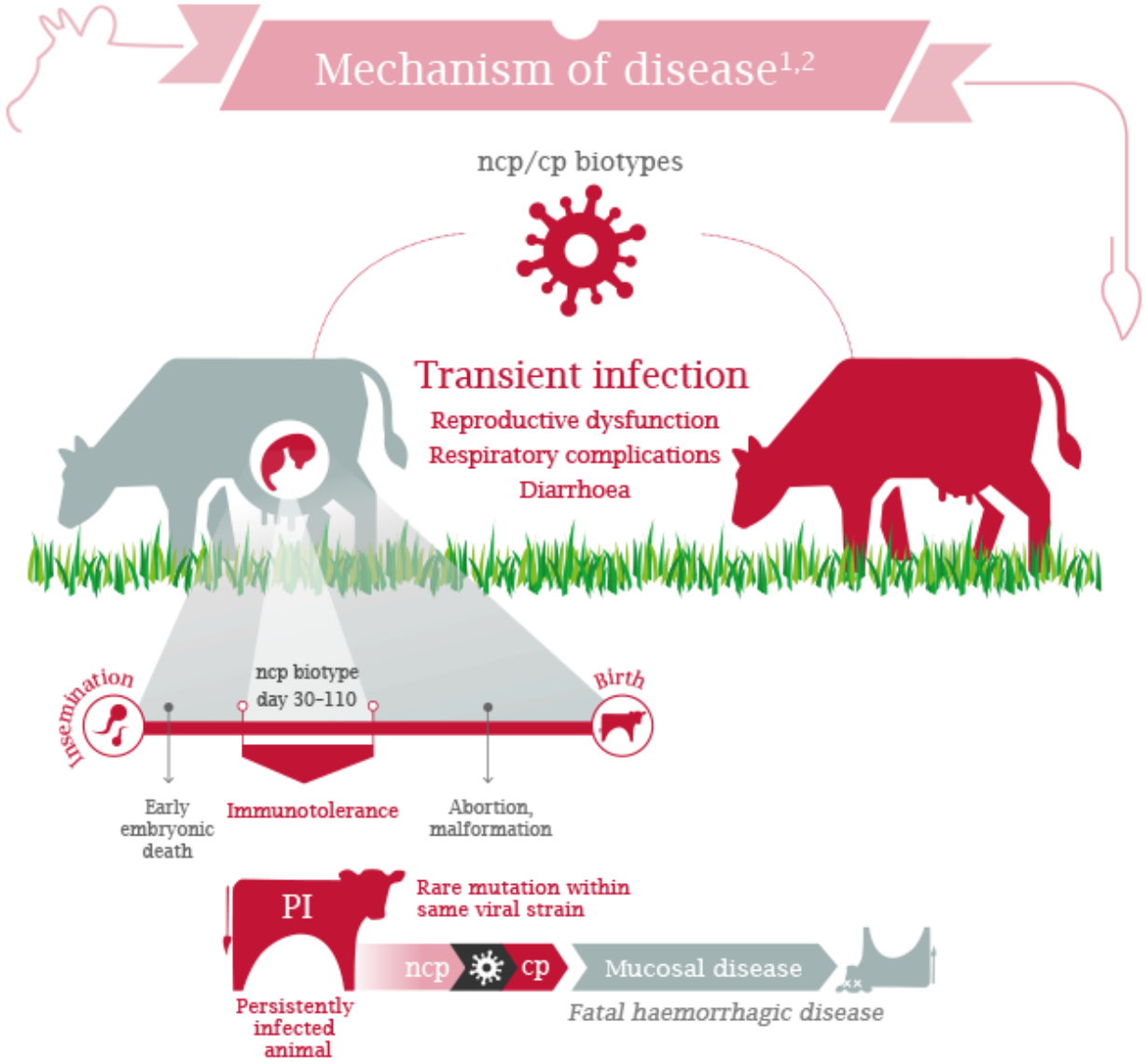
A. During copulation with germ cells

- Infected cells and virus particles adhere to the zona pellucidae.
  - For example, BVD virus with oocyte or IBR virus (BHV-1) with spermatozoon causes infection in this way.

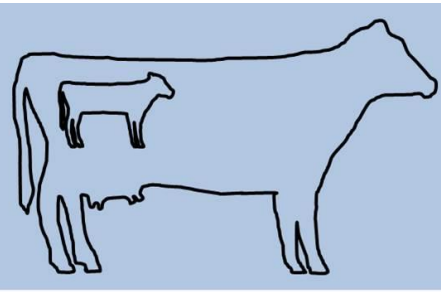
B. When maternal infections are transmitted to the embryo or foetus during pregnancy

1. Inutero (infections in the mucosa or walls of the uterus) BHV-1
2. Transplacental (through the placenta during maternal viremia) Bluetongue, Akkbane, BVDV

B. Example of transplacental (through the placenta during maternal viremia) transmission BVDV infection



How old is the calf foetus?



Months of pregnancy

0	1	2	3	4	5	6	7	8	9

Early embryonic death

Foetal death, the mother could abort

The calf could be born **Persistently infected**

The calf will be born sero-positive, producing antibody to BVD and **not** persistently infected

The calf could be born with congenital defects

https://www.pngegg.com/en/png-opuns
https://www.farmhealthonline.com/disease-management/cattle-diseases/bovine-viral-diarrhoea/

2. Perinatal Period Infections

- Infections that occur after the entry of the agent through the birth canal.

Transmission occurs during or before birth. These infections

1.Maternal Transmission

- With urine and faeces (CMV, BRV)
- Reactivated latent infections (Herpesvirus)

2.Iatrogenic Transmission (As a result of the use of infected materials)

3. Postnatal Period Infections

- Direct contact (Canine Distemper V)
- Inhalation (Aerosol) (IBR, Parainfluenza-3, Pox)
- Oral (Rotavirus, Enterovirus, BSE)
- Conjunctival (Herpesviruses)
- Urogenital (Papillomaviruses, HIV)
- Vectors (Bluetongue virus, Akabane virud, Bovine Ephemeral Fever V)
- Bite (Rabies, FeLV, FIV)
- Cutaneous (Herpes Simplex Virus (HSV), Vaccinia Virus
- Genital (IBR)
- Transfusion (HBV, HCV, HIV)

- For a virus to cause disease -after enters the body through various ways- it must spread to the target organs after primary replication.
  - Primary Replication–The place of primary replication is where the virus replicates after gaining initial entry into the host.
- In this way, viruses are divided into two groups:

I. They can cause infection locally at the site of entry.

- Firstly, the host starts to replicate in areas close to the site of entry into the body. Local infection may occur with primary replication. It can spread to the environment through faeces, body fluids, cough and re-infect susceptible hosts. For example, rotavirus infection.

II. Systemic spread.

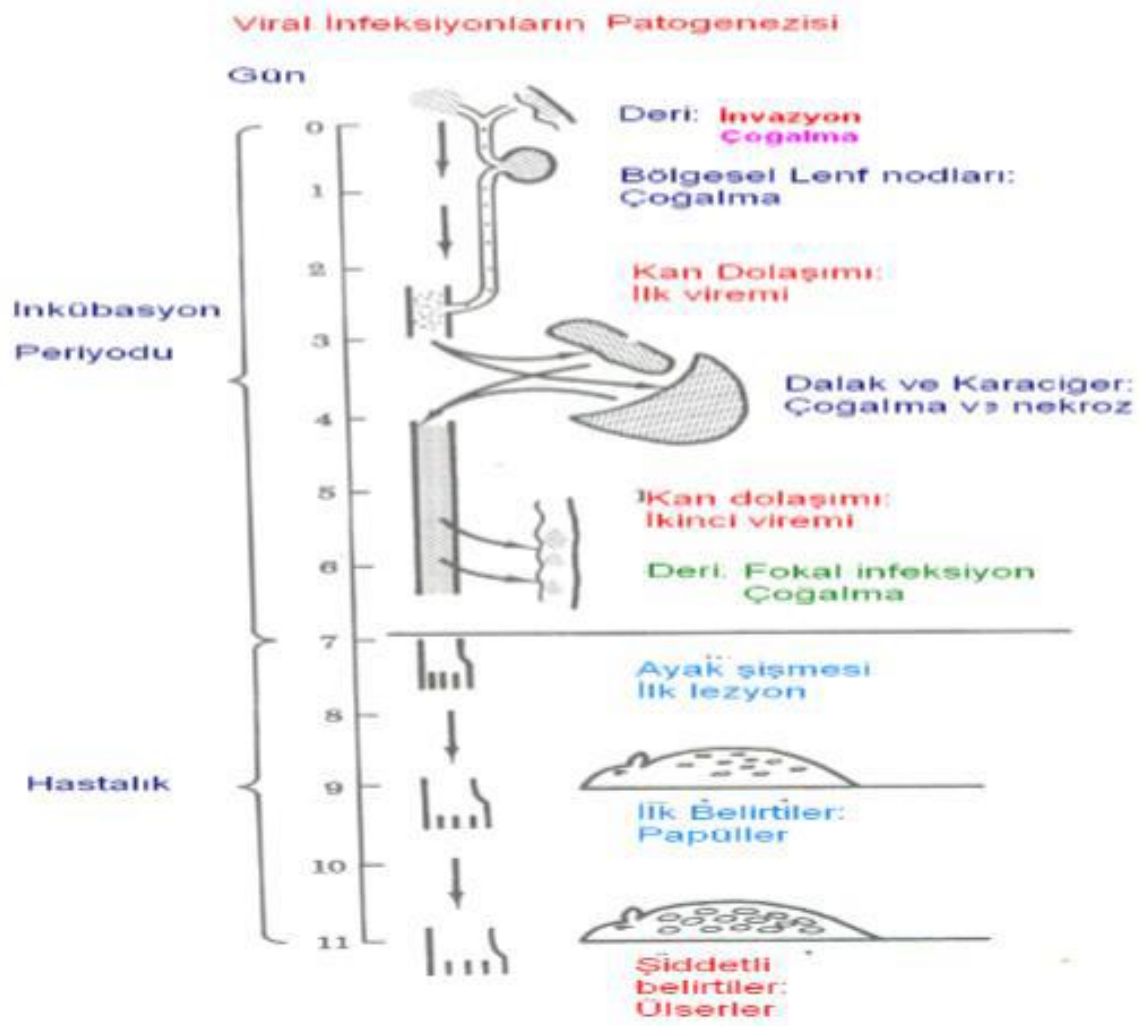
- For this type of infection to occur, the virus crosses the mucosal barrier and spreads to more distant areas. For this purpose, it can use blood circulation, lymph circulation, and nerves to reach organs or tissues with affinity. The virus targets specific cells in the target organ or tissues.
- Systemic spread in viral infections:

➢By blood (viremia):

- It is the period when the virus, which has completed its pre-replication, is carried by blood to reach the cell group to which it has affinity (tropism). The most prominent symptom is fever. In some diseases, there may be two-phase viremia period (pox)
  - Active viremia is caused by the replication of viruses which results in viruses being introduced into the bloodstream. Examples include the measles, in which primary viremia occurs in the epithelial lining of the respiratory tract before replicating and budding out of the cell basal layer (viral shedding), resulting in viruses budding into capillaries and blood vessels.
  - Passive viremia is the introduction of viruses in the bloodstream without the need of active viral replication. Examples include direct inoculation from mosquitoes, through physical breaches or via blood transfusions.

- By blood (viremia):

Frank Fenner Mousepox patogenesiz şeması



➢It is through the nerve pathway. Rabies

Pathogenesis of Rabies

Virus transmitted from saliva to muscle

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Virus travels from neuromuscular junction to peripheral nerves

↓

From PNS to CNS

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Infects brain, salivary gland

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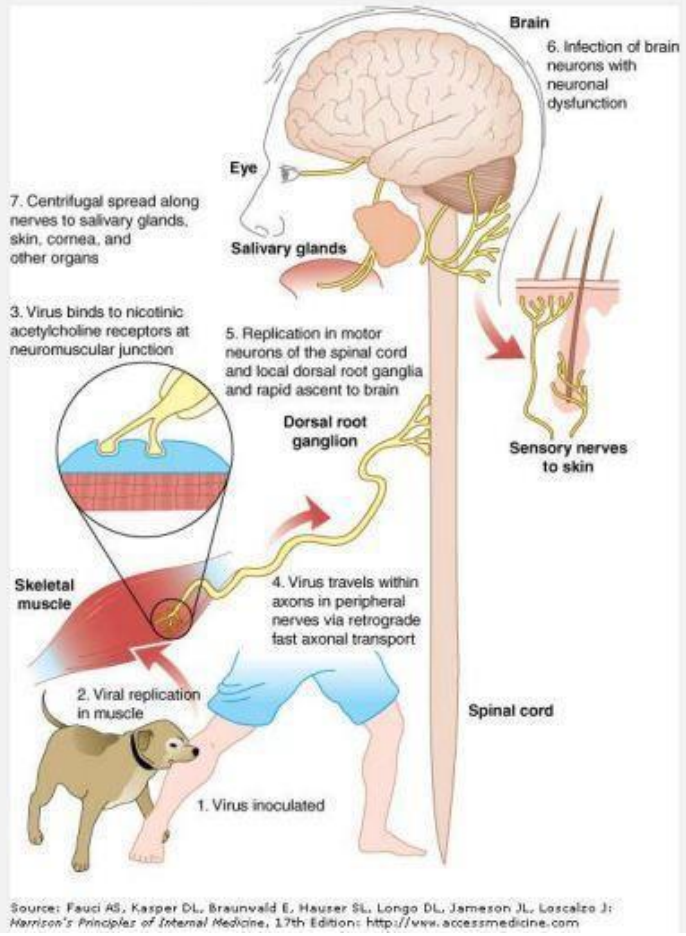
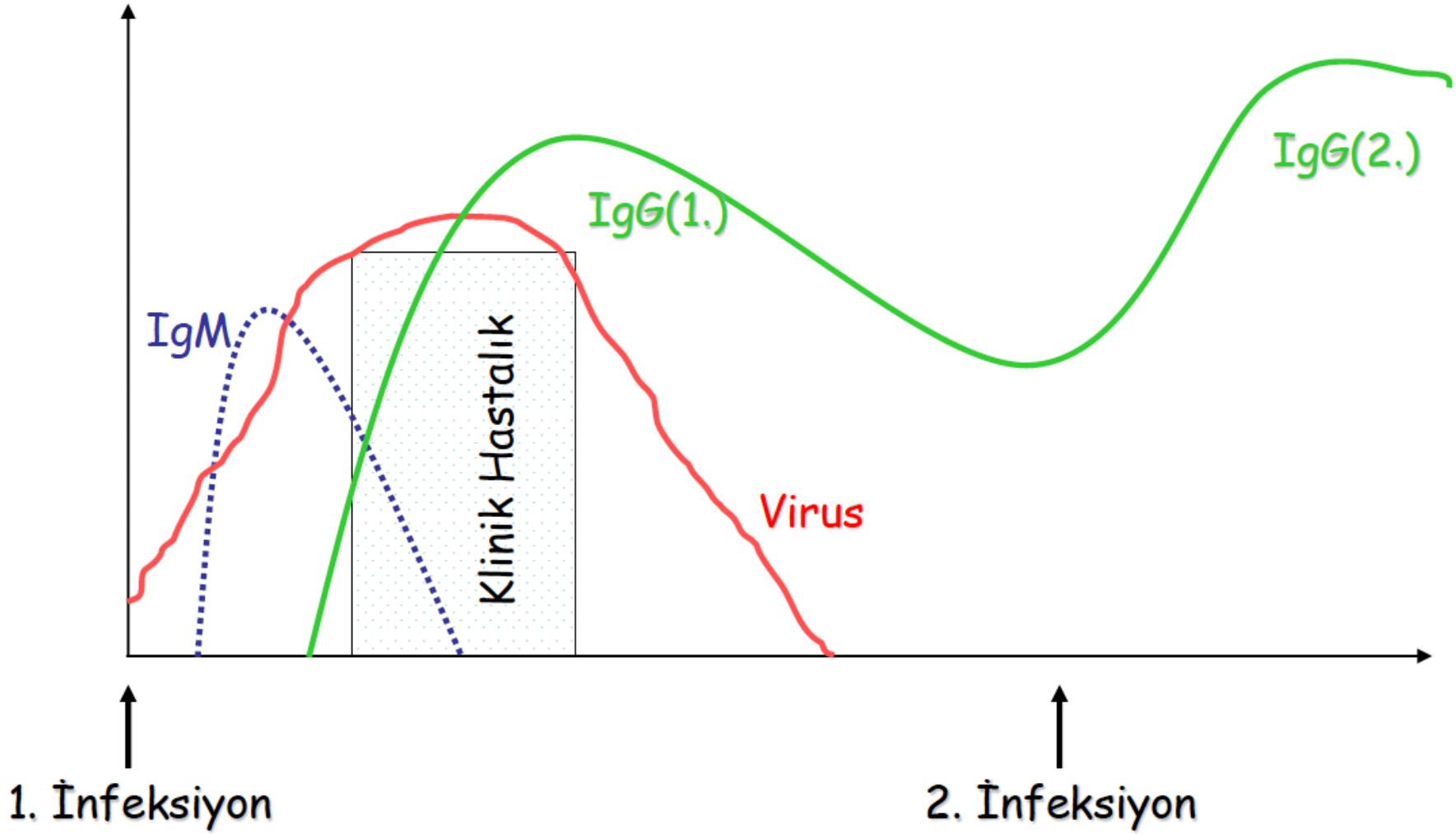
Infects other organs – respiratory tract



Different types of Viral infections

- Postnatal infections may be acute or persistent depending on their progression;
- Acute infection: It is characterized by the development of disease after the agent enters the organism and is eliminated through the immune response. Acute infections are of relatively short duration with rapid recovery.
- Persistent infection: This is a progressive and slowly developing form of infection with a long interval between the entry of the causative agent into the organism and the onset of disease symptoms.
- This may be due to deficiencies in the host immune system, escape of the agent from the immune system and, in some cases, low virulence of the agent.
    1. Chronic Infections
    2. Slow Infections
    3. Latent Infections
    4. immunotolerant infection

Acute infection:



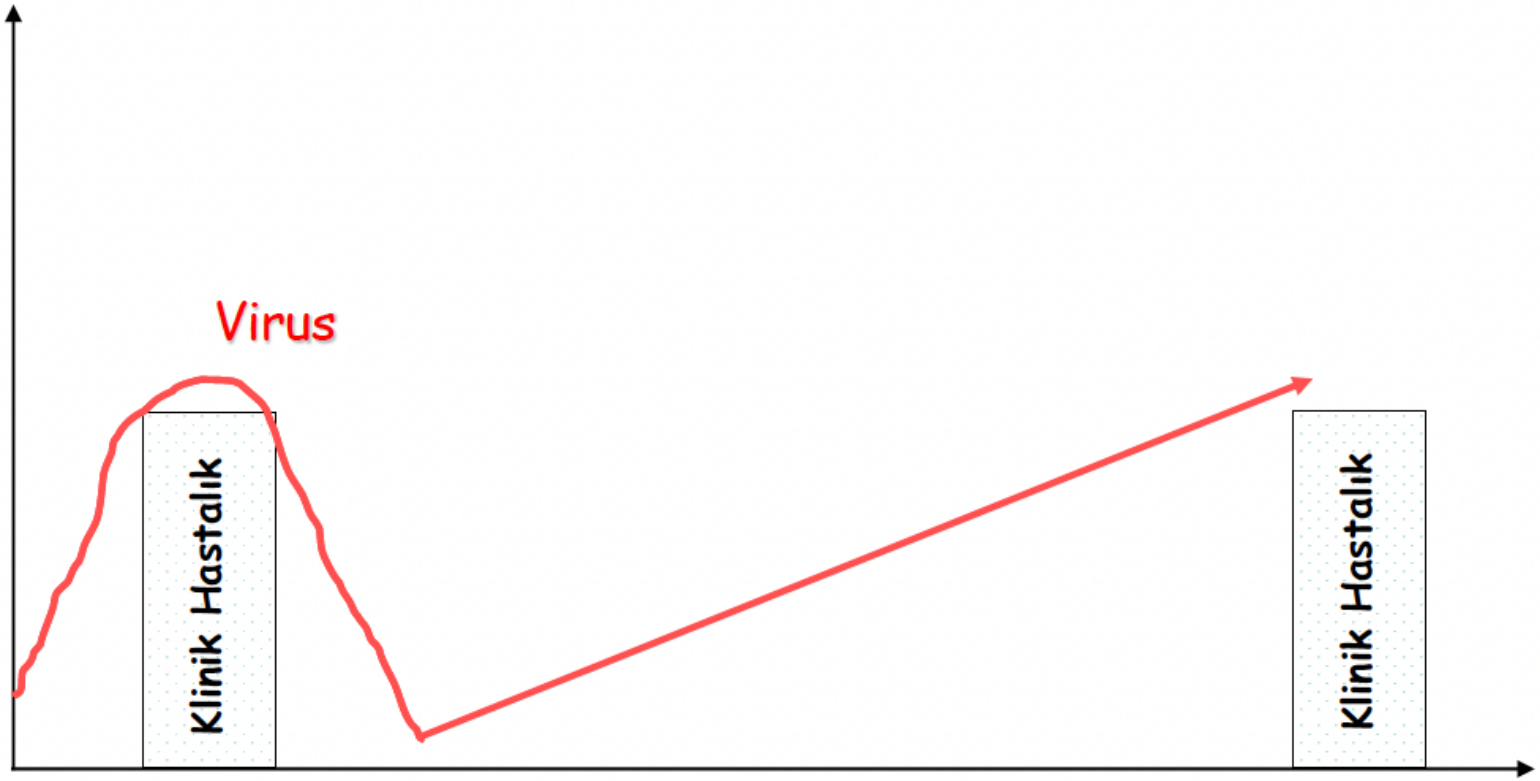
Persistent Infections

1. Chronic Infections (Old Dog Encephalitis)
2. Slow Infections (Retroviral infections; Caprine Arthritis Encephalitis, Maedi-Visna, AIDS, etc.); Prion infections.
3. Latent Infections (All Herpesvirus infections)
4. Immunotolerant infection

1. Chronic Infections

Old Dog Encephalitis, a late complication of canine distemper, is a good example.

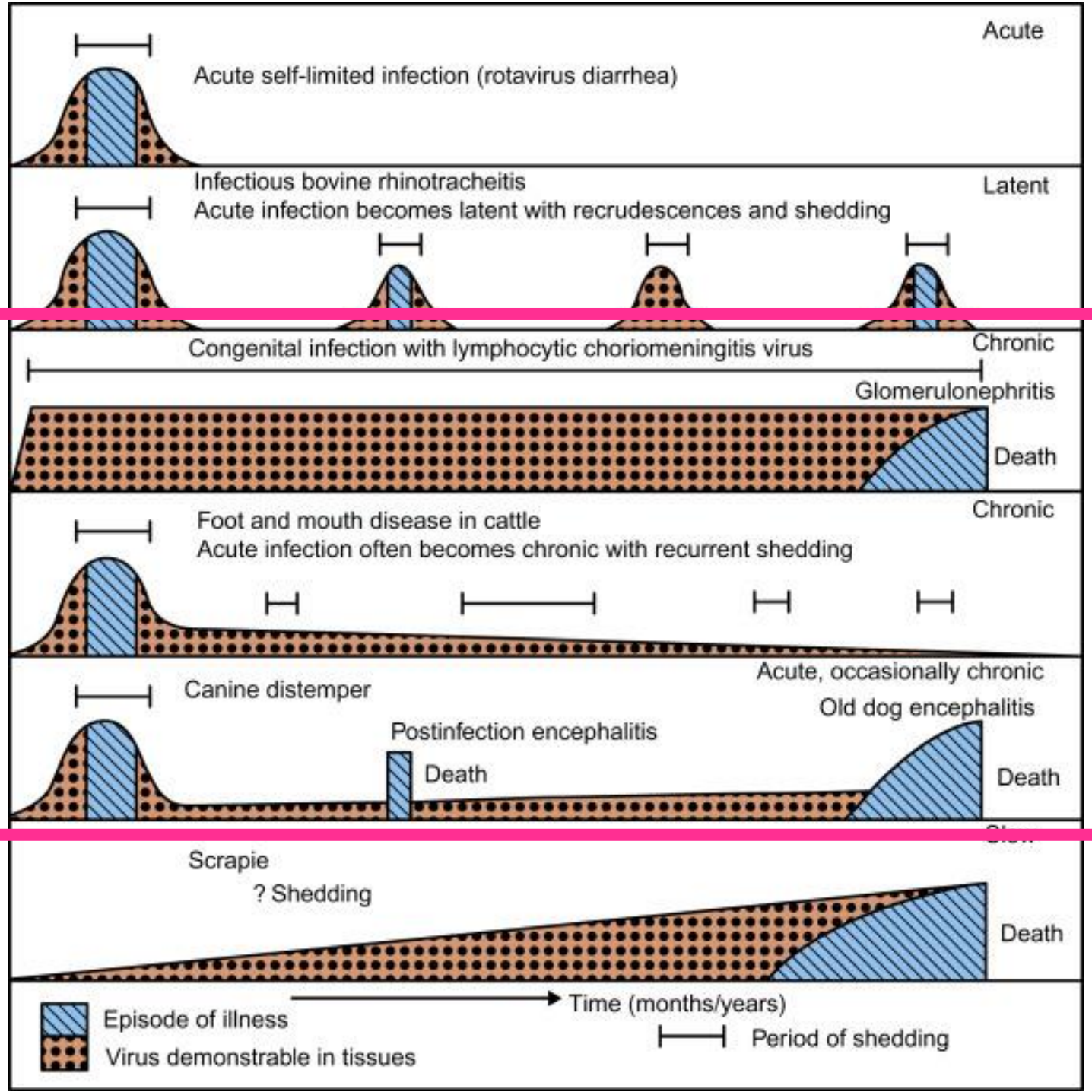
In chronic persistent infections, the virus, which cannot be eliminated following the primary infection, remains in the organism at a certain level or at a gradually decreasing level for a long time.
Although the infection tends to regress, late symptoms of acute infection may occur.



Three different course patterns have been identified for this infection model.

These are the chronic form of

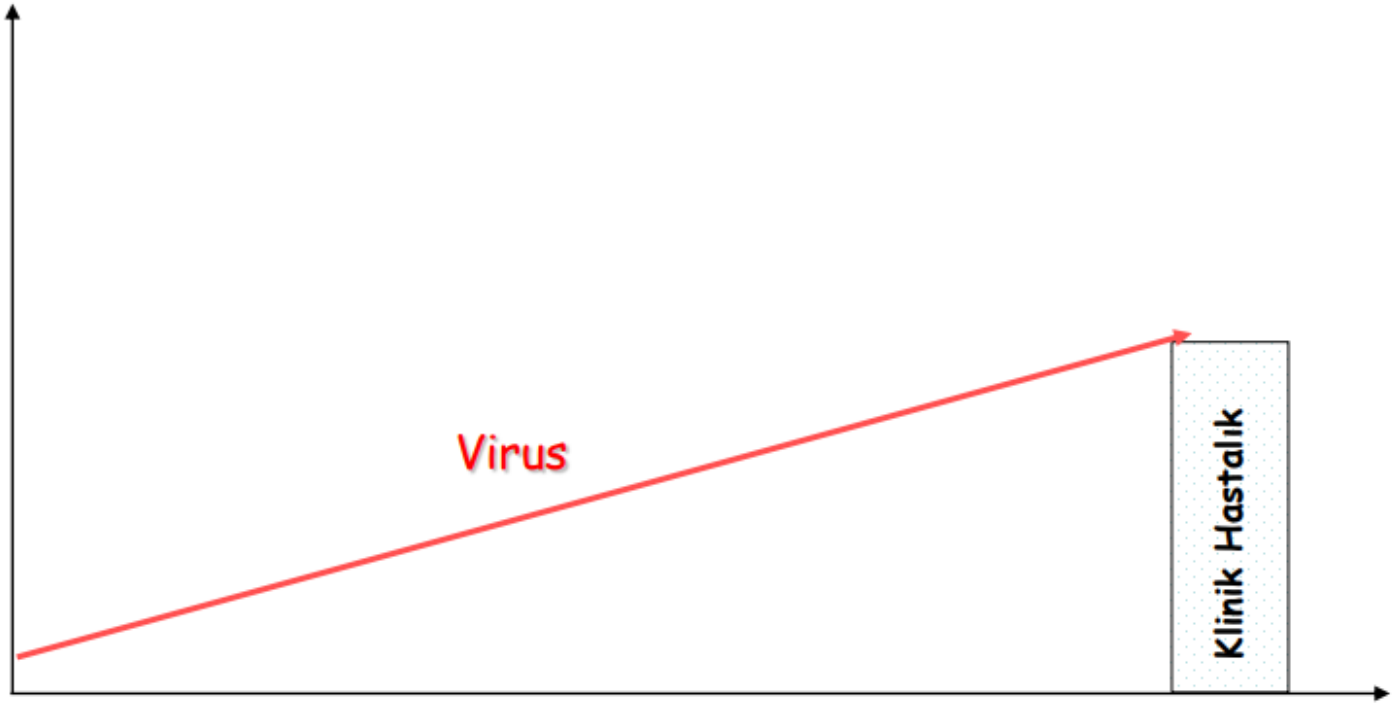
- foot-and-mouth disease,
- the old dog encephalitis form of canine distemper,
- the congenital infection form of lymphocytic choriomeningitis virus.



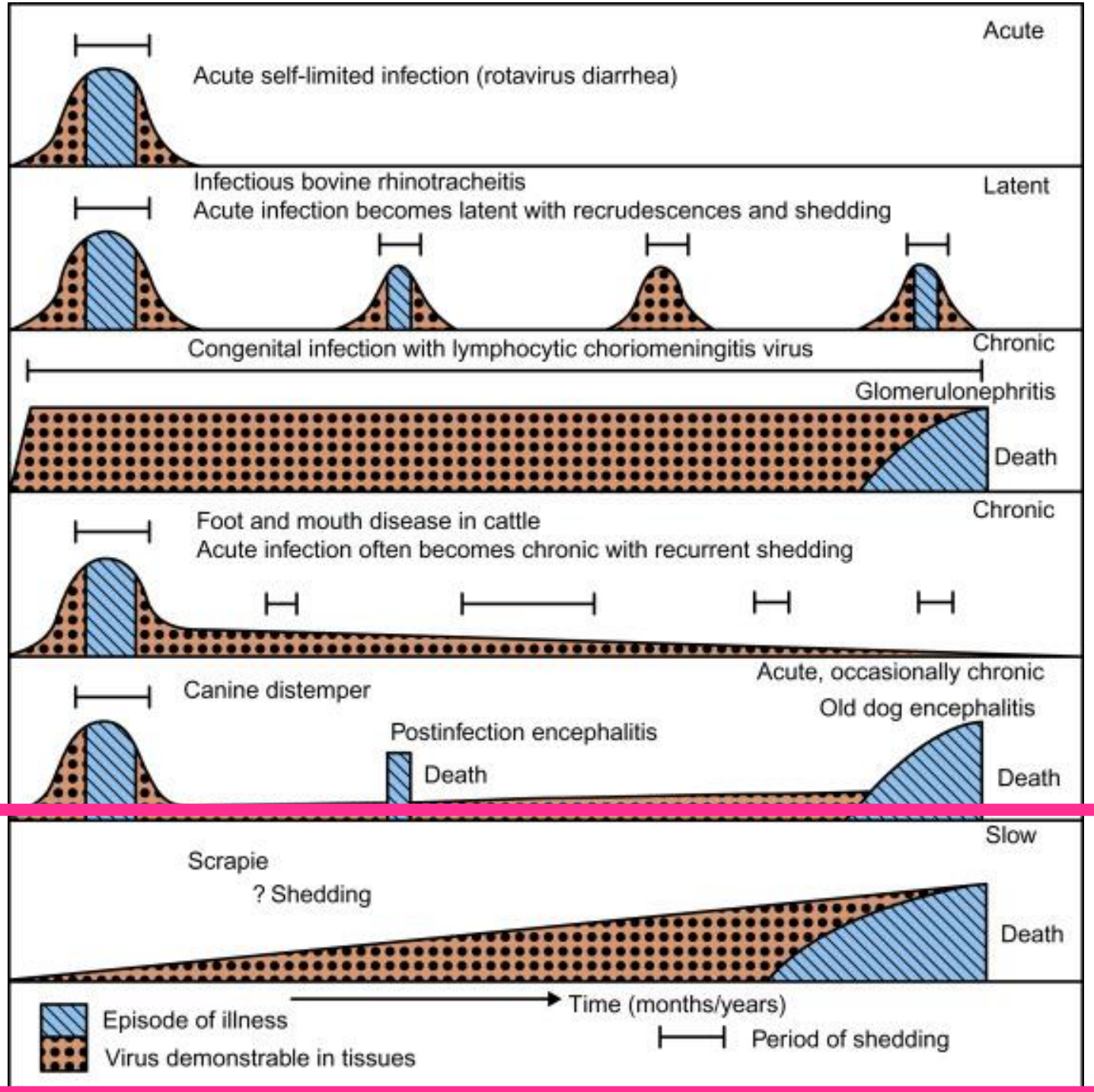
Fenner'sVeterinaryVirology.DOI:http://dx.doi.org/10.1016/B978-0-12-800946-8.00003-9

2. Slow Infections

All retrovirus infections and prion diseases are the best examples of this type of persistent infections.
In these infections, there is a long infection period that progresses very slowly.
During the preclinical period, which can vary from a few months to a few years, the amount of the agent detected in the tissues tends to constantly increase.
In the final stage, disease symptoms appear and these progressive findings result in death.



- Diseases caused by prions (cattle spongiform encephalopathy (BSE), sheep scrapie disease, etc.) and maedi-visna caused by lentiviruses, goat arthritis-encephalitis, feline immunodeficiency syndrome (FAIDS), etc. diseases and some other retrovirus infections (e.g. progressive pneumonia of sheep) are included in this group.



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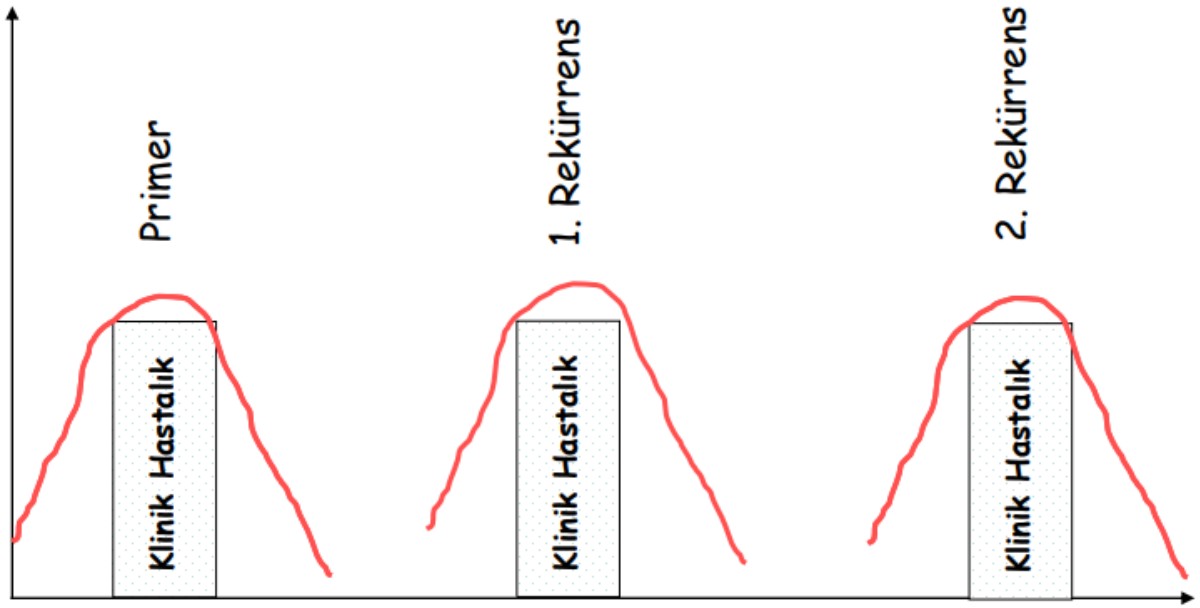
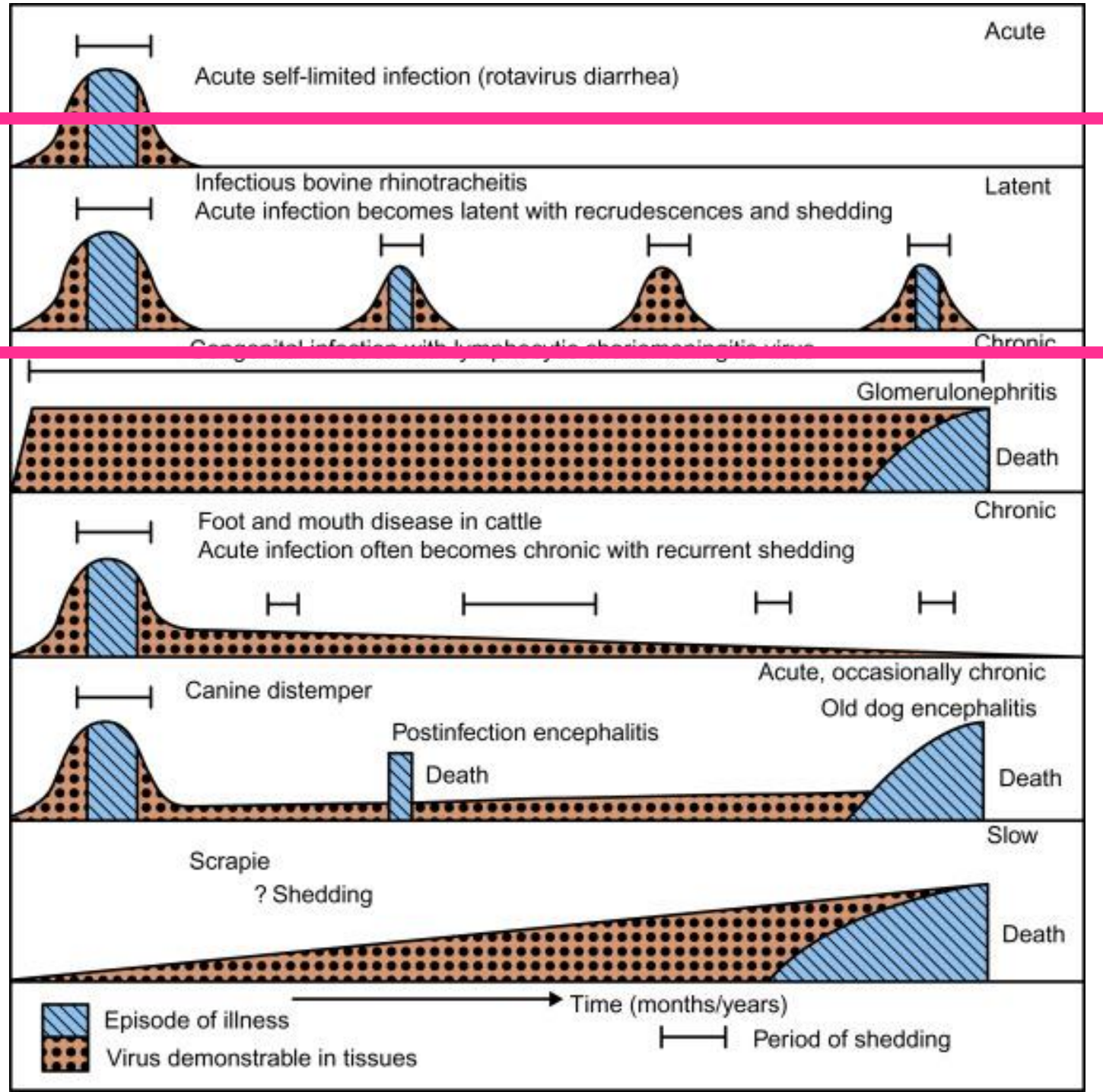
3. Latent Infections

It is characterized by the occasional recurrence of the acute disease picture.

- Herpesvirus infections are the best example of this. The one that occurs first is called primary infection, and the ones that recur are called recurrent infection.
- In the latent infection model, the antibody response is formed following the primary infection phase and specific antibodies are generally detectable throughout life.
- Herpes simplex virus infections (HSV-1 and -2) in humans, bovine herpesvirus type 1 (BHV-1), pseudorabies, equine herpesvirus and feline herpesvirus virus (FHV-1) infections in animals are the most well-known examples of the latent infection model.



- Following primary infection, alphaherpesviruses are transmitted via nerves to the trigeminal or sacral ganglia.
- The viral genome settles in these regions and initiates a lifelong persistent infection.
- In later periods, the virus may become reactivated due to stress factors such as pregnancy, transplantation, and corticosteroid drug use.
- Reactivation is an event that can be repeated throughout life.
- During reactivation periods, virus shedding occurs and virus detection can be made in tissues.
- During these periods, disease symptoms usually reappear, but sometimes reactivation may occur without clinical findings.



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4. Immunotolerant infection

- This infection model seen in **pestiviruses** has a completely different pathogenesis than the other three models.
- In this model, non-cytopathogenic viral strains infect the fetus in utero before the ability to develop an immune response (immunocompetence).
- By the time immunocompetence develops, the virus has already established itself in the organism and is perceived as a structure belonging to the organism.
- There is no immunological response to this virus strain in the organism and a lifelong immunotolerance is formed.
- From the birth of the calf, virological tests give virus (+) results. Antibody (-)
- These individuals, born with immunotolerance and lifelong persistent infection of the immune system, are carriers and transmitters of the virus throughout their lives. ⟶ Persistently Infeted (PI) animals

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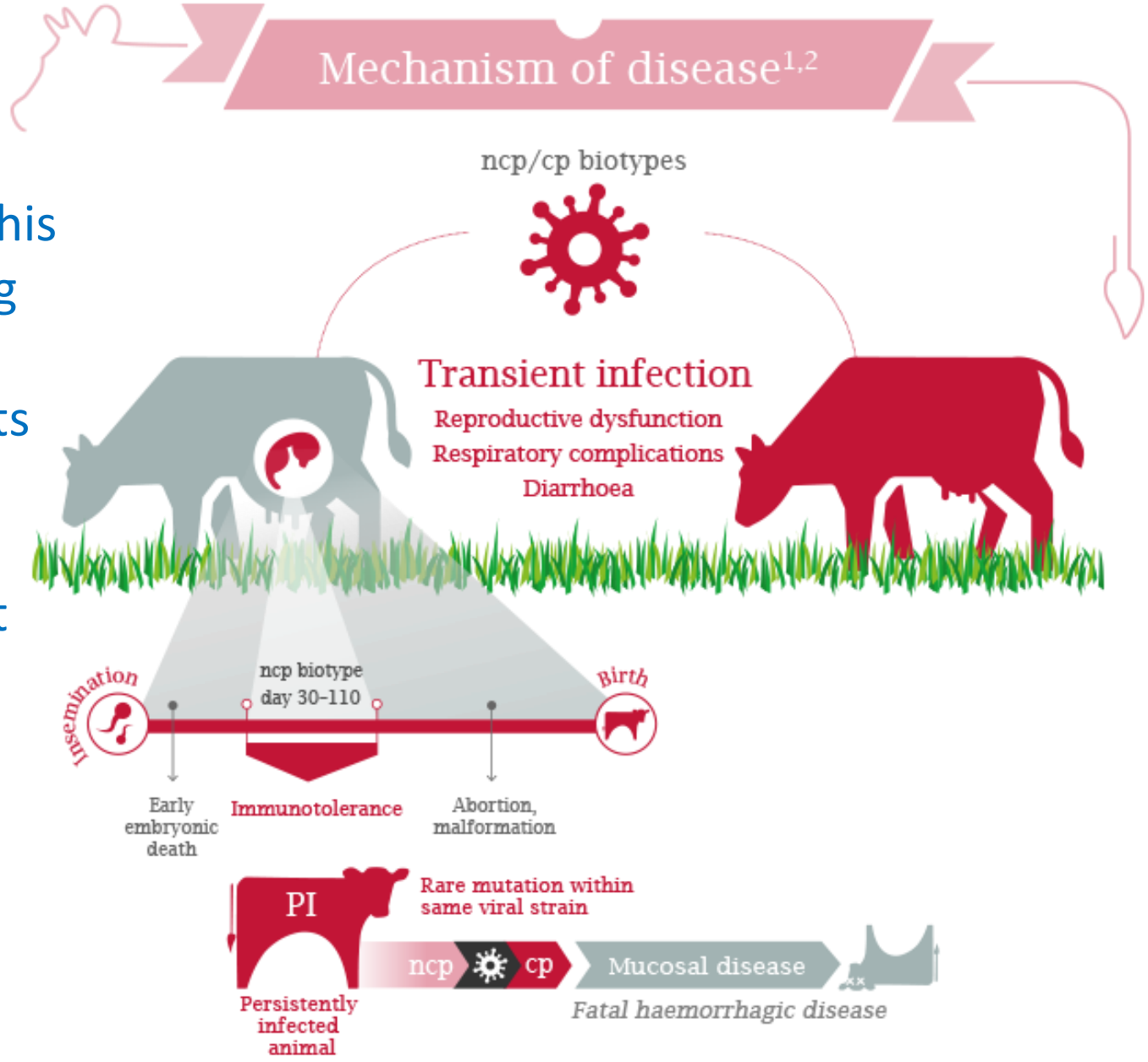

The Importance of Persistent Infections

1. They may become reactive and exhibit an acute illness pattern at any time. They may cause disease outbreaks again due to reactivation (latent infections).
2. They have epidemiological importance. Since these animals do not show clinical signs, they may play a role in transmitting the disease to distant areas.
3. They may lead to re-introduction of disease into disease-free/eradicated areas. They are important in the control/eradication of diseases.
4. They ensure the continuity of infection in nature and allow the continuity of infection in vaccinated individuals or herds.
5. Since the immune system is suppressed, animals are vulnerable to other infections. They may cause the emergence of immunopathological disease complexes.
6. They may cause tumor development.