Lec 2:
Virus Disease in Populations and Individual Animals

The nature of the virus reservoirs:

- **Virus reservoir:** The reservoir of an infectious agent is the habitat in which the agent normally lives, grows, and multiplies.
- Reservoirs include humans, animals, and the environment.

Viruses with human reservoirs:

A significant number of human viruses leading to either mild or life-threatening disease are maintained in human populations. (Polio virus) – eradication possible? Why?

Virus Transmission:

- **Respiratory infection** leads to coughing and sneezing, which spreads an aerosol of droplets containing virus, **e.g. Influenza, SARS**.
- **Herpes Simplex Virus (HSV)** is spread in saliva requiring direct transfer of an aqueous suspension; by contrast, the closely related **varicella zoster (chicken pox) virus (VZV)** is spread by inhalation of a virus-loaded aerosol.
- **Poliovirus** is spread only by virus-containing feces contaminating food or drinks that are then ingested by a susceptible host.
- In the case of **HIV**, body fluids, including blood, breast milk, serum, vaginal secretions, and seminal fluid, are sources of infection.

1. Infection via airborne droplets and particles

2. Contact infection and smear infection (Herpes Simpex virus HSV – contaminated surfaces)

3. Infection via contaminated water and food (Polio/Hepatitis A virus (HAV))

4. Infection via blood and tissue (HIV)

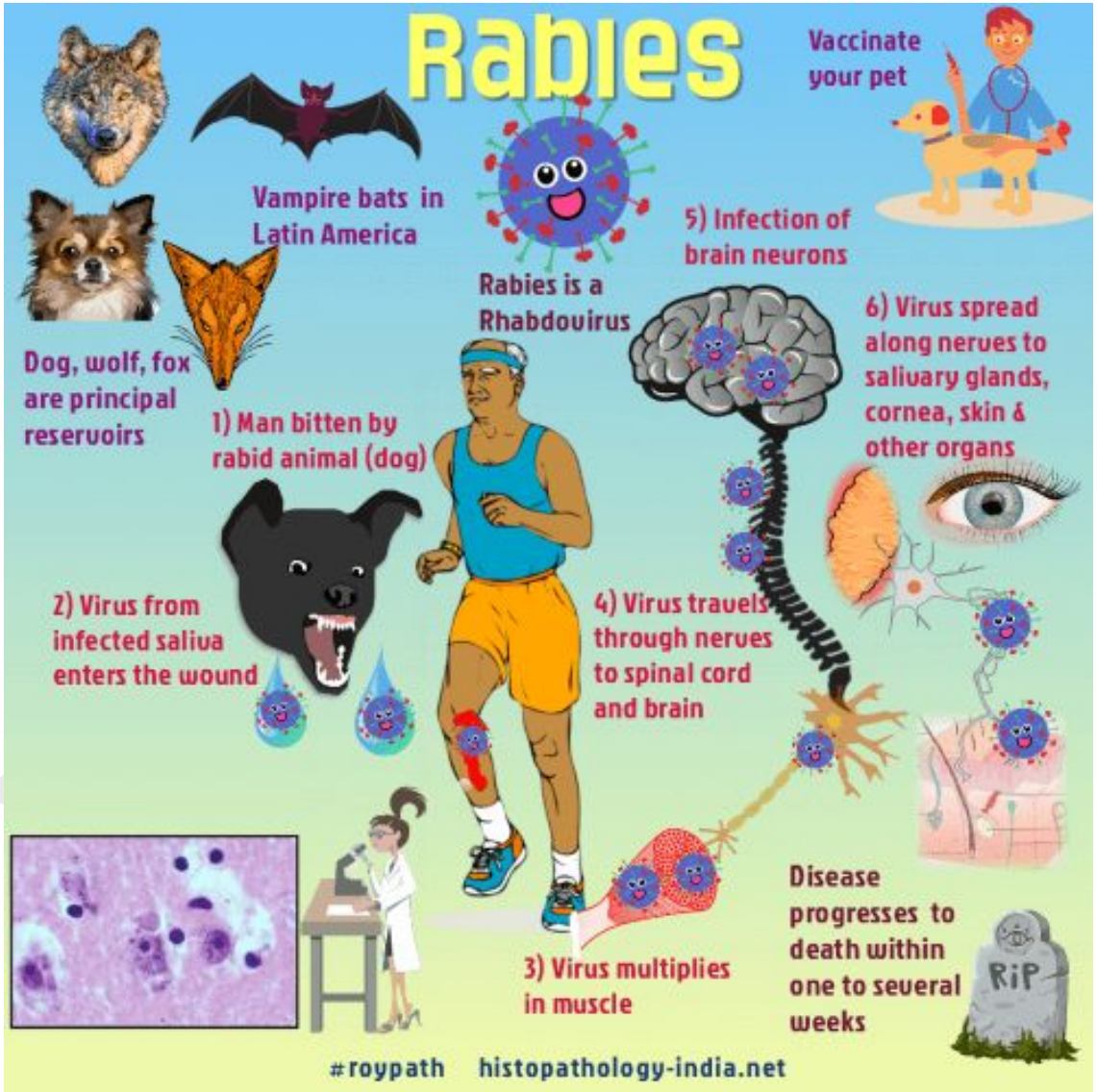
5. Vectors : Ticks/mosquitoes

The nature of the virus reservoirs:

Viruses with vertebrate reservoirs:

- A disease that is transmissible from other vertebrates (mammals, birds, reptiles, amphibians, and fish) to humans is termed **a zoonosis**.
- **Rabies** is a classic example of a zoonosis that affects humans only sporadically.
- **The rabies virus**, which is transmitted in saliva via a bite, is maintained in populations of wild animals (raccoons, bats, and foxes), most generally carnivores.
- **Viral zoonoses** often require the mediation of an **arthropod vector** for spread to humans.
- For viruses with RNA genomes that are transmitted between hosts via arthropods (such as those responsible for **yellow fever**, a number of kinds of encephalitis, and **dengue fever**), virus replication in the vector provides a secondary reservoir and a means of virus amplification.
- This makes spread to a human host highly efficient since even a small inoculation of the virus into the arthropod vector can result in a large increase in virus for transmission to the next host.

Can **Rabies** be eradicated like **Small pox**?



Pathogenic viruses

Virus	Vector/route	Host	Disease
Poliovirus	Human–fecal contamination of water or food	Human	Enteric infection, in rare cases CNS infection (poliomyelitis)
Western equine encephalitis	Mosquito	Horse	Viral encephalitis in the horse – occasional infection of human
La Crosse encephalitis	Mosquito	Squirrel, fox (reservoir), human	No obvious disease in squirrel or fox; viral encephalitis in human
Sin nombre (*Hantavirus*)	Deer mouse	Deer mouse, other rodents (reservoir); human	Hantavirus hemorrhagic respiratory distress syndrome
HIV	Direct injection of virus-infected body fluids into blood	Human	AIDS
Measles	Aerosol	Human	Skin rash, neurological involvement
Yellow fever	Mosquito	Tropical monkeys, human	Malaise, jaundice
Dengue fever	Mosquito	Human, primates	Mild to severe hemorrhagic disease
Ebola	Unknown vector, but nosocomial transmission	Reservoir unknown; humans and primates	Often fatal hemorrhagic fever
Hepatitis A	Fecal contamination of water or food	Human	Acute hepatitis
Hepatitis B	Direct injection of blood	Human	Chronic hepatitis, liver carcinoma
Hepatitis C	Direct injection of blood	Human	Acute and chronic hepatitis
Hepatitis delta	Blood, requires coinfection with hepatitis B	Human	Acute hepatitis
Hepatitis E	Fecal contamination of water or food	Human	Mild acute hepatitis except often fatal to pregnant women

Table 1: Some pathogenic viruses, their vectors or routes of spread, and their hosts. (Basic Virology, 3rd Edition)

Pathogenic viruses

Virus	Vector/route	Host	Disease
Rabies	Bite of infected animal	Vertebrates	Fatal encephalitis
Herpes simplex (HSV)	Saliva, other secretions	Human	Surface lesions followed by latency, rare encephalitis
Varicella-zoster (VZV, chicken pox)	Aerosol	Human	Rash, shingles, latency
Epstein–Barr (EBV)	Saliva	Human	Infectious mononucleosis, latency
Influenza	Aerosol	Human, many vertebrates	Flu
Smallpox	Aerosol	Human	Variola
Myxoma	Insect bite	Rabbits	Variable mortality, skin lesions
Rhinovirus	Aerosol	Human	Colds
Coronavirus	Aerosol	Civet cat (for SARS CoV); human	Colds; SARS
Rubella (German measles)	Aerosol	Human	Mild rash, severe neurological involvement in first-trimester fetus
Adenovirus	Aerosol, saliva	Human	Mild respiratory disease
Papillomavirus	Contact	Human	Benign warts, some venereally transmitted, some correlated with cervical carcinomas
HTLV (human T-cell leukemia virus)	Injection of blood	Human	Leukemia
Tomato spotted wilt (bunyavirus)	Thrip	Broad range of plant species	Necrosis of plant tissue, destruction of crops
Cadang-cadang (viroid)	Physical transmission via pruning	Coconut palm	Coconut palm pathology

Table 1: Some pathogenic viruses, their vectors or routes of spread, and their hosts. (Basic Virology, 3rd Edition)

Viruses in populations:

Epidemiology is **the study of diseases in populations, investigating how, when and why they occur**.

The diseases studied are wide-ranging:

- infectious diseases like coronavirus

-non-infectious diseases like arthritis/High blood pressure

. People who work in this field are referred to as epidemiologists.

- **Viral epidemiology** in small and large populations
- **Viral Epidemiology** is the study (scientific, systematic, and data-driven) of the distribution (frequency, pattern) and determinants (causes, risk factors) of health-related states and events (not just diseases) in specified populations (neighborhood, school, city, state, country, global).
- Its application : to the control the viral infection/ health problems

Viral epidemiology: WHO epidemiology report

A) Viral epidemiology in large population:

In large populations the rate of virus spread greatly surpasses the limitations of the generation of herd immunity and the introduction of a novel pathogenic virus leads to epidemic spread of disease

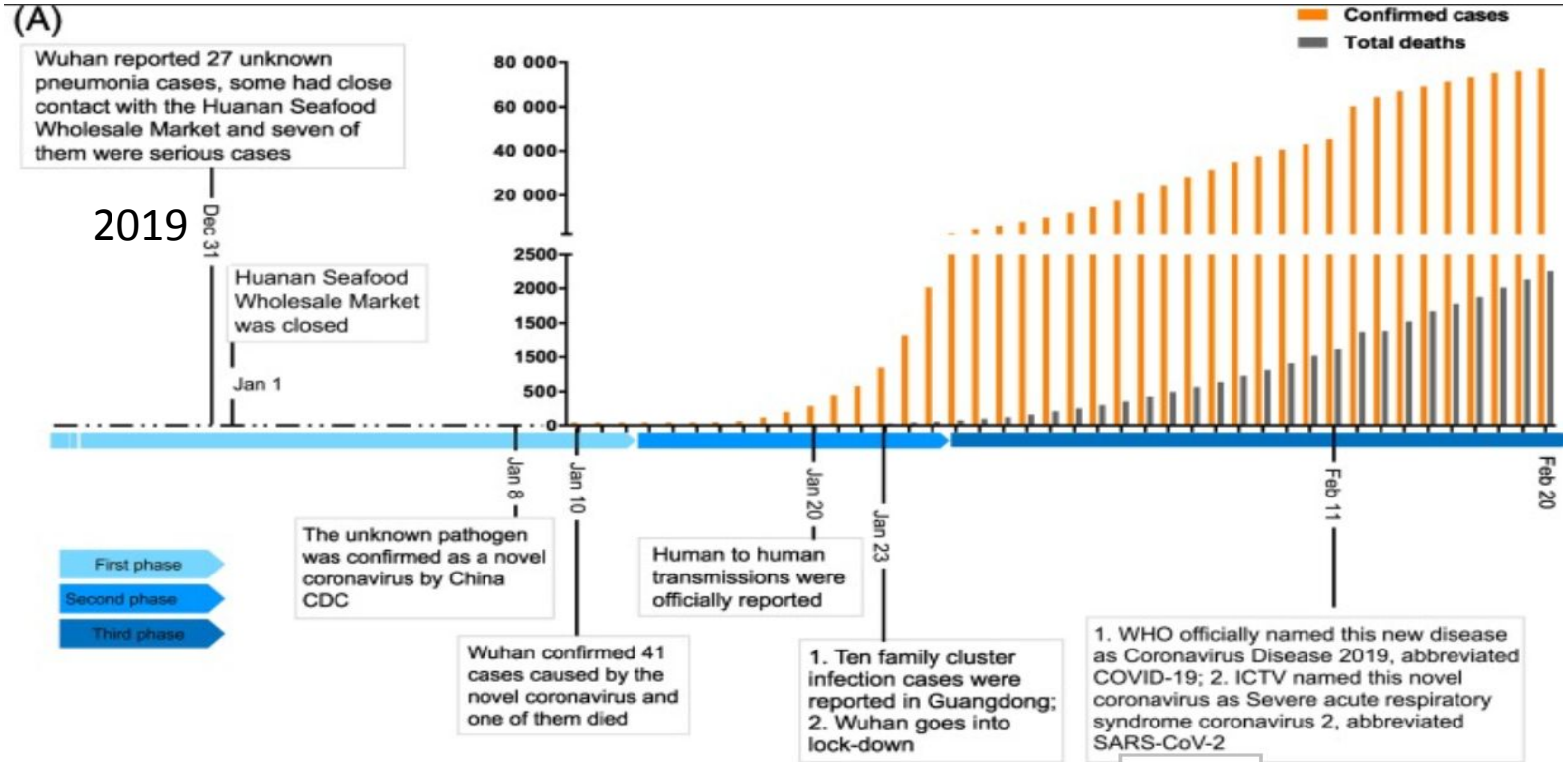


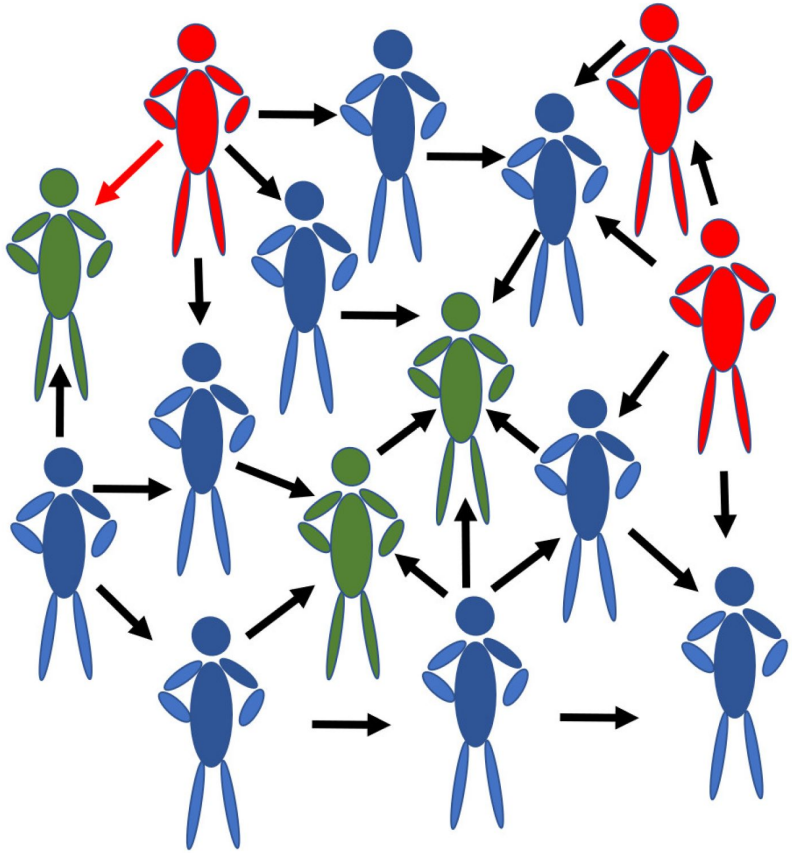
Figure 2: Spreading of the 2019-nCoV Epidemic. Timeline of events during the 2019-nCoV epidemic.(https://www.cell.com/trends/molecular-medicine/fulltext/S1471-4914%2820%2930065-4)

Herd immunity, or community immunity,

When a large part of the population of an area is immune to a specific disease.

Viral Variants/ Mutants – makes it difficult

'Herd immunity', also known as 'population immunity', is the indirect protection from an infectious disease that happens when a population is immune either **through vaccination** or immunity developed through **natural infection**.



COVID-19 POSITIVE

VACCINED OR IMMUNIZED

UNPROTECTED

NO VIRUS SPREADING

VIRUS SPREADING

Factors affecting the control of viral disease in populations

- The generation of **lasting immunity** provides an effective means of controlling and even eradicating certain viral diseases. The **antigenic stability of the smallpox virus and effective immunity** against it allowed effective vaccination programs to eradicate the disease from the population. **Polio and measles** are current candidates for partial or total elimination from the population due to availability of effective vaccines.
- **Antigenic variability: Flu virus** variants arise by **genetic mixing of human and animal strains**, and it is not practical to attempt a widespread vaccination campaign with so many variables.
- HIV remains associated with lymphatic tissue in infected individuals even when antiviral drugs effectively eliminate virus replication. The **intimate (integrate) association of HIV** with the **immune system** may make vaccination campaigns only partially effective
- A major **obstacle to the control of viral and other infectious diseases** in the human population as a whole is **economic**. It costs a lot of money to develop, produce, and deploy a vaccine. Many of the nations most at risk of deadly infectious disease outbreaks are financially unable to afford effective control measures, and pharmaceutical corporations involved with vaccine research and production are primarily interested in bottom-line profit.
- **Lack the political will** and insight to mount effective efforts to counter the spread of viral disease. Such problems constantly change character but are never ending

Polio and measles :
Humans are the only known reservoir of poliovirus

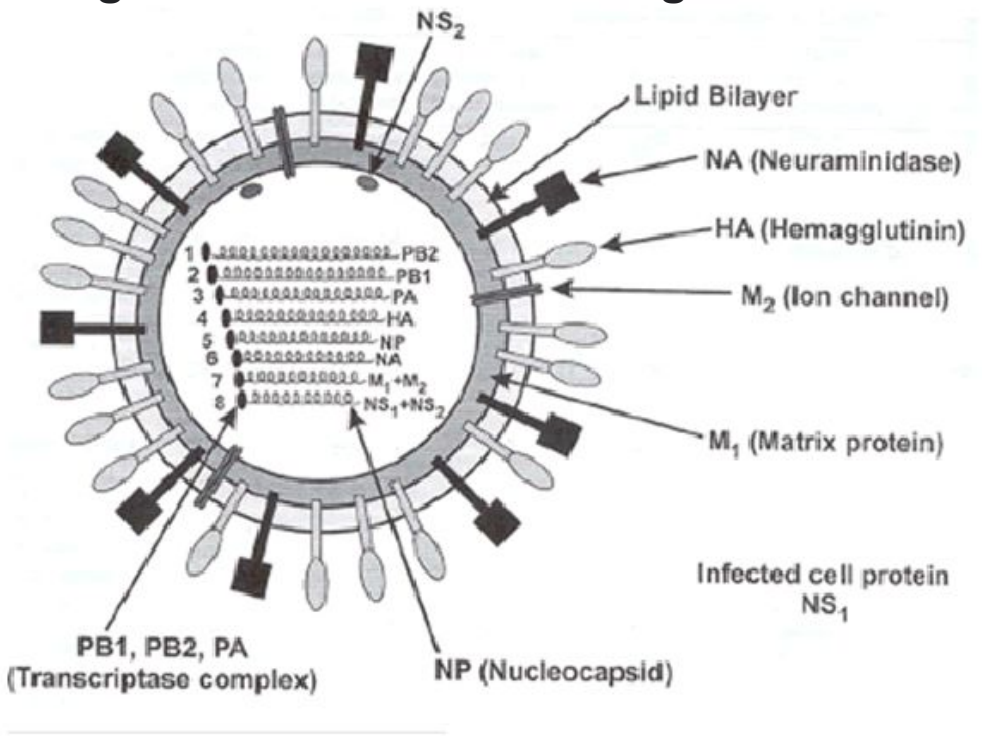
"Antigens" are molecular structures on the surface of viruses that are recognized by the immune system and are capable of triggering one kind of immune response known as antibody production.

Antigenic stability gives: life long protection.
Antigenic variability is characterized by the emergence of sequence distinct variants within a species, circulating between hosts, within hosts, or temporally across populations, for which adaptive immunity elicited by one strain fails to protect against another (1)

Influenza A & B (C,D)

H1N1 strains the Spanish flu 1918 (33%world population)
, the 1977 Russian flu pandemic and the 2009 swine flu pandemic.

8 single-stranded –ve RNA segments



16 different types of HA
9 different types of NA,

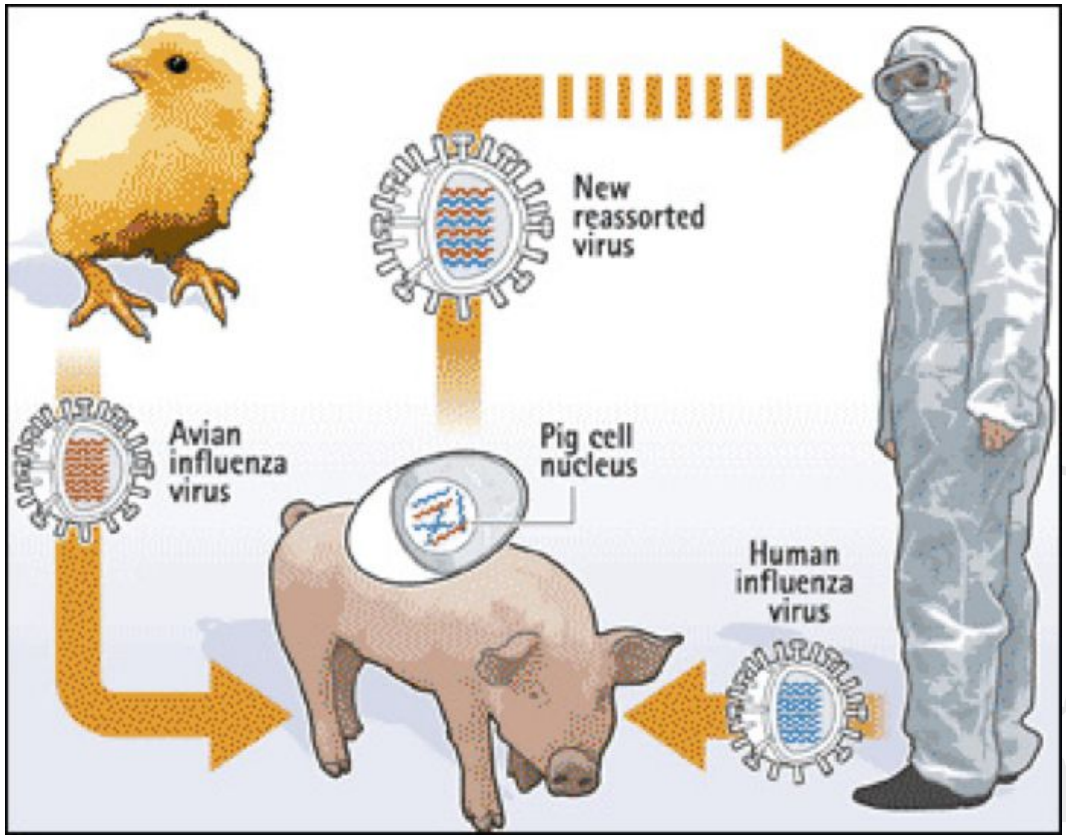
potentially 144 different subtypes of influenza A viruses.

Among them, **two subtypes of influenza A,**

H1N1 and H3N2, most commonly infect humans.

Flu virus variants arise by **genetic mixing of human and animal strains**

Genetic mixing: Influenza strains



*A process known as "**reassortment.**" Historically, pigs have been good "mixing vessels" for this process, since pig cells -unlike bird or human cells-can be infected by both bird and human viruses. Inside the pig-cell nucleus, genetic segments of the two types of viruses replicate and mix, producing offspring with genes from both parent viruses.*

What was once a bird flu now has genes that enable it to spread more easily among humans.

How to study viruses?

- Viral pathogenesis?
- Viral transmission?
- Viral drugs?
- Viral vaccines?

Animal model to study viral pathogenesis:

- One extremely effective way to obtain reliable data on the dynamics of disease and its course in an individual is to **develop an accurate animal model.**
- Another important reason for using an animal model to study virus infection is that useful information can often be obtained with **very simple experimental processes.**
- The ability of a virus to cause specific symptoms can be **determined by careful control of the viral genotype and site of inoculation in the animal**, followed by observation of the symptoms as they develop.
- The passage of a virus throughout the body during infection can be studied by **dissection of specific organs, careful gross and microscopic observation**, and **simple measurement (assay) of virus levels in those organs.**
- Many of the models developed for the study of viral pathogenesis involve the use of **mice**. These animals have an **excellent immune system, can be infected with many viruses** adapted from human diseases, and are relatively inexpensive to use.

Mouse models have been used to elucidate **adapted mutations** related to host interactions and viral pathogenicity through experimental infection (infection and repeated passage are required for the adaptation of human virus to mice, resulting in mutations in multiple genes)

Viral pathogenesis

- Viral pathogenesis describes the processes by which viral infections cause diseases and involves virus–host interactions at the cellular and systemic level that determine whether a virus will cause a disease,
- what form that disease takes
- how severe the disease is?

A simple view of viral pathogenesis is that viruses replicate and kill cells, thus causing disease.

Eg:

Death of liver cells (hepatocytes) causes hepatitis eg: virus?

Death of enterocytes may cause diarrhea: eg: virus?

Death of respiratory epithelial cells may cause severe respiratory tract disease eg virus?

HIV- infects what cells? Kills what cells? Causes what disease?

Animal models

- German physicist (microbiologist) Robert Koch (1843-1910)
- Awarded the Nobel Prize for Physiology or Medicine in 1905.
- The founder of modern bacteriology
- Proved the bacterial cause of anthrax, cholera, and tuberculosis.
- Sheep cow human-anthrax blood of infected animal had bacteria

His team developed ways of staining bacteria for easier viewing under a microscope, and his assistant Julius Richard Petri

- Julius Richard Petri who expanded upon their work in developing a gelatinous substance for growing the bacteria, created the **Petri dish.**

German bacteriologist **Julius Richard Petri.**

- A Petri dish is a shallow transparent lidded dish that biologists use to hold growth medium in which cells can be cultured, originally, cells of bacteria, fungi and small mosses.
- The container is named after him.
- It is the most common type of culture plate.

Robert Koch rules:

He formulated a set of rules for demonstrating that a specific microorganism is the causative agent of a specific disease.

Rules are as follows:

1 The same pathogen must be able to be cultured from every individual displaying the symptoms of the disease in question.

2 The pathogen must be cultivated in pure form.

3 The pathogen must be able to cause the disease in question when inoculated into a suitable host.

Ethically cannot do this…use human as host..so use animals

History: Nazi on prisoners; Blacks/Negros in USA 1930-1940s syphilis (bacteria)

Now: How are human trials done? Placebo (sugar tablets)

Virus propagation: animal cell culture

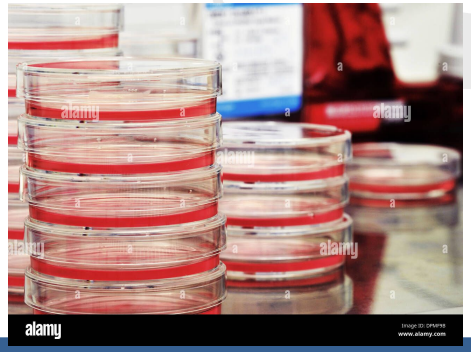
Petri dishes

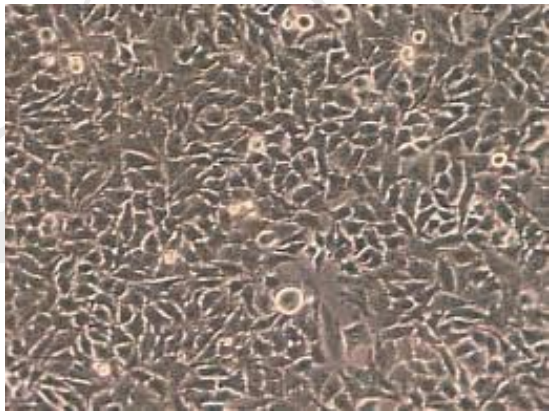
Culture flasks

Multi-well plates

Cell scrapers

Fig. 2. Vessels and accessories for animal cell culture.





FBS used

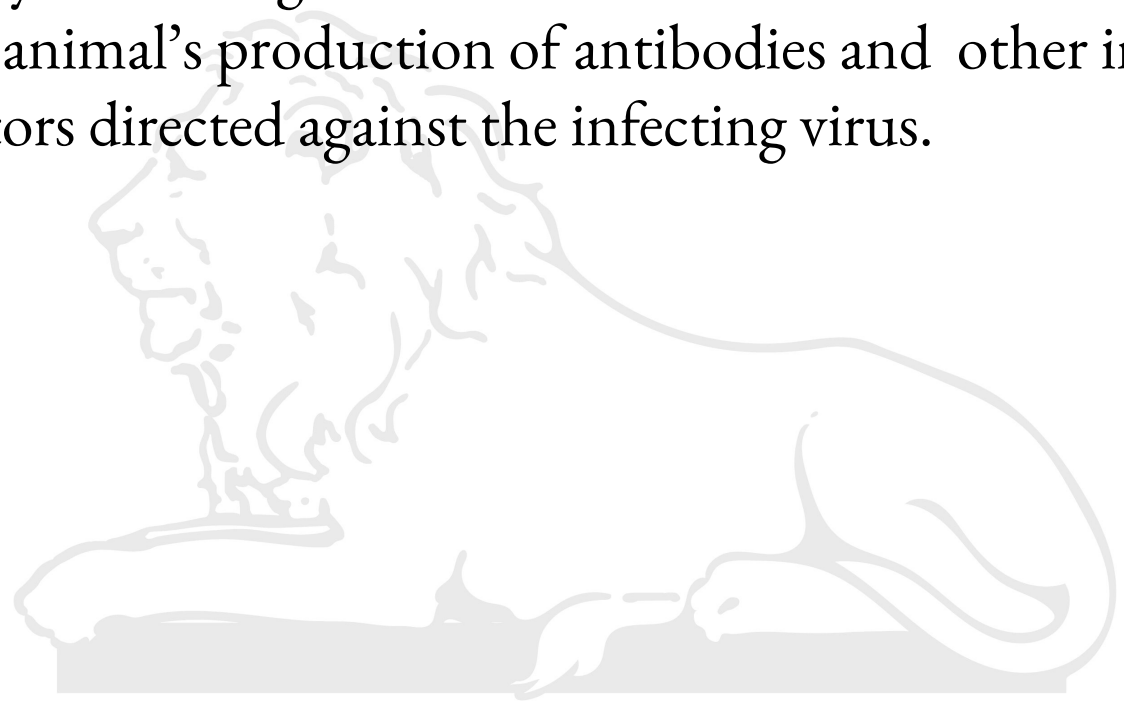
Max Theiler (nobel prize 1951) Succeeded in transmitting the YF virus to mice, When the virus was transmitted between mice, a weakened form of the virus was obtained that could make apes immune.

Live attenuated 17D - YFV vaccine

Specific-pathogen-free (**SPF**) is a term used for laboratory **animals** that are guaranteed free of particular pathogens.

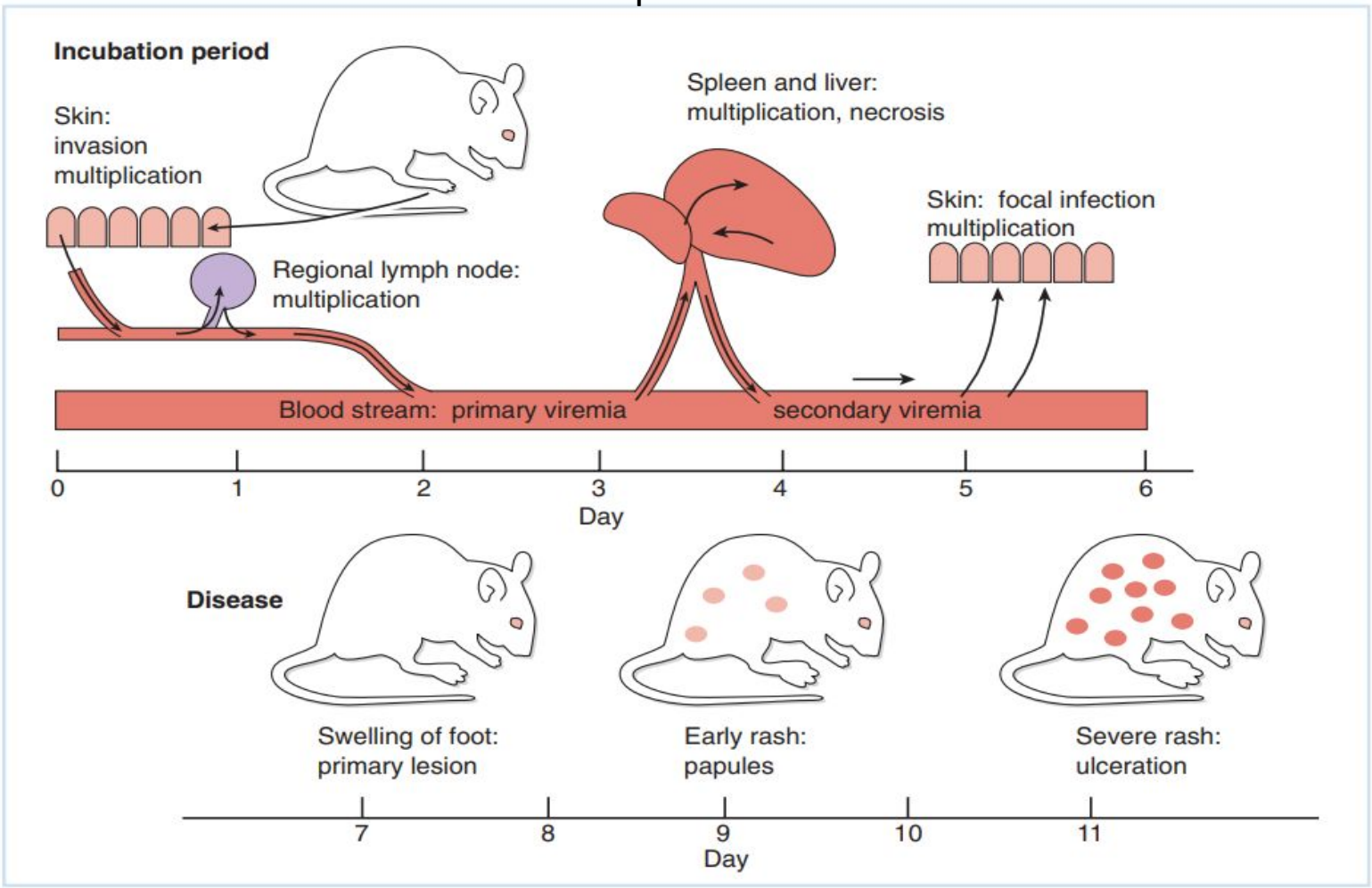
The host response to infection can be determined (in part, at least) by measuring

- the animal's production of antibodies and other immune factors directed against the infecting virus.



Mice as a model for poxvirus infection

Mouse pox- 1950s



subcutaneous injection of the footpad,

>virus yields in various organs,
> antibody titer,

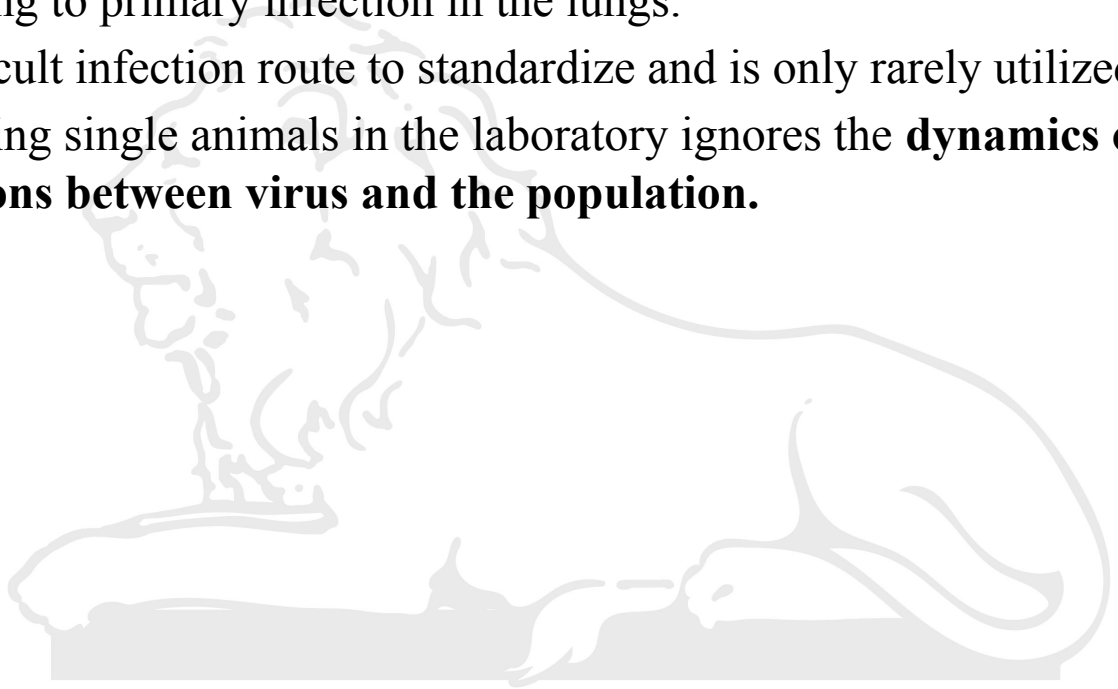
- rash scored
- Animal sacrificed and organ system assayed

Figure 3: The course of experimental poxvirus infection in laboratory mice. (Basic Virology, 3rd Edition)

Mice as a model for poxvirus infection

Limitations:

- It does not completely describe **virus infection in the wild**. An example of a significant deviation from one "natural" mode of infection is when poxvirus is transmitted as an aerosol, leading to primary infection in the lungs.
- This is a difficult infection route to standardize and is only rarely utilized.
- Also, examining single animals in the laboratory ignores the **dynamics of infection and the interactions between virus and the population.**



Rabies virus

- One of the puzzles of rabies virus infection is the very long incubation period of the disease.
- it is clear that animals (or humans) infected with the virus can be vaccinated *after* infection and still mount an effective immune response.
- The footpad of several experimental animals was injected with virus at day 0 and then the inoculated foot was surgically removed from different groups at days 1, 2, 3, and so on, after infection. Mice whose foot was removed as long as 3 weeks after infection survived without rabies, but once neurological symptoms appeared, the mice invariably died. Since removal of the foot saved the mice, it is clear that the virus remained localized there until it invaded the nervous system.
- Viral load: (Mice reinoculation CNS -12-24 hrs but in rabid wild animal takes as long as a week to 10 days)

Mice as a model for Rabies infection

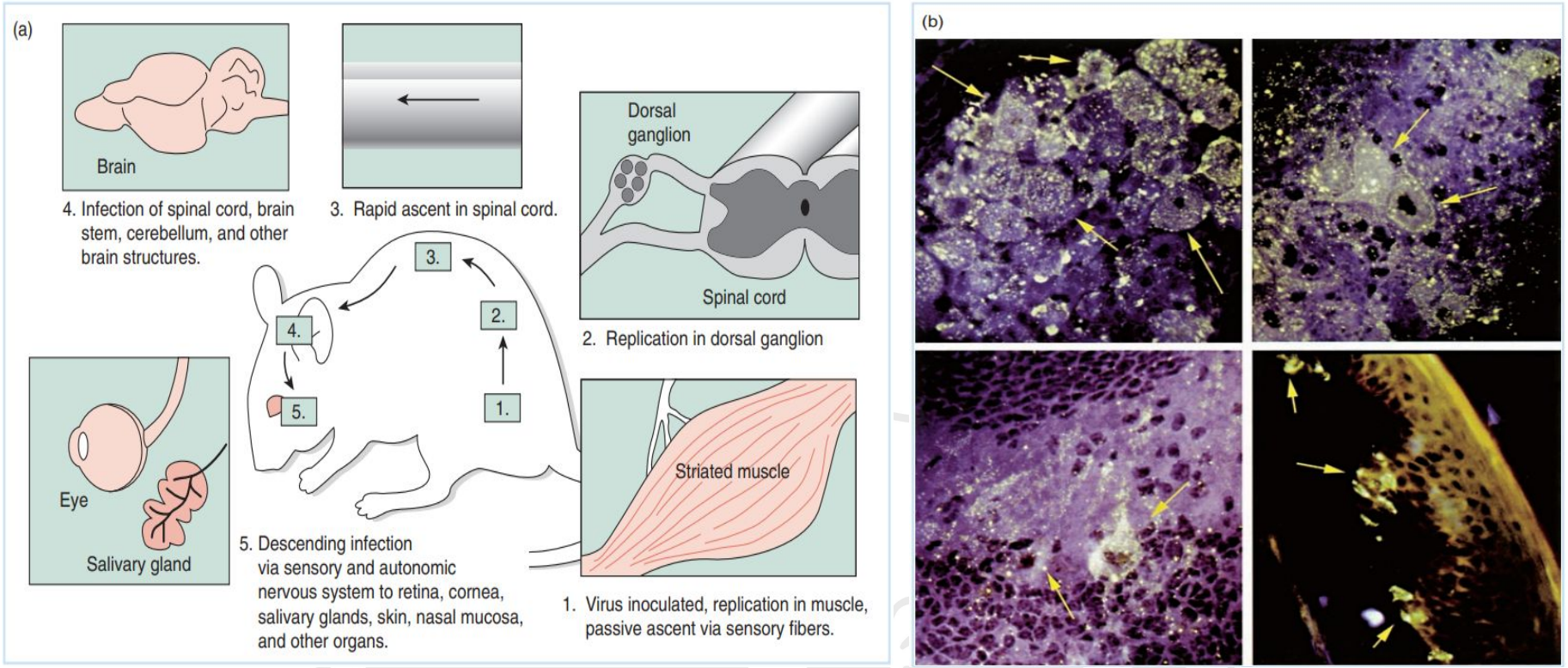


Figure 4: Visualization of rabies virus-infected neurons in experimentally infected animals. (a) A schematic representation of the pathogenesis of rabies in an experimentally infected laboratory animal. (b) Immunofluorescent detection of rabies virus proteins in neurons of infected animals. (Basic Virology, 3rd Edition)

Mice as a model for HSV infection

Herpes simplex virus: type 1 (facial, HSV-1) and type 2 (genital, HSV-2).

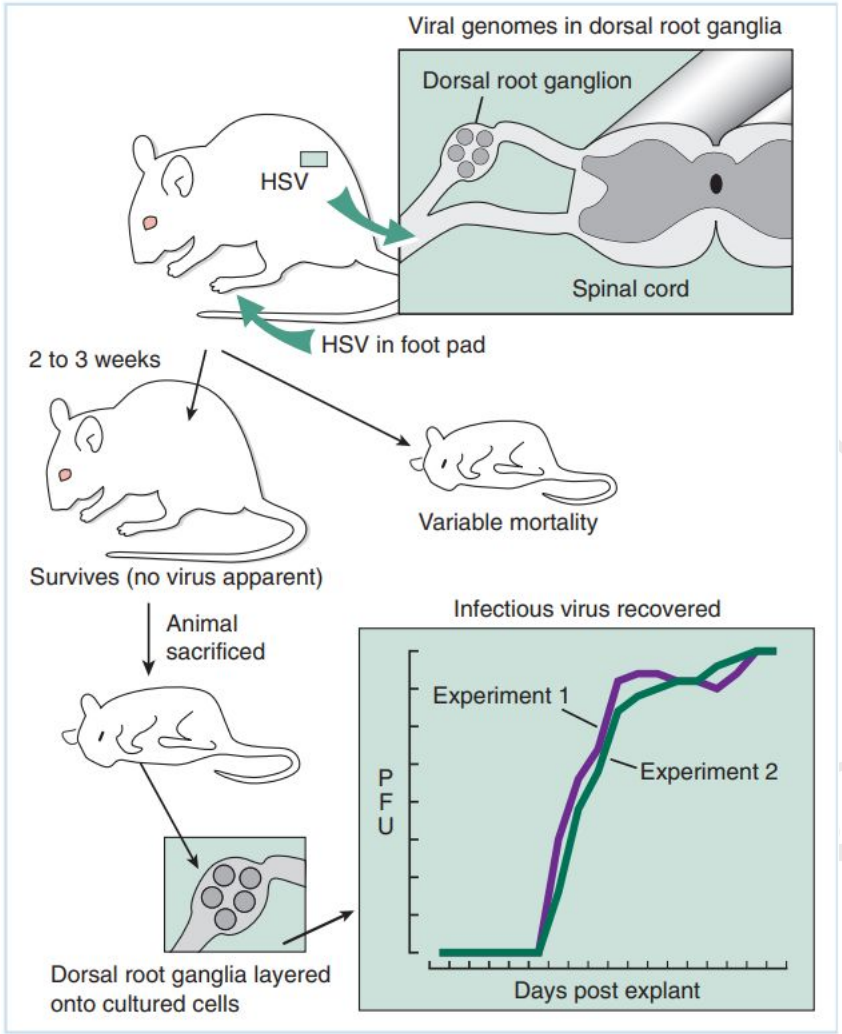


Figure 5: Analysis of the establishment and maintenance of latent HSV infections in mice. (Basic Virology, 3rd Edition)

Mice do not clinically reactivate HSV, the physiological process of reactivation, where virus can be recovered at the site of initial infection, cannot be effectively studied in mice.

During this **latent** infection, no infectious virus can be recovered from nerve tissue, but if the nerve ganglia are **explanted** (dissected, dissociated and maintained on a **feeder layer** of cultured cells), virus will eventually appear and begin to replicate.

Rabbit and Guinea pig models (for HSV better reactivation occurs)

- Infection of **rabbit eyes with HSV** leads to localized infection and recovery. The rabbits maintain virus in their **trigeminal ganglia**, and viral DNA or virus or both can be recovered using methods described for the murine model. Unlike mice, **rabbits spontaneously reactivate HSV** and virus occasionally can be recovered from the rabbit's tear film.
- **Rabbits**, because HSV can reactivate in them, are vital to the design of experiments to **investigate induced reactivation**, although they are more expensive to purchase and keep than mice.

- **Guinea pigs** are favored experimental animals for the study of infection and disease because they are **readily infected with many human pathogens**. They are an important model for the study of **HSV-2,** which cannot be studied effectively in the murine and rabbit models just described.
- Guinea pigs can be infected vaginally with inoculation of virus, and following a localized infection, latency can be established. As occurs in the murine and rabbit models, virus or viral DNA can be recovered from latently infected neurons (those enervating the vaginal area in this case\

Chapter 4

Human viral diseases

Dynamics of the virus–host interaction

- **The stable association of viruses with their natural host places specific constraints on the nature of viral disease and mode of persistence**
- Viruses are maintained by active rounds of infection somewhere in **their reservoir**. **Virus infection leading to immunity to reinfection will lead to virus extinction in a small population once the pool of susceptible individuals is exhausted**.
- **Virus infection directly or indirectly leads to death of a large enough number of individuals, the host population may become extinct.** Clearly, a virus, which can only replicate within that population, will also become extinct.
- These limitations, which can be described with precision using the mathematics of population biology and epidemiology, lead to a number of evolutionary constraints on the **dynamics of the virus–host interaction.**
- Notably **a number of viruses using RNA as their genetic material, have a broad host range and can readily jump from one species of host to another**. With such a virus, the constraints on the mortality of the disease caused in the novel or ancillary target population do not exist. It is not particularly surprising, then, that mortality rates of some diseases caused by zoonotic viruses are quite high, **e.g. Influenza, SARS.**

Patterns of Some Viral Diseases of Humans

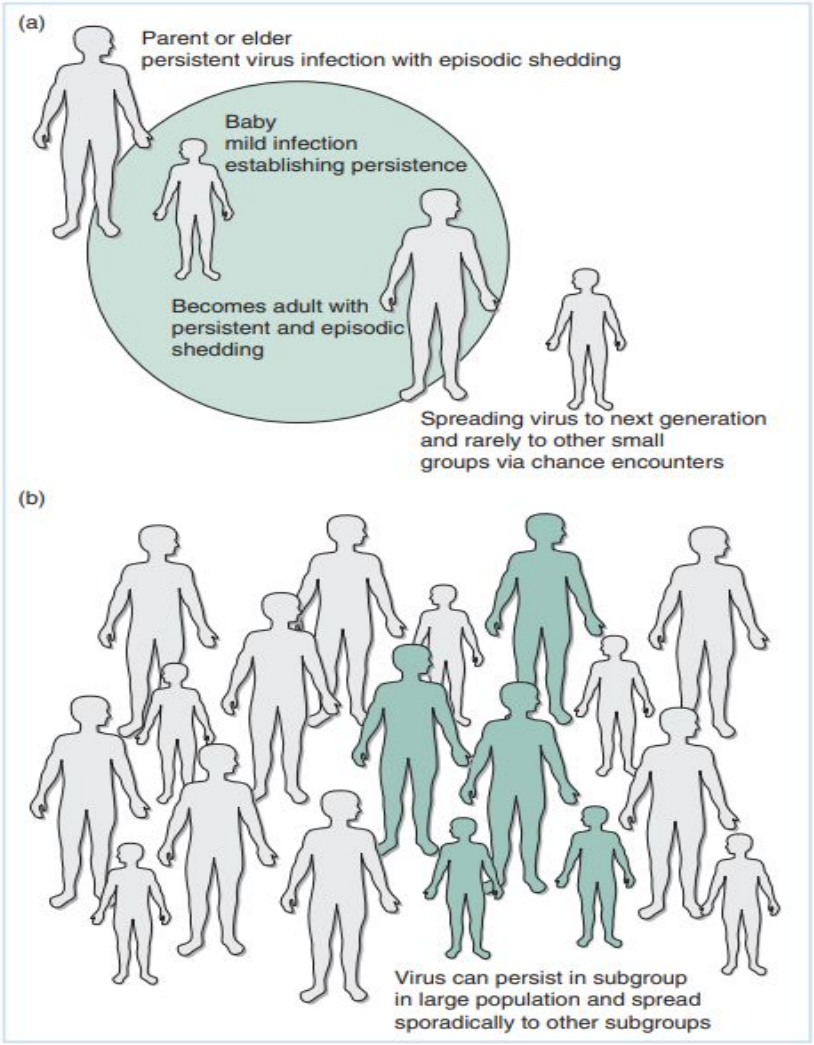


Figure 6: Virus maintenance in small and large populations. (Basic Virology, 3rd Edition)

1. Narrow host range to infect just one species or type of host. (expected to have low mortality otherwise host will get extinct) (HSV-1 and HSV-2: Humans are the only natural **reservoirs**, and no vectors are involved in transmission, **Latency,** HSV mother to fetus)

2. A number of viruses using RNA as their genetic material (no RT and no host integration-evolutionary pressure), have a **broad host range** and can readily jump from one species of host to another.
>With such a virus, the constraints on the mortality of the disease does not exist (therefore for **zoonotic viruses-high mortality** generally)

Incubation time more than lifespan of host (mortality no issue for virus to survive in a population) – virus survives

Rabies virus

- Rabid animals are the only source of infection. Virus is shed in the saliva some days before the onset of clinical signs and transmitted through a bite or a scratch to the skin or mucous membranes.
- Average incubation period in cats is 2 months, but may vary from 2 weeks to several months, or even years.
- Incubation period in dog 2 weeks to 4 months
- Humans: incubation period days to 2 yrs (Confirmed rabies has occurred as long as 7 years after exposure, but the reasons for this long latency are unknown)

Viral diseases leading to persistence

- We have seen that **two basic** patterns occur in the course of virus replication in humans – persistent infections with **incomplete virus clearing**, **and acute infections with efficient virus clearing** upon recovery from the acute infection.
- It might be argued that **persistent infections (immunocompromised)** represent associations between virus and host that have stabilized over time, such that the viruses are maintained within the host population without a large negative effect.
- Conversely, **acute infections** may involve viruses that have recently moved from a different host. In the case of humans, such viruses may originate from zoonotic infections.
- While influenza A viruses and hantaviruses are examples that support this model, human rhinoviruses, among others, would not, since there are no known animal reservoirs.

Viruses infecting humans

Virus group	Genome	Primary reservoir	How long associated with humans	Virus type	Acute disease	Primary infection	Mortality rate	Persistent/ latent?	Reactivation	Chronic disease/ complications
Herpesvirus	DNA	Humans	Ancient	HSV-1	Facial lesion	Epidermis	Nil	Yes	Frequent at site	Encephalitis (rare)
				HSV-2	Genital lesion	Epidermis	Nil	Yes	Frequent at site	Encephalitis (rare)
				VZV	Chickenpox	Epidermis	Nil	Yes	Once	Shingles/ disseminated infection upon immune suppression
				HCMV	Mononucleosis	Hematopoietic tissue	Nil	Yes	Asymptomatic/ infrequent?	Disseminated infection upon immune suppression/ retinitis
				EBV	Mononucleosis	Lymphoid tissue	Nil	Yes	Asymptomatic/ infrequent?	Lymphoma/ carcinoma
				HHV-6	Roseola	Lymphoid tissue	Nil	Yes	Asymptomatic/ infrequent?	?
				HHV-7	?	Lymphoid tissue	Nil	Yes	Asymptomatic/ infrequent?	?
				HHV-8	?	Lymphoid tissue	Nil	Yes	Asymptomatic/ infrequent?	Kaposi's sarcoma
Polyomavirus	DNA	Humans	Ancient	JC	None	Kidney/bladder	Nil	Yes	Infrequent shedding?	Encephalitis upon immune suppression
				BK	None	Kidney/bladder	Nil	Yes	Infrequent shedding?	Kidney infection
Papillomavirus	DNA	Humans	Ancient	>60 types	Warts	Epidermis	Nil	Yes	Constant shedding at site	Cervical carcinoma (types 6, 11, 16, and 18)
Adenovirus	DNA	Humans	Ancient?	>12 types	Mild respiratory	Respiratory tract	Nil	Yes	Infrequent shedding?	?
Poxvirus	DNA	Humans	Recent	Variola	Smallpox	Epidermis	Moderate to high	No	N/A	None

Table 2: Viruses infecting humans. (Basic Virology, 3rd Edition)

Viruses infecting humans

Virus group	Genome	Primary reservoir	How long associated with humans	Virus type	Acute disease	Primary infection	Mortality rate	Persistent/ latent?	Reactivation	Chronic disease/ complications
Orthomyxovirus	RNA	Birds, pigs	Sporadic/ current	Influenza A	Influenza	Respiratory tract	Usually low/ rare high	No	N/A	None
		Humans	Sporadic/ current	Influenza B	Influenza	Respiratory tract	Nil			None
Coronavirus	RNA	Humans	?	Human coronavirus	Cold	Nasopharynx	Nil	No?	N/A	None
		Palm civets	Current	SARS	Acute respiratory failure	Respiratory tract	Moderate to high	No	N/A	None
Picornavirus	RNA	Humans	Recent ?	Poliovirus	None to mild digestive upset	GI tract	Nil	No	N/A	Paralysis
		Humans	Recent ?	Hepatitis A virus	Hepatitis	Liver	Low	No	N/A	Rare
		Humans	?	Rhinoviruses	Cold	Respiratory tract	Nil	No?	N/A	None
Hepevirus	RNA	Humans	?	Hepatitis E	Hepatitis; severe in newborns	Liver	Nil, except pregnant women; moderate in newborns	No	N/A	Rare
Flavivirus	RNA	Birds	Sporadic/ current	West Nile	Encephalitis	Brain	Low	No	N/A	Neurological
		Primates	Sporadic/ current	Yellow fever	Encephalitis	Brain	Moderate	No	N/A	Neurological
		Humans	?	Hepatitis C virus	Hepatitis	Liver	Low	Occasional	Chronic hepatitis with no virus shedding	Liver failure/ carcinoma
Rhabdovirus	RNA	Carnivores	Sporadic/ current	Rabies	Encephalitis	Brain	100%	No	N/A	N/A
Togavirus	RNA	Horses	Sporadic/ current	Equine encephalitis virus	Encephalitis	Brain	Low	No	N/A	Neurological

Table 2: Viruses infecting humans. (Basic Virology, 3rd Edition)

Viruses infecting humans

Virus group	Genome	Primary reservoir	How long associated with humans	Virus type	Acute disease	Primary infection	Mortality rate	Persistent/ latent?	Reactivation	Chronic disease/ complications
		Humans?	?	Rubella virus (German measles)	Rash	Skin/developing nerve tissue	Nil in adults; severe neurological symptoms in developing fetus	No	N/A	Fetal infection
Paramyxovirus	RNA	Carnivore?	Recent	Measles	Rash	Respiratory tract	Low/moderate	Yes/no	Chronic virus antigen present/no infectious virus	SSPE
		Human	?	Mumps	Glandular inflammation	Respiratory tract	Nil	No	N/A	Infertility
		?	?	Respiratory syncytial virus	Mild respiratory in adults	Nasopharynx	Nil in adults	Yes	Virus shed from nasopharynx	Infections of newborns
Hepatitis delta	RNA	Humans	?	Hepatitis D	Hepatitis	Liver	Usually low but infection with hepatitis B leads to acute liver failure	Yes	Virus antigen present and infectious in blood	Liver failure
Bunyavirus	RNA	Mosquitoes	?	LaCrosse encephalitis virus	Encephalitis	CNS	Low; more severe for children	No	N/A	None
		Rodents	?	Hantavirus	Severe respiratory failure	Respiratory tract	Moderate especially in young adults	No	N/A	Respiratory failure
Hepadnavirus	RNA/DNA	Humans	?	Hepatitis B	Hepatitis	Liver	Low	Yes	Virus antigen present and infectious in blood	Liver failure/ carcinoma
Retrovirus/RNA tumor virus	RNA/DNA	Humans	Ancient	Human T-cell leukemia	None	Lymphoid tissue	Nil?	Yes	Infectious virus shed?	Lymphoma/ paraparesis
Retrovirus/ lentivirus	RNA/DNA	Chimpanzees/ mangabeys	1930 +/–20 years?	HIV-1/HIV-2	None/influenza or mononucleosis like symptoms	Lymphoid tissue	100%	Yes	Infectious virus shed	Immunodeficiency

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Classification of human disease-causing viruses according to virus–host dynamics

- 1. **Acute infections followed by virus clearing**

  >Severe infections: points to zoonosis (SARS-CoV2)

  > Influenza (bird, pigs, human)

  > Hanta (rodents?) – 50% fatality;

  > WNV (Avian and insect) - encephalitis

- 2**. Persistent viral infections incomplete virus clearing**

  > Viruses maybe constantly shed while persistent infections with some viruses leads to loss of any detectable virus.

  > HSV, human papilloma virus (HPV); hepatitis B and hepatitis D viruses – chronic infection leading to liver damage

  >Associations between virus and host that have stabilized over time, such that the viruses are maintained within the host population without a large negative effect

  > Human Rhinovirus – common cold (human only reservoir)

Viral diseases leading to persistence

- A number of important human viruses are either **asymptomatic or cause relatively mild symptoms** of primary infection which is followed by a stable association between virus and host that lasts as long as the latter lives.

- During this more or less stable association some viruses are **constantly shed** while persistent infections with others leads to loss of any detectable virus. In the latter case, various types of stress to the host can lead to viral recrudescence (reappearance of infectious virus along with mild or no symptoms) with the **potential for virus spread to other individuals.**

Viral diseases acute and severe infection

- Those viruses characterized by an **acute, severe infection with variable or high mortality** rates **suggests a virus that has either a primary reservoir other than humans (a zoonosis)** or has recently "jumped" from such a reservoir to establish and maintain itself in the human population.

- Influenza A virus: Primary reservoir for this virus is birds, but its broad host range allows it to establish secondary reservoirs in pigs as well as humans.

- The great worldwide epidemic of **influenza (H1N1)** in **1918–19** (also called a pandemic) was the result of a direct transmission of the virus from birds to humans, with subsequent mutation to allow human to human spread.

- Numerous other examples of zoonotic viruses associated with severe human disease exist. The recent **COVID 19 pandemic is caused due to SARS CoV 2**, which has jumped from different animal species to humans.

Viral diseases HIV: zoonosis

The most devastating virus introduced into the human population from a zoonosis in recent time is the human immunodeficiency virus, HIV, which is the causative agent of AIDS.

- There are two types of HIV, which differ in sequence by 25%. Both types of virus have been shown to be **closely related** to **retroviruses carried asymptomatically in nonhuman primates in West Africa** and clearly entered the human population through contact with such animals, probably in their use as a delicacy in local cooking.
- The virus is spread through **sexual contact and intravenous drug usage.**
- Human (bad) behavior has favored its establishment as a formidable threat to public health, especially in the third world.

Patterns of special viral diseases of human

Acute infections followed by virus clearing:

- **Viruses spread as aerosols : Cold viruses (rhinoviruses, adenoviruses, and coronaviruses).** Infection is localized within the nasopharynx, and recovery involves immunity against that specific virus serotype.
- The vast array of different cold viruses and serotypes ensures that there will always be another one to infect individuals. Although generally these types of respiratory diseases are mild, infection of an immune-compromised host or a person having complications due to another disease or advanced age can lead to major problems.

Influenza

- The epidemiology of influenza is an excellent model for the study of virus spread within a population. While symptoms can be severe, in part due to **host factors, the virus infection is localized, and the virus is efficiently cleared from the host**.
- Flu viruses have evolved unique mechanisms to ensure constant generation of genetic variants, and the constant appearance of new influenza virus serotypes leads to periodic epidemics of the disease.
- Some strains of the virus cause more severe symptoms with accompanying complications than others. At least one strain, the **Spanish strain of 1918 (H1N1),** caused a worldwide epidemic with extremely high mortality rates.

Persistent viral infections

Persistent viral infections often indicate a long history of coevolution between virus and host, the lack of serious consequences to the vast majority of those infected does not mean that debilitating or lethal consequences are not possible.

- This is especially the case in situations where the immune system of the infected individual is compromised or has not yet developed.

Herpesvirus infections and latency:

- hallmarks of herpesvirus infections are an initial acute infection followed by apparent recovery where **viral genomes are maintained in the absence** of infectious virus production in specific tissue.
- Latency is characterized by **episodic reactivation (recrudescence)** with ensuing (usually) milder symptoms of the original acute infection. Example viruses include **HSV, Epstein–Barr virus , and Varicella-zoster virus.**

Persistent viral infections

- In a latent infection, the **viral genome** is maintained in a **specific cell type** and does not actively replicate.

  HSV maintains latent infections in **sensory neurons**

  Epstein–Barr virus maintains itself in **B lymphocytes**.

  (EBV, is one of the most common human viruses in the world. It spreads primarily through saliva. EBV can cause **infectious mononucleosis, also called mono, and other illnesses**. Most people will get infected with EBV in their lifetime and will not have any symptoms, however: linked to cancers and autoimmune disorders)

- Latent infections often require the expression of specific virus genes that function to ensure the survival of the viral genome or to mediate the reactivation process.
- Such a decline can be triggered by the **host's reaction to physical or psychological stress**. **HSV reactivation** often correlates with a **host stressed by fatigue or anxiety.**
- **Varicella-zoster virus** reactivation leads to shingles, a very painful recrudescence throughout the **sensory nerve net serving** the site of the latent virus.

Other complications arising from persistent infections

- **Persistent infections** caused by some viruses can (rarely) **lead to a neoplasm (a cancerous growth) due to continual tissue damage and resulting in mutation of cellular genes controlling cell division (oncogenes or tumor suppressor genes).**
- Examples include infections with slow transforming retroviruses such **as human T-cell leukemia virus (HTLV), chronic hepatitis B and hepatitis C** infections of the liver, certain **genital papilloma virus infections**, and **EBV infections**. The latter require the additional action of auxiliary cancer-causing factors (co-carcinogens).
- Autoimmune diseases such as **multiple sclerosis (MS)** are thought by many investigators to result from an **abnormal immune response to viral protein antigens** continually present in the body due to a persistent infection. Such persistent infections need not result in the reappearance of infectious virus.
- For example, infection with **measles virus** usually leads to rash and recovery although portions of viral genomes and antigens persist in certain tissues, including neural tissue.

Viral and subviral diseases with long incubation periods

Rabies:

- Some viral diseases have very **high mortality rates** despite their being well established in a population. With rabies, for example, injection of virus via the saliva of an animal bearing active disease leads to unapparent early infection followed by **a long incubation period.**
- **During this time**, the infected animal is a walking "time bomb." The symptoms of disease (irritability, frenzy, and salivation) are all important parts of the way the virus is **spread among individuals.**
- The very long incubation period allows animals bearing the disease to carry on normal activities, even breed, before the symptoms almost inevitably presaging death appear. A hypothetical viral infection that might lead to these physiological and behavioral changes but that resulted in a quick death could not be spread in such a way.

HIV–AIDS:

- AIDS, which is characterized by a latent period in which HIV can be transmitted, followed by severe disease, is an example of a "new" viral disease. In humans, virus spread is often the result of behavioral patterns of infected individuals during HIV's long latent period. This pattern of spread makes it unlikely that there is any selective pressure over time toward amelioration of the late severe symptoms.

Viral infections of the liver (viral hepatitis)

- The liver hold a special place in many types of medicine, both because of the **important physiological role** of this organ and because all circulating blood and lymph pass through the liver frequently.
- A number of different and unrelated viruses target the liver; these are collectively known as **hepatitis viruses**. All hepatitis viruses cause liver damage that can be devastating to the infected host.
- Currently, there are five reasonably well-characterized human **hepatitis viruses: A, B, C, delta (D), and E.**

Hepatitis A:

- This virus is related to poliovirus. It is spread by contaminated water or food, and causes a potentially severe but controllable loss of liver function and general malaise. Proper medical care will generally result in full recovery of liver function and full clearance of virus from the host, with effective immunity against reinfection. A relatively effective hepatitis A vaccine is available for individuals at risk of infection.

Viral infections of the liver (viral hepatitis)

Hepatitis B

- **Hepatitis B** virus is related to but clearly distinct from **retroviruses**.
- Unlike the situation with hepatitis A, the B virus is spread mainly through blood, either during sexual activity or during other **blood contamination events (sharing of needles, for instance),** and primary infection is followed by persistent viremia and liver damage.
- Hepatitis B infection is a special risk to medical personnel owing to the possibility of transmission by needle stick from contaminated blood, and is also a virus endemic among **intravenous drug users, commercial sex partners, and their customers**. The disease is endemic in Southeast Asia where the virus can be spread from mother to infant by birth trauma.
- Hepatitis B virus infection can lead to acute disease with attendant liver failure or can be asymptomatic. In many cases, virus is completely cleared leading to full or partial recovery of liver function. Unfortunately, a large number of infected individuals go on to become asymptomatic chronic carriers of the virus.
- Indeed, **chronic hepatitis B infections** are a leading factor in certain human liver cancers (carcinomas) prevalent in Southeast Asia. A third form of the hepatitis B virus infection (fulminant infection) is marked by **rapid onset of extensive liver damage and often death.**

Viral infections of the liver (viral hepatitis)

Hepatitis C

- Hepatitis C virus is caused by a virus that, at first, seemed to have some general relationships to a large group of plant, animal, and bacterial viruses, including poliovirus and hepatitis A virus. However, it has been determined that this virus is a member of the Flaviviridae.
- The virus is **transmitted by contaminated blood and blood products**, and is thought to cause as much as **25% of acute viral hepatitis worldwide**.

Hepatitis D

- **Hepatitis delta (D)** virus is a defective virus in that it cannot replicate without the **aid of another virus, the hepatitis B virus.**
- Despite this requirement, it is not particularly prevalent in Southeast Asia, a major center of hepatitis B infection. Hepatitis D and B coinfection in the same individual does not lead to a much higher incidence of acute or chronic liver disease than does infection with hepatitis B virus alone. By contrast, hepatitis D virus infection of a person previously infected with hepatitis B virus is often correlated with acute disease followed by chronic virus secretion and cirrhosis of the liver.

Viral infections of the liver (viral hepatitis)

Hepatitis E

- Like hepatitis A virus, hepatitis E virus is spread by contaminated water and possibly by food. It is found throughout the world and has caused significant epidemics in India and Russia through problems with drinking water.
- The disease caused by this virus is usually mild, but can **have high mortality rates in pregnant women.** Recovery from acute infection is generally complete, and there is no evidence of chronic infection following the acute phase.

Reference

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