VIRUSES CAUSING HUMAN DISEASES

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I. EPIDEMIOLOGY OF VIRUSES

Epidemiology studies the distribution and dynamics of diseases and factors influencing their occurrence in populations. It examines how virus characteristics, host susceptibility, and environmental factors impact infection risk. By analyzing quantitative data, virus epidemiology seeks to understand disease patterns, identify outbreak sources, develop prevention strategies, and explore the role of viruses in disease. It also aids in evaluating transmission modes and testing vaccines and treatments on a large scale.

II. DEFINITIONS

1. **Epidemics:** Disease outbreaks that occur in a specific community or region, and they exceed the normal or expected rate of occurrence. The Ebola outbreak in West Africa in 2014-2016, resulted in thousands of deaths and spread across multiple countries. The Zika virus outbreak in Brazil in 2015-2016, led to a significant increase in cases of microcephaly and other birth defects.

2. **Endemics:** Endemic diseases are those that are consistently present in a particular geographic area or population. They occur at a relatively stable rate and are considered part of the normal environment. Malaria in sub-Saharan Africa is endemic due to the presence of the Anopheles mosquito vector and suitable environmental condition. The endemic Dengue fever cases in parts of Southeast Asia occur regularly during the rainy season.

3. **Pandemics:** Pandemics are global outbreaks of a disease that spread across multiple countries or continents, affecting a large number of people. Examples include- the Spanish flu pandemic of 1918-1919, which infected an estimated one-third of the world's population and resulted in tens of millions of deaths. The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, began in late 2019 and led to widespread illness, death, and significant societal disruption worldwide.

III. SURVIVAL STRATEGIES ADAPTED BY VIRUS IN THE HOST CELL

Viruses rely on continuous transmission between living cells for their survival, with disease occurrence not always necessary. Infections may be symptomatic or asymptomatic, with the latter often more abundant and facilitating viral spread. Epidemiologists identify three survival patterns (Table 13) in mammalian hosts:

- Acute infections without reservoirs
- Persistent infections with human reservoirs, and
- Those involving animal reservoirs

Table 1: Survival Strategies Adapted by Virus in the Host Cell

Infecton		**Survival Strategies**	**Examples**
Acute infection (self-limiting)	Long-lasting immunity	No reservoir; requires sustained transmission within a large population	Measles, mumps, rubella, polio, hepatitis A, enteroviruses, dengue
	Transient (short-term) immunity	No reservoir; reinfections observed, virus can persist in smaller populations	RSV, rotavirus, influenza, coronaviruses, rhinoviruses
Persistent infection	Periodic viral replication (with or without shedding)	Human reservoir; infected individuals can serve as lifelong carriers of the virus	HSV, varicella-zoster, CMV, EBV
	Continuous replication	Human reservoir; infected individuals can act as a persistent source of the virus throughout their lives.	HIV, HBV, HCV, Human T lymphotropic virus-1 (HTLV-1), HPV
Zoonotic infection	No human to human spread	Survival relies on maintaining enzootic infection within an animal reservoir and subsequent transmission to humans.	Most arboviruses except dengue, yellow fever (urban cycle). Avian influenza, rabies, Hendra
	Human to human spread with strong significance	Survival relies on maintaining enzootic infection within an animal reservoir and subsequent transmission to humans.	Marburg/Ebola, Hantaan, Nipah, dengue, yellow fever (urban cycle)

Most viral infections in humans are acute and self-limiting. Viruses that cause systemic infections and provide lifelong immunity typically require large, densely populated areas for optimal transmission. In contrast, viruses causing superficial mucosal infections with temporary immunity can persist in smaller populations and more contained environments, often aided by antigenic drift.

Virus Transmission: Transmission cycles involve virus entry, replication, shedding, and dissemination to new hosts. Horizontal transmission is the most common mode among at-risk populations. Virus shedding typically occurs from body openings or surfaces involved in viral entry. In localized infections, entry and exit occur at the same site, while generalized infections may use various shedding modes. Viruses like hepatitis B, HIV, and cytomegalovirus are shed from multiple sites, including semen, cervical secretions, milk, and saliva. The amount of shed virus is crucial for transmission; low concentrations may be negligible unless in large volumes, while some viruses can transmit with less than 1 µl of material.

1. Respiratory Droplets

- Respiratory viruses are shed as aerosols during coughing, sneezing, while systemic infections like measles, chickenpox, and rubella shed viruses from the respiratory tract.
- Some viruses (HSV, CMV, and EBV) are shed into the oral cavity and transmitted through activities like kissing.
- Aerosols are most infectious during peak virus replication. Respiratory virus spread involves three components:
  - ❖ **Small-Droplet Aerosols (<10 µm)** causing rapid outbreaks and distant transmission
  - ❖ **Large-Droplet Aerosols (10 to 100 µm)** requiring closer contact, and
  - ❖ **Fomite Transmission** from contaminated objects to respiratory tracts, particularly in poor hygiene conditions.
- Airborne transmission can originate from environmental sources like virus-contaminated dust (arenavirus) or aerosols carrying infected urine from rodents (arenaviruses) or bats (rabies).
- However, most respiratory viruses, being enveloped, are not robust and cannot survive for long periods outside the body unless they remain moist in secretions.

2. Gastrointestinal Transmission

- Enteric viruses are released in feces and vomit, with higher fluid output leading to increased environmental contamination, these viruses can survive longer.
- Two distinct epidemiological patterns associated with enteric virus transmission:
  - ❖ **Point source outbreaks-** Multiple individuals consume contaminated food or water (observed at weddings). This is commonly linked to the consumption of items such as salads, raw shellfish, or water from unsafe sources contaminated with sewage.
  - ❖ **Person-to-person transmission via the fecal-oral route-** Progress gradually, especially in households lacking adequate sanitation facilities, running water, or education. This mode of transmission is characterized by poverty and hygiene.

3. Skin Contact

- Intact skin is an effective barrier against virus entry, with minimal virus shedding. Systemic blood-borne infections do not pose transmission risk through intact skin.
- Minor skin abrasions are significant for transmission through direct contact (molluscum contagiosum, HPV warts).
- Blood-borne infections can be transmitted through bleeding from broken skin, with hepatitis B showing potential for horizontal transmission.
- Poxviruses like cowpox, vaccinia, orf, and pseudocowpox can spread between animals and humans through contact with skin lesions.
- Transmission of rabies virus and B virus (Macacine herpesvirus 1 or herpesvirus simiae) can occur through the skin via the bite of an infected animal.

4. Blood-Borne Transmission

- Viremia (presence of viruses in bloodstream) serves as a significant pathway for virus dissemination both within individual hosts and between hosts.
- Hepatitis B, C, and D viruses, HIV, and HTLV are transmitted through blood transfusions, prompting rigorous testing of donated blood to mitigate risks.
- Blood-borne transmission is more prevalent among intravenous drug users, primarily due to contaminated needles and paraphernalia.
- Blood serves as the primary source from which arthropods acquire viruses during blood meals, such as mosquitoes, ticks, and sandflies.
- In contrast, some arthropods like horseflies passively transmit viruses through contamination of their mouthparts during interrupted blood feeding on multiple hosts.

5. Urogenital (Sexual) Transmission

- Viruses can be present in semen or vaginal secretions. Sexual transmission of virus infections through mucosal contact is efficient due to the virus's moisture retention and lack of need for long-term survival outside the body.
- Key examples of sexually transmitted viruses include HIV, HBV, human papillomavirus, and herpes simplex type 2, alongside other herpesviruses, hepatitis B, and HTLV I, which also spread easily through sexual contact.
- Viruria (presence of virus in urine) persists throughout the lifespan of rodents infected with arenaviruses, serving as the primary mode of contamination by these viruses.
- However, while certain human viruses like mumps and cytomegaloviruses replicate in kidney tubular epithelial cells and are shed in urine.

6. Other Routes

- **Opthalmic Transmission:** Virus infection can reach the eye through various routes, including contact with contaminated fingers (e.g., herpes simplex, vaccinia), exposure to infected swimming pools (adenoviruses), use of inadequately sterilized ophthalmic equipment (adenoviruses, prions), inhalation of aerosols (enterovirus 71), or systemic infection leading to bloodstream transmission (measles).

- **Breast Feeding:** Certain viruses, such as cytomegalovirus, HIV-1, and HTLV-1, can be excreted in breast milk, potentially transmitting the infection to newborns. Despite the risk of transmission through breastfeeding, it may still be recommended in situations where infectious diseases or malnutrition pose significant threats to infant health, even though the risk is comparatively smaller than vertical transmission during childbirth.

No virus is shed from the brain or other internal organs that lack communication with body openings or surfaces. However, replication in these internal organs often precedes shedding from other sites or infection of blood-sucking arthropods, contributing to the long-term survival of the virus in nature.

IV. ELEMENTS INFLUENCING THE DYNAMICS OF VIRAL INFECTIONS

1. **Virus Transmissibility:** Transmissibility depends on virus properties, shedding of virus and social interactions. Respiratory viruses (enveloped, less stable) spread through explosive sneezing or coughing and enteric viruses (non enveloped, stable on surfaces) shed in feces, contaminating surfaces. Socio-economic improvements have reduced childhood infections, but some diseases affect older age groups, potentially leading to multiple cases. Zoonotic diseases usually arise from close contact with animals or arthropod vectors.

2. **Seasonality:** Viral infections exhibit seasonal variations in both temperate and tropical climates. In temperate regions, arbovirus infections from mosquitoes and sand-flies are more common in summer, while tick-borne infections peak in spring and early summer. Respiratory infections, including RSV and influenza, peak in winter, and some childhood rash diseases peak in spring. Enteric virus infections vary, with enteroviruses peaking in summer, rotaviruses in winter, and caliciviruses lacking a clear seasonal pattern. In tropical regions, wet and dry seasons influence infection patterns. Measles and chickenpox peak late in the dry season, declining with the rainy season onset. Influenza and rhinovirus infections peak during the rainy season.

   Certain viruses, such as measles and influenza, thrive in low humidity, while others, like polioviruses and adenoviruses, do better in high humidity, aligning with seasonal prevalence. Changes in host susceptibility, possibly due to environmental factors like smoke exposure or indoor heating, also impact infection rates. Social activities significantly affect virus transmission. In winter, crowded indoor environments in temperate climates facilitate transmission, while monsoonal rains limit movement but increase transmission within families in smoke-filled dwellings. In urban areas, young children often introduce viruses into families, shedding larger amounts of virus as they lack developed immunological resistance.

3. **Threshold Community Size:** The survival of viruses causing acute, self-limiting infections relies on a large and dense susceptible host population. As individuals acquire immunity, the pool of susceptible hosts diminishes, potentially leading to the disappearance of these viruses from a population. Persistent viruses, however, can endure in small populations across generations. The critical community size needed to sustain transmission varies widely depending on factors like immunity duration and virus shedding patterns, illustrated by examples such as measles and chickenpox.

4. **Impacts of Immunity:** Immunity from prior infection or vaccination greatly affects the spread of viral diseases. Lifelong immunity, primarily from IgG antibodies, is common in generalized infections like measles and poliomyelitis. In contrast, mucosal infections in the respiratory tract have shorter-lived immunity. Viruses like rhinoviruses, coronaviruses, and enteroviruses cause recurrent colds due to a lack of cross-immunity between serotypes, relying on IgA antibodies in nasal secretions for protection. Most respiratory viruses shed briefly, but rhinoviruses can shed for up to three weeks, extending transmission.

   In isolated communities, respiratory diseases require a steady influx of susceptible individuals or new viral serotypes to persist. Arctic and Antarctic explorers remain free

from these illnesses until they re-establish contact with others, showing the role of repeated infections in maintaining population immunity. Antigenic shift (resulting from genetic reassortment) in influenza A, though less frequent than antigenic drift (accumulation of small mutations), can cause widespread epidemics due to the lack of immunity to the new virus.

5. **Chronic (Persistent) Infection**: Persistent viral infections, whether symptomatic or not, help in the perpetuation of viruses. Individuals with chronic infections can intermittently or continuously shed the virus, reintroducing it into populations. Herpesviruses particularly benefit from this transmission pattern, aiding their survival in small populations. The persistence of infection, disease production, and virus transmission are not always linked. Arenaviruses, for example, persist in rodent reservoir hosts without causing significant harm but maintain efficient transmission. In contrast, viruses like the measles virus in subacute sclerosing panencephalitis (SSPE) persist in the central nervous system and are lethal but not epidemiologically significant since they do not shed infectious virus.

6. **Non-Human Reservoir:** The regular reintroduction of infection from non-human sources, as seen in zoonoses, aids in the persistence of viruses in human populations and influences the spread and severity of these infections. Examples include various arboviruses, rabies, and hantaviruses. The level of human infection is influenced by the frequency of contact with the animal source and the prevalence of infection within that source. The presence and potential size of an animal reservoir are crucial factors when devising strategies for regional elimination or global eradication of any human viral disease.

7. **Arthropod Transmission:** Arthropod transmission, involving arboviruses, is the most ecologically complex virus transmission mode. These viruses replicate in both vertebrate hosts and blood-feeding arthropods like mosquitoes or ticks, causing asymptomatic infections, encephalitis, fever with joint and muscle pain, rash, and hemorrhagic fever. Arthropods acquire the virus from viremic animals or humans, with replication occurring in their gut and salivary glands before transmission to new hosts.

   This enables viruses to cross species barriers, with wild mammals or birds serving as reservoirs. Vertebrate hosts typically recover quickly and develop lasting immunity, while arthropods carry the virus for their short lifespan. Humans in areas with enzootic arboviruses are vulnerable, especially those without acquired immunity like tourists, soldiers, and forest workers. Arboviruses can overwinter through transovarial transmission in arthropods or possibly in hibernating vertebrates. Human activities such as population movements, deforestation, irrigation, urbanization, air travel, bird migration changes, and climate change can disrupt arbovirus life cycles and increase disease prevalence.

8. **Nosocomial/Iatrogenic Transmission:** Nosocomial transmission occurs within hospitals or clinics, while iatrogenic transmission refers to transmission caused directly by medical personnel. The 1976 Ebola virus outbreak in Zaire is a well-known example of both iatrogenic and nosocomial infection. Common examples of nosocomial virus infections include chickenpox, influenza, and respiratory syncytial virus, often spread through the respiratory route in healthcare settings. Hepatitis B and C viruses, as well as HIV, can be

transmitted by healthcare providers like doctors, dentists, acupuncturists, and tattooists, with attending staff and laboratory personnel also at risk through needle stick injuries. Factors such as infectious patients congregating in healthcare facilities and invasive procedures increase the risk of nosocomial transmission. Health professionals take particular care to prevent such transmission events.

V. EPIDEMIOLOGICAL ASSESSMENT

1. **Disease Incidence and Prevalence:** Comparison of disease occurrence across populations relies on rates, indicating events in a standard population size, e.g., 100,000. Incidence and prevalence are key rates used. Incidence measures events over time, crucial for acute diseases, while prevalence reflects current cases in a population. Attributes like age, sex, and immune status affect rates. Incidence accounts for both population size and time, often lower due to immunity and subclinical cases. Secondary attack rate gauges virus infectiousness. Prevalence captures disease frequency at a point in time, influenced by incidence and disease duration. Seroprevalence denotes antibody frequency in a population. Mortality rates categorize deaths from a disease, either cause-specific or case-fatality rate.

2. **Laboratory Diagnosis**

   - **Seroepidemiology:** Seroepidemiology (Figure 1) offers a more precise method than traditional disease surveillance by detecting antibodies in sera, enabling accurate assessment of virus prevalence and transmission. It correlates serological findings with clinical data to determine the ratio of clinical to sub-clinical infections, supporting public health policies. Utilizing various sources of human sera, such as blood banks and hospitals, seroepidemiology aids in evaluating immunization programs and investigating emerging viruses like HIV, HBV, and HCV. Additionally, it helps measure total infections, estimate their prevalence and incidence, analyze age-specific patterns, assess exposure risks, and identify natural reservoirs of infections. Sentinel animal studies, like using sentinel chickens, are employed to monitor seasonal arbovirus prevalence.

   - **Molecular Epidemiology:** Advancements in molecular epidemiology, facilitated by rapid sequencing techniques, enable the analysis and comparison of virus genome sequences to address key epidemiological inquiries. For instance, partial genome sequencing distinguishes poliovirus vaccine strains from wild strains and identifies changes indicating vaccine strain reversion. Sequencing also helps trace the geographical origins of viruses like West Nile virus, aiding in outbreak investigations. Moreover, genome sequencing assists in predicting virus sources, assessing drug sensitivity, and determining transmission routes, crucial for prompt response to emerging infections.

3. **Regular Surveillance:** Gathering accurate disease data demands significant effort and creativity. While population data are typically accessible, obtaining precise case information poses challenges. Some cases are legally mandated for reporting, but underreporting by physicians and individuals who refuse medical assistance is common. To address this, public health authorities establish sentinel practices and engage

diagnostic labs for integrated data collection. Information on infectious diseases is disseminated through platforms like CDC's Morbidity and Mortality Weekly Report (MMWR) and WHO's Weekly Epidemiological Record. Special surveillance programs target priority issues such as HIV/AIDS, influenza strains, and acute flaccid paralysis. Prompt responses to outbreaks involve task forces of experts, as seen in investigations of SARS, H5N1 avian flu, and Ebola outbreaks.

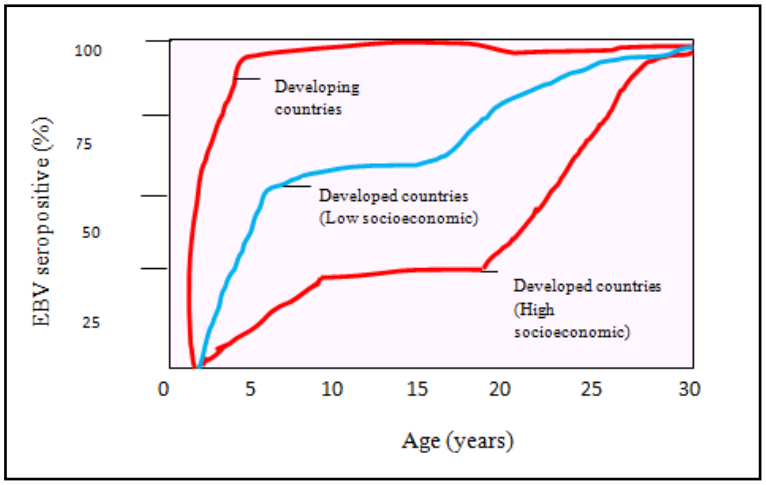

Figure 1: *The seroepidemiological analysis of Epstein-Barr virus infection concerning socioeconomic factors. The vertical axis depicts EBV antibody prevalence across age groups in three populations. [In developed nations with high socioeconomic status, transmission peaks occur among <1 to 5-year-olds and 15 to 25-year-olds, likely due to increased salivary contact]*

4. Epidemiological Case Studies

- **Cross-Sectional Study:** A cross-sectional study provides a rapid assessment of a population's prevalence for a specific marker. However, population heterogeneity can lead to skewed results, particularly if a small subgroup at high risk contributes most cases. For example, blood donors, often selected based on low-risk criteria, may not accurately represent the broader population. Age-specific prevalence rates offer deeper insights into virus transmission patterns and historical changes.

- **Case-Control Study:** A case-control study is retrospective, aiming to identify the cause of a disease by comparing cases with controls. Careful selection of both groups is essential to avoid bias, along with precise choice of questions and tests. For instance, it can determine if an enteric virus causes disease by comparing virus excretion rates between children hospitalized with gastroenteritis and age-matched controls hospitalized for other reasons.

- **Cohort Study:** Cohort studies, typically prospective, investigate a potential cause or risk (like a new treatment or vaccine) by tracking an exposed group over time to uncover significant associations such as disease outcomes or vaccine effectiveness. These studies involve ongoing data collection and require a well-matched control group. Despite being costly and time-consuming, they provide robust evidence for

cause-and-effect relationships, particularly in evaluating vaccine safety and understanding disease progression. The connection between rubella virus and congenital defects highlights the importance of both retrospective and prospective studies. In the early 1940s, Norman Gregg's observations of congenital defects in children whose mothers had rubella led to studies confirming this link, thus defining congenital rubella syndrome.

- **Human Volunteers:** The advancement in controlling viral diseases owes much to the participation of human volunteers. Early investigations into diseases like yellow fever, viral hepatitis, and respiratory infections depended on human subjects due to the absence of suitable animal models. Obtaining informed consent from volunteers, or their parents in the case of minors, has been imperative. Presently, governmental agencies closely regulate human subject research in most countries, with institutional review boards (IRBs) ensuring ethical oversight. Precautionary measures such as isolating subjects during studies help mitigate the risk of secondary transmission to others.

Mathematical Modelling: Mathematical modelling of epidemiology (Figure 14) involves mathematical equations and computational methods to study the spread and control of diseases within populations.

Table 2: Mathematical Modelling of Epidemiology

Model Construction	Epidemiological models are constructed using mathematical equations that represent various aspects of disease transmission and population dynamics. These equations may describe factors such as population size, demographics, disease transmission rates, and the effectiveness of interventions.
Types of Models	Compartmental models such as Susceptible-Infectious-Recovered or SIR, agent-based models, and network models. Each type has its own strengths and limitations, and the choice of model depends on the specific research question and available data.
Simulation and Prediction	Epidemiological models simulate disease spread over time by using parameters like initial conditions, transmission rates, and intervention strategies. These models help researchers predict future disease spread and evaluate the control measures.
Parameter Estimation	Models often rely on parameter values that may be estimated from epidemiological data, clinical studies, or experimental research. Parameter estimation involves fitting the model to observed data to determine the most likely values for these parameters.
Validation and Calibration	It's crucial to validate and calibrate epidemiological models to ensure their accuracy and reliability. Validation involves comparing model predictions with real-world data, while calibration adjusts model parameters to better match observed outcomes.
Policy and Decision Making	Epidemiological models provide valuable insights for policymakers and public health officials. They help inform decisions about disease control measures, resource allocation, and intervention strategies to minimize disease transmission and mitigate the impact on public health.

Challenges	Epidemiological models, while valuable, face challenges such as incomplete data, underlying assumptions, and the complexity of real-world disease dynamics. Sensitivity analysis and scenario testing are employed to evaluate how robust model predictions are to these uncertainties.

Epidemiological Parameters: Epidemiological parameters are essential components used to quantify various aspects of disease transmission and outbreak dynamics within populations. They provide valuable insights into the characteristics of infectious diseases and help in understanding how they spread and affect communities. Here are some key epidemiological parameters and their significance:

1. **Basic Reproductive Number (R0):** This parameter represents the average number of secondary infections produced by a single infected individual in a completely susceptible population. R0 is a fundamental measure of disease transmissibility and helps determine whether an outbreak will spread or decline. If R0 is greater than 1, it indicates sustained transmission within the population.

2. **Infectivity Rates:** These rates quantify the likelihood of an infected individual transmitting the disease to others. High infectivity rates suggest that the pathogen spreads easily from person to person, leading to more rapid transmission within the community.

3. **Transmission Dynamics:** Transmission dynamics describe how infections are transmitted from one individual to another and how this process changes over time. Understanding transmission dynamics helps in predicting the course of an outbreak and designing effective control measures.

4. **Incubation Period:** The incubation period is the time interval between exposure to the infectious agent and the onset of symptoms in the infected individual. It is a crucial parameter for determining the duration of infectiousness and implementing timely interventions to prevent further transmission. The average incubation period for COVID-19 is estimated to be around 5 to 6 days, although it can range from 2 to 14 days. This means that individuals infected with the virus may develop symptoms within this time frame after exposure. The incubation period for influenza typically ranges from 1 to 4 days, with an average of about 2 days. This relatively short incubation period contributes to the rapid spread of the flu virus during seasonal outbreaks. The prolonged incubation period of HIV virus (months to years) poses challenges for early detection and prevention efforts, as individuals may remain asymptomatic for an extended period while still being able to transmit the virus. The incubation period influences vaccination strategies, particularly for diseases with shorter incubation periods. Vaccination programs may target individuals before they become infectious, aiming to provide immunity within the window of susceptibility and reduce the likelihood of transmission during the latent period.

5. **Mortality Rates:** Mortality rates indicate the proportion of infected individuals who die from the disease. These rates provide important insights into the severity of the illness and help in assessing the impact of the outbreak on public health.

6. **Effectiveness of Control Measures:** Epidemiological parameters also help evaluate the effectiveness of control measures such as vaccination, quarantine, and social distancing. By monitoring changes in key parameters over time, public health officials can assess the impact of interventions and adjust strategies accordingly.

Understanding the epidemiology and transmission patterns of infectious diseases is essential for devising effective prevention and control measures. Incidence, prevalence, and mortality data help prioritize prevention and control efforts, while insights into viral characteristics and transmission modes inform strategies such as vaccine development, environmental enhancements, nutritional improvements, hygiene promotion, and behavioural interventions.

VI. VIRUSES CAUSING DISEASES

DNA Viruses

Hepadnavirus: Hepadnaviruses, particularly Hepatitis B virus (HBV), cause significant liver disease, leading to both acute and chronic infections. Hepatitis B, once known as "serum hepatitis," is primarily transmitted parenterally.

1. Hepatitis B

Structure: The virus particle is 42 nm, with a dense core (27 nm) and an outer envelope containing HBsAg. Infected liver cells produce excess surface antigen, which is secreted in 22-nm particles and tubular structures (Figure 2). The virion's surface contains large surface proteins, including pre-S1 and pre-S2 regions, which are absent in 22 nm particles but may be found in tubular forms in highly viremic individuals. The nucleocapsid contains the viral genome and HBcAg. The genome is 3.2 kilobases with two linear DNA strands in a circular configuration.

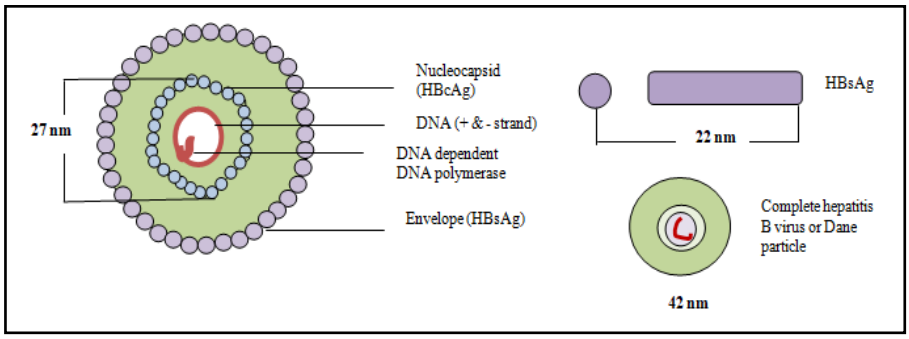

Figure 2: *Structure of Hepatitis B*

Clinical Presentation: Hepatitis B, a type of liver disease, typically lasts 1-6 months and can cause complications like arthralgia, urticaria, and polyarteritis. Most adults recover within 1-2 months, but a mortality rate of 0.5-2.0% is higher in post-transfusion cases. About 1% of patients develop fatal fulminant hepatitis, and 1-10% become chronically infected. There are two stages: acute and chronic.

Pathogenesis: HBV infects hepatocytes and replicates through reverse transcription. Immune responses, including natural killer and cytotoxic T cells, target infected cells, but the virus can evade clearance, leading to chronic infection and complications.

Antigens and Antibodies: HBsAg signifies ongoing infection, with variations across strains; Anti-HBs indicates immunity from infection or vaccination; HBcAg is within the viral core and triggers robust immune responses; Anti-HBc indicates past exposure, persisting long-term; HBeAg signals active viral replication and high infectivity; Anti-HBe denotes reduced replication (Figure 3); HBxAg is implicated in viral replication and linked to hepatocellular carcinoma, its detection indicating heightened cancer risk.

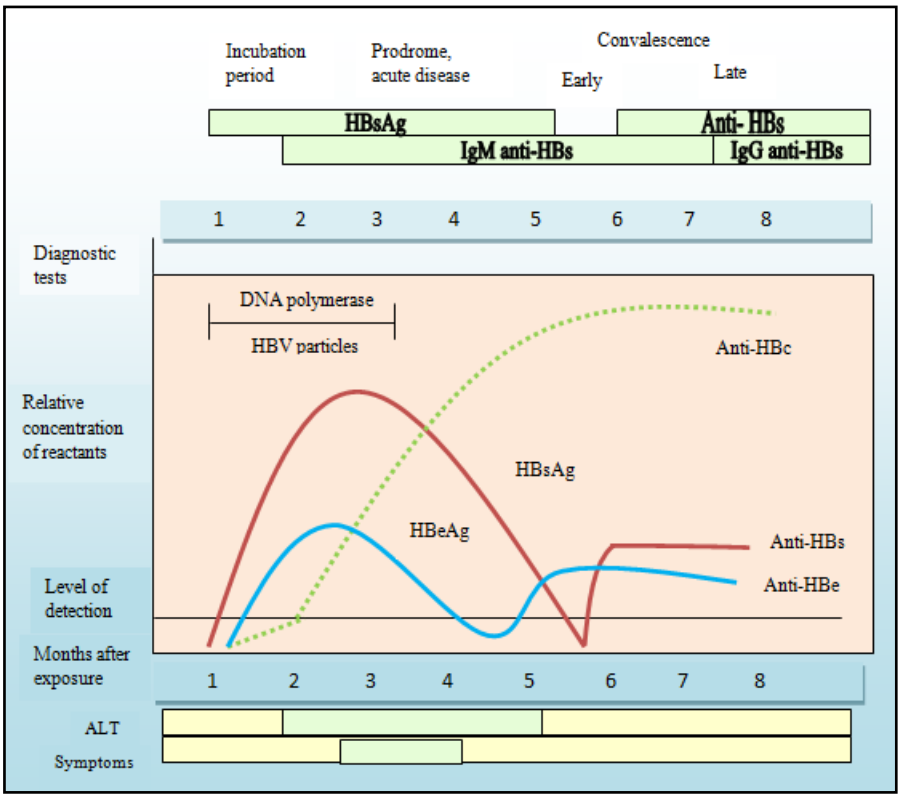

Figure 3: *Clinical and serological events in HBV*

Genome: The S gene directs the synthesis of surface proteins crucial for viral entry and immune recognition. The C gene generates core antigens and HBeAg, markers of viral replication and infectivity. The P gene encodes DNA polymerase, essential for viral genome replication. The X gene encodes HBxAg, which is implicated in viral replication and associated with an increased risk of hepatocellular carcinoma.

Epidemiology: HBV affects millions worldwide, with a significant carrier population, particularly in certain geographic regions. Transmission occurs through blood, sexual contact, and perinatal routes.

Laboratory Diagnosis

1. **Serological Assays:**
   - **HBsAg Detection:** Indicates current infection.
   - **Anti-HBs:** Signifies immunity.
   - **Anti-HBc:** Confirms prior exposure.
   - **HBeAg and Anti-HBe:** Assess viral replication status.
2. **Biochemical Parameters:** Used to assess liver damage and fibrosis.
3. **Molecular Diagnostics:** HBV DNA quantification, genotyping, and detection of drug resistance mutations.

Treatment: Interferon Therapy activates antiviral defense but has significant side effects. Active immunization involves using genetically engineered vaccines of HBV S gene into baker's yeast and Passive immunization uses hyperimmune hepatitis B immune globulin (HBIG).

2. **Hepatitis C:** HCV can cause acute and chronic liver diseases, including cirrhosis and liver cancer. Structurally, HCV is a single-stranded RNA virus resembling flaviviruses, classified under Hepacivirus in the Flaviviridae family. Primarily transmits through blood contact. High-risk groups include injectable drug users and those with compromised immune systems. The global prevalence varies widely, with significant cases in India.Screening is advised for high-risk individuals, with ELISA and PCR tests used for confirmation. Treatment for chronic hepatitis C includes antiviral drugs like sofosbuvir and daclatasvir.

3. **Hepatitis D:** The virus was discovered in 1977 by Rizzetto's team in Italy. It's a defective RNA virus that depends on hepatitis B (HBV) for replication. HDV has a 36 nm spherical particle with an outer coat of hepatitis B surface antigen and a circular RNA genome. It is classified under the genus Deltavirus. HDV is transmitted like HBV and can cause co-infection or superinfection, leading to severe chronic illness. Liver transplantation is sometimes necessary for fulminant liver failure due to HDV, although recurrence post-transplant is possible. HDV is primarily spread through parenteral exposure. Testing involves anti-HDV antibodies and HDV RNA quantification. Treatment focuses on interferon therapy, although its efficacy is limited. Research on new antiviral agents is ongoing.

4. **Poxvirus:** Poxviruses (Figure 15) are large, complex DNA viruses that infect a wide range of hosts, including humans and animals. Their unique structure, replication cycle, and pathogenesis make them significant in virology and immunology.

5. **Smallpox (Variola Virus):** Variola virus, an Orthopoxvirus, caused smallpox, a highly contagious and deadly diseaseTransmission was via inhalation of airborne particles. Variola major was more virulent with a 30% fatality rate, while Variola minor had less than 1%. Symptoms included high fever, body aches, and a rash progressing from red spots to pustules. Smallpox was eradicated in 1980 after a global vaccination campaign.

6. **Vaccinia Virus:** Edward Jenner's use of cowpox virus in 1796 led to the development of the smallpox vaccine. Over time, vaccinia virus replaced cowpox in vaccines. It was crucial for smallpox eradication due to its thermal stability and robust immune response.

Table 3: Classification of Poxviridae

Family	Genus	Species with Features
Chordopoxviridae (infect vertebrates)	Orthopoxvirus	Variola (major)- causes smallpox; narrow host range (humans); eradicated globally
		Variola (minor) – causes alastrim or moderate smallpox, narrow host range (humans); characterized by a rash of pus-filled lesions; seen in Europe, Asia, Africa.
		Vaccinia virus – causes vaccinia; localized pustule and mild discomfort; complications such as eczema vaccinatum or generalized vaccinia may occur; broad host range (humans, cattle, buffalo, swine, rabbits); spread worldwide
		Cowpox virus- causes cowpox; skin lesion ulcerates in a specific area; transmitted from cats, okapi, cattle or rodents (broad host range); observed in regions across Asia and Europe.
		Monkeypox virus-causes monkeypox; characterized by pustules; 15% mortality rate; broad host range (Squirrels, monkeys, anteaters, great apes, humans); observed in Western and central Africa
	Parapoxvirus	Orf virus-Causes contagious pustular dermatitis; broad host range (sheep, goats, humans); spread worldwide
		Pseudocowpox – causes Milker's nodules (occupational skin disease; occurs in cattle herd); narrow host range (cattle, humans); spread worldwide
		Bovine papular stomatitis virus- causes bovine papular stomatitis; papules and ulcers in mouth; narrow host range (cattle, humans); seen worldwide
	Capripoxvirus	Sheeppox virus- causes shippox; characterized by fever, respiratory symptoms; nodules and scabs on the skin; narrow host range (sheep, goats); observed in Africa, Asia
		Goatpox virus- causes goatpox; respiratory distress and skin lesions; narrow host range (goats, sheep); seen in Africa, Asia
	Leporipoxvirus	Myxoma virus 9myxomatosis or skin tumor) and Rabbit fibroma virus (fibroma or benign tumor) - Narrow host range [rabbits (Oryctolagus and Sylvilagus spp.)]; found in Americas, Europe, and Australia
	Avipoxvirus	Fowlpox virus, canarypox, crowpox,

		pigeonpox; narrow host range (chickens, turkeys, other bird species); spread worldwide
	Suipoxvirus	Swinepox virus- causes swinepox; skin lesions and pustules; narrow host range (swine); seen worldwide
Entomopoxvirinae (infect insects)	Molluscipoxvirus	Molluscum contagiosum virus- causes molluscum contagiosum; dome shaped bump; skin contact; broad host range (humans, nonhuman primates, birds, kangaroos, dogs); seen worldwide
	Yatapoxvirus	Yabapox virus- causes localized skin tumors; narrow host range (monkeys, humans); observed in West Africa
		Tanapox virus- causes localized skin lesions; transmission from arthropod bites; found in West Africa

Structure: Poxviruses are oval or brick-shaped (Figure 4) particles (200-400 nm), first observed by Buist in 1887. They have an external enveloped virion and intracellular mature virion. The genome is a single, linear dsDNA with over 100 proteins. Poxviruses are resistant to freeze-drying, heat, and some disinfectants but are deactivated by formalin and oxidizing agents.

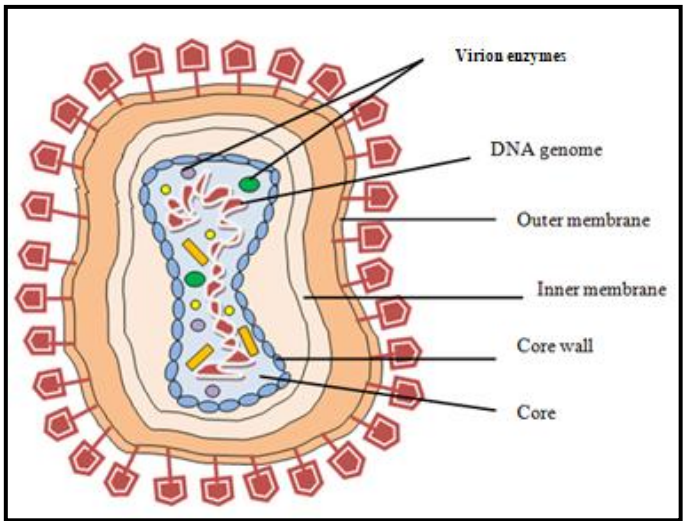

Figure 4: *Structure of poxvirus*

Clinical Presentation: Smallpox had an incubation period of 7-17 days, followed by a prodromal stage with flu-like symptoms. The rash stage featured lesions starting on the face and spreading. Lesions evolved from red spots to pustules. The crust and scab stage involved the formation of scabs that left scars. The convalescent stage marked recovery but could involve complications like pneumonia and encephalitis.

Pathogenesis: Pathogenesis includes initial infection through the skin or respiratory tract, viremia, and subsequent spread to the skin. Host immunity involves antiviral antibodies and T cells. Poxviruses evade immune responses using immunomodulatory proteins.

Laboratory Diagnosis

- **Clinical Evaluation:** Lesion examination and patient history
- **Microscopic Examination:** Direct microscopy for Guarnieri bodies; electron microscopy for virion visualization
- **Molecular Techniques:**PCR for viral DNA detection; sequencing for strain identification
- **Serological Assays:** ELISA and IFA for antibody detection
- **Cell Culture:** Cell culture for virus isolation and identification. Poke formation occurs on the chorioallantoic membrane (CAM) of 11-13-day-old chick embryos within 48-72 hours. Variola pocks appear small, shiny, white, convex, and non-necrotic whereas vaccinia pocks are larger, flat, greyish, often necrotic. The 'ceiling temperatures' where pock formation stops differ: vaccinia at 41°C, variola major at 38°C, and variola minor at 37.5°C (Figure 5).
- **Immunohistochemistry:** Staining of tissue sections with poxvirus-specific antibodies.

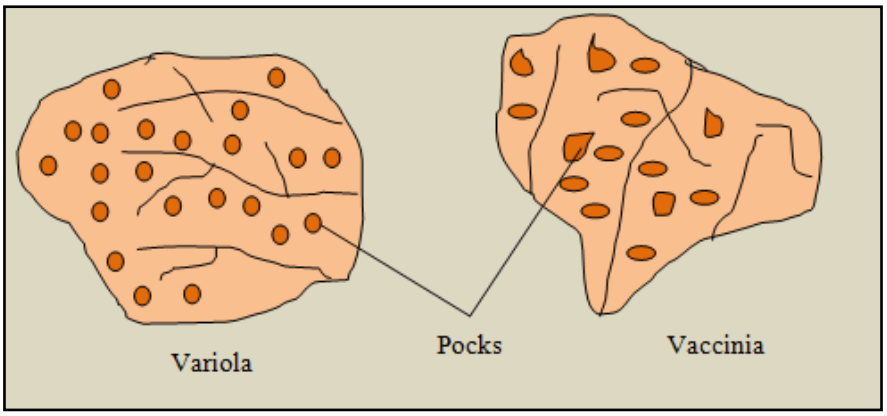

Figure 5: *Pocks formation*

7. **Molluscum Contagiosum:** It is a common viral skin infection characterized by benign, self-limiting lesions. It primarily affects humans and occasionally other animals like horses and chimpanzees. Transmission occurs through direct skin contact and fomites. The virus replicates in the deeper layers of the skin, causing characteristic lesions known as molluscum bodies. These lesions are dome-shaped, pearly nodules with a central depression, often appearing in clusters. They can persist for months and are commonly found on the trunk, extremities, and genital areas. Diagnosis is typically clinical based on lesion appearance. Electron microscopy of expressed material may reveal characteristic brick-shaped virions. PCR can confirm the presence of the virus in suspected cases.

8. **Monkeypox:** Monkeypox is a zoonotic infection caused by the monkeypox virus, characterized by fever and skin lesions. It was first identified in monkeys and later found to infect humans.The virus is large, brick-shaped, and spreads through contact with

infected animals or humans. It can cause outbreaks, with recent cases reported outside Africa, including in the United States and the United Kingdom. In humans, monkeypox presents with fever, lymphadenopathy, and distinctive skin lesions progressing through various stages. Diagnosis relies on laboratory tests such as PCR and viral culture. Treatment focuses on supportive care, as specific antiviral therapies are limited.

9. **Parapoxviruses:** Parapoxviruses infect both humans and animals, causing localized skin lesions. Examples include Orf virus causes contagious pustular dermatitis in sheep and goats, and Milker's node, caused by paravaccinia virus, affects cattle handlers, presenting as ulcerating nodules.

10. **Avipoxviruses:** Avipoxviruses infect birds, causing diseases like Fowlpox and Canarypox, with significant economic impact on poultry farming and wild bird populations.

11. **Yata, Tana and Yaba Poxviruses:** Yatapoxviruses include Tanapox virus affecting humans in Africa and Yaba monkey tumor virus primarily found in African green monkeys.

Herpesvirus: Herpesviruses (Table 4) encompass a diverse family of DNA viruses known for causing latent infections and periodic reactivation, impacting both humans and animals.

Table 4: Classification of Herpesviridae

Sub Family	Species	Common Name with Abbreviation	Site of Infection	Disease Caused
Alpha	Human herpesvirus type 1	Herpes simplex virus type 1 (HSV-1)	Neuronal epithelial cells	Oral herpes, herpes keratitis, herpes gladiatorum, congenital defects, genital herpe
	Human herpesvirus type 2	Herpes simplex virus type 2 (HSV-2)	Neuronal epithelial cells	Genital herpes, congenital defects
	Human herpesvirus type 3 (HHV-3)	Varicella zoster virus (VZV)	Neuronal epithelial cells	Chickenpox, shingles, herpes zoster ophthalmicus, postherpetic neuralgia
Beta	Human herpesvirus type 5 (HHV-5)	Cytomegalovirus (CMV)	Secretory glands, kidneys, Monocytes	Congenital defects, mononucleosis
	Human herpesvirus type 6	Human B cell lymphotropic virus (HBLV)	Lymphocytes, monocytes, neural	Roseola infantum

	(HHV-6)		cells	
	Human herpesvirus type 7 (HHV-7)	R K virus	Lymphoid tissues	Roseola infantum
Gamma	Human herpesvirus type 4 (HHV-4)	Epstein-Barr virus (EBV)	Lymphoid tissues, epithelial cells, B cells	Mononucleosis, Burkitt lymphoma, Hodgkin lymphoma
	Human herpesvirus type 8 (HHV-8)	Kaposi sarcoma–associated herpesvirus (KSHV)	B cells, endothelial cells	Kaposi sarcoma, lymphoma

Structure and Replication: Herpes simplex virus (HSV) virions are spherical particles enveloped in a lipid bilayer, housing an icosahedral capsid containing the viral DNA. Replication occurs within host cell nuclei, utilizing viral glycoproteins for cell entry and spread. Glycoproteins like gD, gB, gH, and gG facilitate viral attachment, fusion, and immune evasion during HSV infection.

1. **HSV-1:** HSV-1 primarily infects epithelial cells, establishes latency in neurons, and periodically reactivates, leading to recurrent lesions in mucosal and cutaneous tissues (Figure 6A). HSV-1 is highly prevalent globally, transmitted through non-sexual contact with infected saliva or lesions. Neonatal infections occur during childbirth, posing significant risks. HSV-1 infections present variably across different sites, including orolabial herpes, genital herpes, and ocular infections, each with distinctive clinical features and complications. Antiviral medications such as acyclovir and valaciclovir are effective for managing HSV-1 infections, with early intervention crucial for severe cases like encephalitis.

    - **Eczema Herpeticum:** A type of eczema, causes widespread ulceration and atopic dermatitis, often seen in children (Figure 40B).
    - **Herpetic Whitlow (Occupational Herpes):** Involves deep blisters on digits, potentially leading to lymphadenopathy, seen in healthcare workers (for eg, doctors, nurses, dentists).
    - **Herpes Gladiatorum (Mat Herpes):** Skin infection commonly linked to contact sports like wrestling. The virus spreads through direct contact by infected skin lesions or secretions, with symptoms including painful blisters.

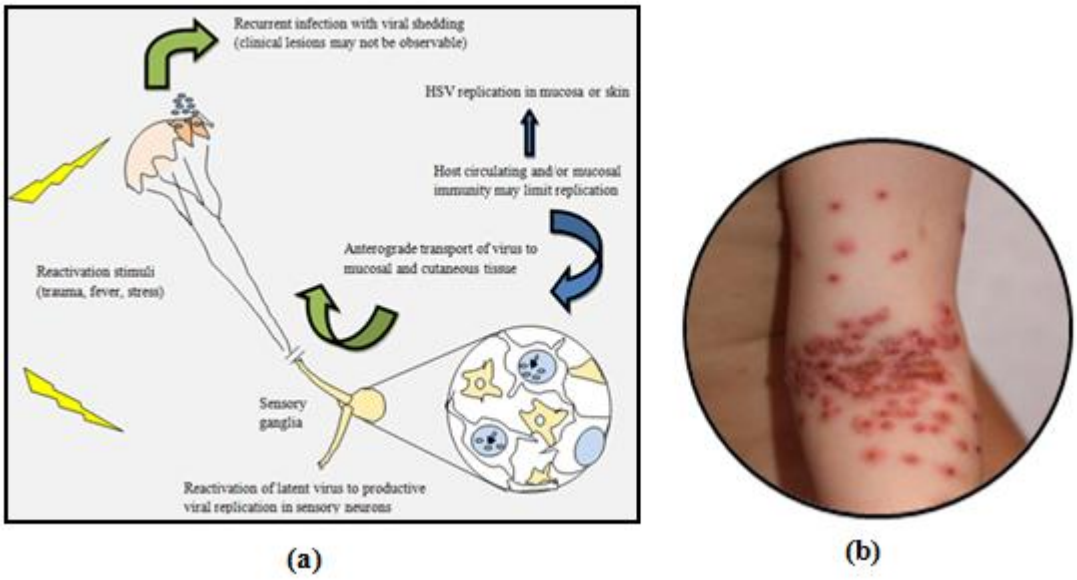

Figure 6: *(a) The recurrence pattern and asymptomatic shedding of HSV-1 (b) Eczema herpeticum (Damour et al., 2020)*

2. **HSV-2:** HSV-2 affects approximately 22% of adults in the United States and is the primary cause of genital lesions (Figure 7). It often presents with nonspecific symptoms like itching and irritation, which can delay diagnosis and treatment. HSV-2 spreads through direct contact with shedding sections of a seropositive individual, targeting skin and mucous membranes. The virus becomes dormant in sensory nerve sheaths for about 10 to 14 days. Reactivation can occur later in life, with the virus traveling through sensory nerves to mucocutaneous sites, causing vesicular clusters at dermatological sites. HSV-2 typically causes genital herpes, characterized by painful, recurrent genital lesions.

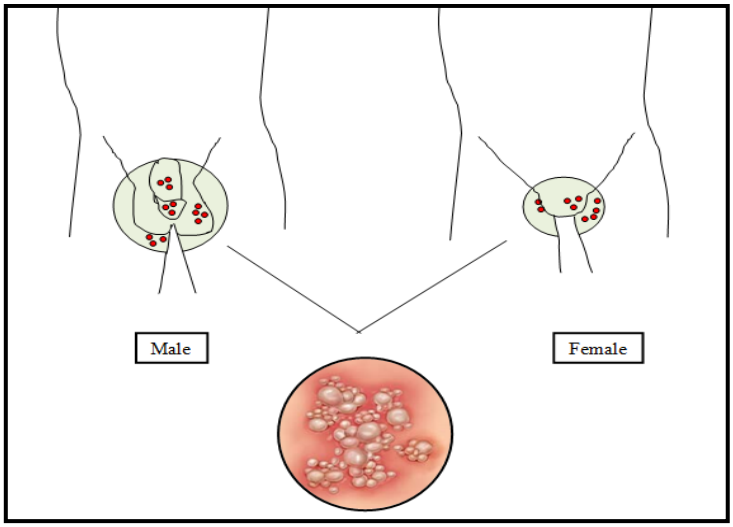

Figure 7: *Genital herpes by HSV-2*

Laboratory Diagnosis: The laboratory diagnosis of HSV-2 involves various techniques aimed at detecting the virus-

- **Viral Culture:** Clinical specimens are inoculated onto cell culture monolayers. Cytopathic effects indicative of viral replication are observed microscopically.
- **Microscopy:** Tzanck smear from lesions is stained and examined for multinucleated giant cells and intranuclear inclusion bodies.
- **Antigen Detection:** Enzyme immunoassays (EIAs) or direct fluorescent antibody (DFA) tests detect HSV antigens in clinical specimens.
- **Nucleic Acid Amplification Tests (NAATs):** Techniques like PCR or NASBA amplify and detect HSV DNA in clinical specimens, providing high sensitivity and specificity.
- **Serological Tests:** ELISAs or immunofluorescence assays (IFAs) detect HSV-specific antibodies in serum samples, useful for detecting past infections.
- **Direct Immunofluorescence Assay (DFA):** Clinical specimens are stained with fluorescent-labeled antibodies specific to HSV antigens, providing rapid results and high sensitivity.

3. **Varicella Zoster Virus (VZV):** VZV causes varicella (chickenpox) and herpes zoster (shingles). While vaccination has decreased varicella incidence, herpes zoster remains prevalent, especially in older adults. VZV has a symmetrical icosahedral structure with dsDNA and glycoprotein spikes. Chickenpox primarily affects children, spreading via close contact, while herpes zoster affects around 20% of the population, especially the elderly and immunocompromised individuals. VZV infection triggers immune responses, becoming latent in sensory nerve ganglia and potentially reactivating as herpes zoster.

   Clinical presentation of chickenpox includes a rash, fever, and malaise, with potential complications like CNS involvement and Reye's syndrome. Shingles presents as a unilateral vesicular rash with complications including ophthalmic infections and postherpetic neuralgia and Ramsay Hunt syndrome. Diagnosis involves PCR, serological tests, viral culture, microscopy (Multinucleated giant cells and type A intranuclear inclusion bodies can be observed in Tzanck smears), and immunofluorescence. Treatment includes antivirals (acyclovir), hygiene practices, and vaccination, with an inactivated Oka vaccine under study for herpes zoster prevention post-stem cell transplantation. Zostavax was recommended for elders (>60 yrs) affected by zoster.

4. **Cytomegalovirus (CMV):** Cytomegalovirus, the largest herpesvirus, causes a range of clinical conditions from congenital neonatal infections to infectious mononucleosis in young adults. It is widespread, infecting 60-70% of people in U.S. cities and nearly 100% in some parts of Africa. Structurally, CMV has an icosahedral shape with four key components: an outer lipid envelope, tegument, nucleocapsid, and an internal nucleoprotein core. Transmission occurs through contact with infectious bodily fluids and through solid organ and stem cell transplantation. CMV enters host cells via viral glycoproteins interacting with cellular receptors and then establishes latency in various cell types, leading to the production of CMV-specific IgM and IgG antibodies. Clinically, most cases are asymptomatic with prolonged latency and occasional reactivation. In newborns and infants, CMV can result from maternal infection during pregnancy, causing severe outcomes like fetal death or cytomegalic inclusion disease. Cytomegalic cells, characterized by "owl's eye" inclusion bodies, in centrifuged deposits from urine or saliva (Figure 8).

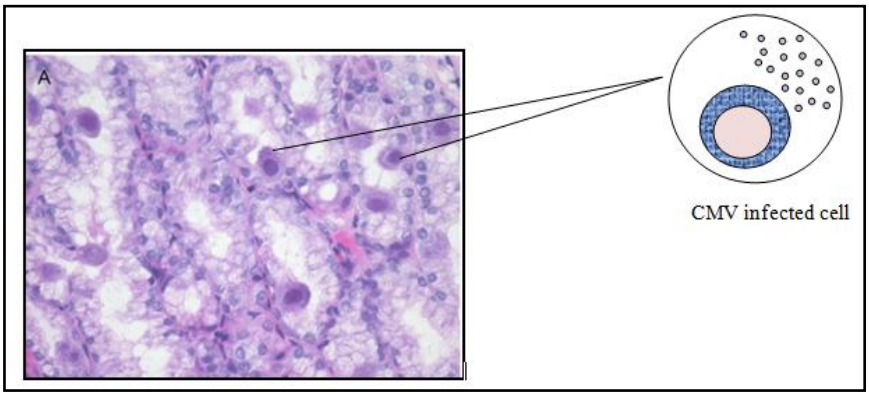

Figure 8: *CMV owl's eye inclusion in gastrointestinal tract of HIV patients*

5. **Epstein-Barr Virus (EBV):** Discovered in 1964, Epstein-Barr virus (EBV) is the first identified human oncogenic virus and can persist silently in the body for life. EBV features a double-stranded DNA genome within an icosahedral protein nucleocapsid, enveloped by a lipid membrane with viral glycoproteins. By adulthood, EBV antibodies are widespread in both developed and developing countries. Transmission primarily occurs through saliva, often via intimate contact like kissing ("Kissing Disease"), and less frequently through blood transfusions or organ transplants.

   EBV infects B lymphocytes with CD21 receptors and nasopharyngeal epithelial cells, establishing latency and occasionally reactivating to cause conditions such as infectious mononucleosis and EBV-associated malignancies like Burkitt's lymphoma and nasopharyngeal carcinoma. Diagnosis relies on serological tests (Paul-Bunnell test), detection of specific EBV antibodies, and occasionally virus culture or DNA detection. Treatment focuses on supportive care, while prevention efforts include vaccine development targeting viral components like glycoprotein gp350.

6. **Human Herpesvirus 6 (HHV-6):** Human herpesvirus 6 (HHV-6), discovered in 1986 in patients with lymphoproliferative disorders and HIV, has two variants: HHV-6A and HHV-6B, with HHV-6B primarily causing exanthem subitum (Roseola Infantum or Sixth Disease).

7. **Human Herpesvirus 7 (HHV-7):** HHV-7 was discovered by Frenkel and colleagues in 1990 in a healthy individual and subsequently linked to exanthem subitum. HHV-6 and HHV-7, collectively known as Roseolovirus. Primary HHV-7 infection may be asymptomatic or present with fever, febrile seizures, or nonspecific symptoms like upper respiratory tract disease.

8. **Human Herpesvirus 8 (HHV-8):** Kaposi's sarcoma-associated herpesvirus (KSHV), also known as HHV-8, was identified in 1994, linking it to Kaposi's sarcoma (KS) and other diseases like primary effusion lymphoma (PEL) and multicentric Castleman's disease.

Adenovirus: Adenovirus infections are common, responsible for 5-10% of febrile illnesses in infants and young children.

Structure: Adenoviruses (Figure 9) exhibit a distinctive icosahedral capsid structure composed of 252 capsomeres, including 240 hexons forming the capsid faces and 12 pentons located at the vertices, each with a fiber. These nonenveloped viruses carry dsDNA genomes and are known for their robust environmental stability.

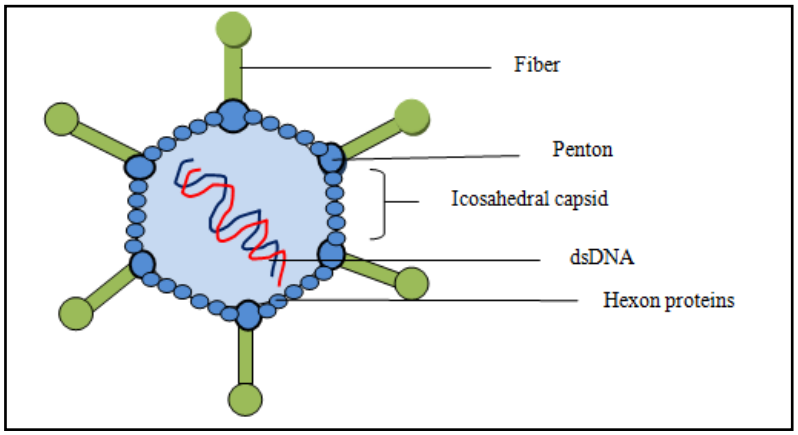

Figure 9: Structure of adenovirus

Classification: They belong to the Adenoviridae family, categorized into two genera: Mastadenovirus (infecting mammals) and Aviadenovirus (infecting birds), with over 50 human serotypes grouped into six species (A-F).

Pathogenesis: Pathogenesis involves specific tissue tropism targeting epithelial cells lining mucosal surfaces in respiratory, gastrointestinal, and ocular tracts. Viral replication triggers immune responses, leading to cytokine release, inflammation, and potential dissemination to other organs, particularly in immunocompromised individuals.

Clinical Presentation: Clinical manifestations (Table 5) range from mild to severe respiratory tract Adenovirus infections in children often present with pharyngitis, otitis media, and febrile illnesses, while in adults, they can cause pneumonia and conjunctivitis.

Table 5: Adenovirus SYNDROMES

Serotypes	Disease
1,2,5,6	Respiratory infections in children
3,4,7,14,21	Febrile illness, sore throat, pneumonia
4,7,21	acute respiratory distress (ARD) in military individuals
3,7	Follicular conjunctivitis (related to swimming pool)
8,19,37	Epidemic keratoconjunctivitis (shipyard eye)
40,41	Diarrhoea

Laboratory Diagnosis: Diagnosis involves various methods such as tissue culture, antigen detection (IFA, ELISA), serology (a rise in antibody titers in paired sera) and PCR for viral DNA detection. Adenoviruses, except types 40 and 41, can be detected via routine tissue culture, with a typical cytopathic effect observed within days. Trypsinised monkey kidney cells or transformed human embryonic kidney cells are essential. "Smudge cells" inclusions are observed in histopathology examination

Treatment: Adenovirus infections are preventable through hygiene measures, especially in closed settings like schools and healthcare facilities. Vaccines targeting serotypes 4 and 7 are used in military populations to prevent outbreaks.

Viral Vector: Adenoviruses are extensively studied as vectors for gene therapy and vaccine development due to their ability to carry large DNA inserts and induce robust immune responses. They are modified to be replication incompetent for safety, used in clinical trials for diseases like SARS-CoV-2, malaria, tuberculosis, and cancers.

1. **Adeno-Associated Viruses (AAVs):** AAVs are small, non-enveloped viruses from the Parvoviridae family that do not cause human diseases and are considered relatively harmless. They have become prominent in biomedical research for their role as efficient and safe gene delivery vectors. Electron microscopy reveals small icosahedral particles (20-25 nm) in adenovirus preparations, identified as defective or adenosatellite viruses, which cannot replicate independently and require helper viruses (adenoviruses or herpesviruses) for multiplication. AAVs have a single-stranded DNA genome with two open reading frames encoding Rep and Cap proteins. AAVs offer advantages for gene therapy, including transduction of both dividing and non-dividing cells.

2. **Polyomavirus**: Human polyomaviruses JC virus (JCV) and BK virus (BKV) were discovered in 1971 and are widespread globally. They are asymptomatic in healthy individuals. Additionally, three newer polyomaviruses—WU, KI, and Merkel cell carcinoma virus (MCV)—have been identified, with WU and KI found in respiratory tract secretions.

    - **JCV:** Primarily transmitted via respiratory routes or ingestion of contaminated food or water, remaining latent in the kidneys and lymphoid tissues. It can lead to progressive multifocal leukoencephalopathy (PML) in immunocompromised individuals. JCV may require both a serotonin receptor and a sialylated glycan for entry into central nervous system cells. Brain biopsy is the gold standard for PML diagnosis. Serology measures antibodies against JCV.

    - **BKV:** BKV establishes latency in renal tubular epithelial cells, with reactivation causing nephropathy, ureteral stenosis and hemorrhagic cystitis. Transmission routes include respiratory secretions, fecal-oral transmission, and possibly blood transfusions or organ transplantation. Urine cytology detects BKV viruria and renal biopsy confirms BKV-induced nephropathy. Urinalysis reveals blood and other abnormalities in urine.

3. **Other Polyomaviruses:** In 2007, two novel polyomaviruses, KI and WU, were characterized and found in children's respiratory secretions. Merkel cell polyomavirus (MCV) was identified in 2008, primarily found in tissues with Merkel cell carcinoma. These viruses share genetic and protein similarities with BKV and JCV, but their infectious nature remains uncertain. New human polyomaviruses, including HPyV6, HPyV7, TSPyV, HPyV9, and MWPyV, are under investigation for their roles in respiratory and urinary tract infections.

4. **Papillomavirus:** The term 'papova' originates from the names of viruses within this group, such as papilloma and polyoma viruses. The family Papovaviridae encompasses two genera: Polyomavirus, including SV40, JC and BK, and Papillomavirus, which causes human infections.

Structure: HPVs are small (Figure 10), nonenveloped viruses with an icosahedral capsid enclosing a ds circular DNA genome. The genome consists of approximately 7900 base pairs and is organized into three functional regions: upstream regulatory region, early region (E1-E7), and late region (L1 and L2).

Pathogenesis: HPV infects basal cells of stratified squamous epithelium and replicates as cells differentiate, establishing episomal DNA and integrating into the host genome in malignancy. The E6 and E7 gene products interfere with cellular growth regulation, promoting cellular proliferation and inhibiting apoptosis, which can lead to cancer over time.

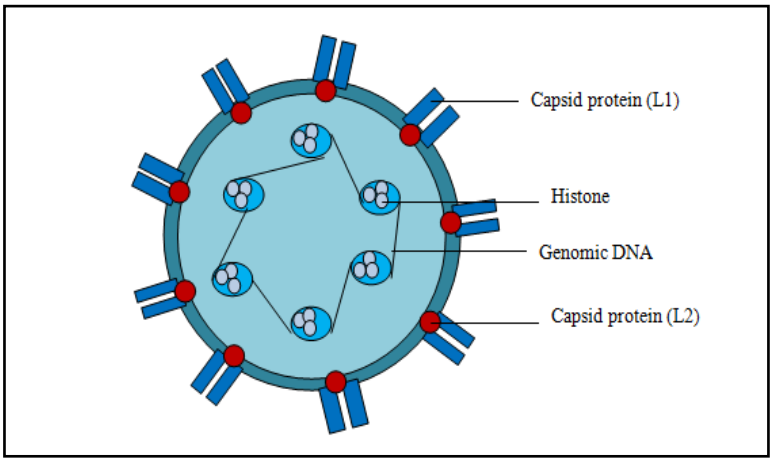

Figure 10: *Structure of human papillomavirus*

Clinical Presentation

- **Cutaneous Warts:** Include deep plantar warts, common warts, and plane warts, each with distinct morphological features and locations.
- **Epidermodysplasia Verruciformis:** Characterized by flat warts and a risk of malignant transformation, especially in sun-exposed areas.
- **Anogenital Warts:** Flesh-colored papules in the anogenital area that may transform into squamous cell carcinomas.
- **Recurrent Respiratory Papillomatosis:** Lesions in the upper respiratory tract, potentially life-threatening in children.
- **Other HPV Infections:** Oral squamous cell papillomas, conjunctival and periungual squamous cell carcinomas, and various skin lesions.

Epidemiology: HPV infections vary from clinical to subclinical, with transmission primarily through skin-to-skin contact and sexual activity. Genital/mucosal infections are most common in individuals aged 15-44, and high-risk types are strongly associated with cervical cancer.

Laboratory Diagnosis: Methods include cervical swabs, biopsies, and molecular tests like PCR-based HPV DNA testing. Immunologic assays are inadequate, and cytology (Pap smear) remains crucial for detecting cervical abnormalities. Colposcopy aids in visualizing cervical tissues post-abnormal screening.

Treatment: Noninvasive lesions are treated with cryotherapy, laser therapy, or topical agents like imiquimod. Invasive procedures like LEEP are used for cost-effectiveness and tissue preservation.

Cervical Cancer: High-risk HPVs (16, 18, 31, 33, 45, 55) are precursors to cervical cancer, progressing from mild cervical intraepithelial neoplasia (CIN1) to more severe neoplasias (CIN2 or CIN3) and eventually to invasive cancer. Early detection and treatment of HPV infections are vital in preventing cervical cancer progression.

Parvovirus: The name "Parvovirus" originates from Latin, meaning small. Parvoviridae, one of the smallest DNA viruses, is divided into Parvovirinae (vertebrate infecting) and Densovirinae (invertebrate infecting). Parvovirinae includes genera such as Parvovirus, Dependovirus, Erythrovirus, Bocavirus, and Amdovirus. Parvovirus B19 discovered in 1974 during hepatitis B surface antigen testing.

Structure: Parvoviruses are small, nonenveloped viruses (~22 nm), comprising an icosahedral capsid with VP2 as the major capsid protein and VP1 enhancing infectivity due to its phospholipase A2 motif.

Pathogenesis: B19V targets human erythroid progenitor cells and CD36-positive erythroblasts in bone marrow, causing transient cessation of red cell production. It specifically infects cells expressing globoside (P antigen), found on erythroid lineage cells, endothelial cells, and fetal myocytes.

Transmission: Primarily transmitted via respiratory routes, B19 can also spread through blood. Antibody response to B19V involves IgM and persistence IgG production.

Clinical Presentation

- **Erythema Infectiosum (Fifth Disease)-** Characterized by flu-like symptoms followed by a "slapped-cheek" rash (Figure 11A) and subsequent rash on the trunk and limbs. Joint pain (arthropathy) may occur, resolving within weeks.
- **Aplastic Crisis-** Transient severe anemia observed in individuals with hemolytic anemias, potentially requiring blood transfusions.
- **Fetal Hydrops-** Severe fetal complications including hydrops fetalis can occur if B19V crosses the placenta during pregnancy, leading to fetal anemia and edema (Figure 11B).

Laboratory Diagnosis: Detection relies on PCR for viral DNA in serum, antigen detection in throat secretions, and antibody detection (IgM and IgG) in serum to confirm recent or past infection. Fetal infection can be diagnosed via amniotic fluid or fetal blood sampling.

Treatment: In most cases, B19V infections are self-limiting, requiring only symptomatic relief. Severe cases may necessitate blood transfusions or intravenous immunoglobulin for individuals with underlying hematologic conditions.

Other Human Parvoviruses

- **Human Dependoviruses (AAVs):** Nonpathogenic viruses used as vectors in gene therapy.

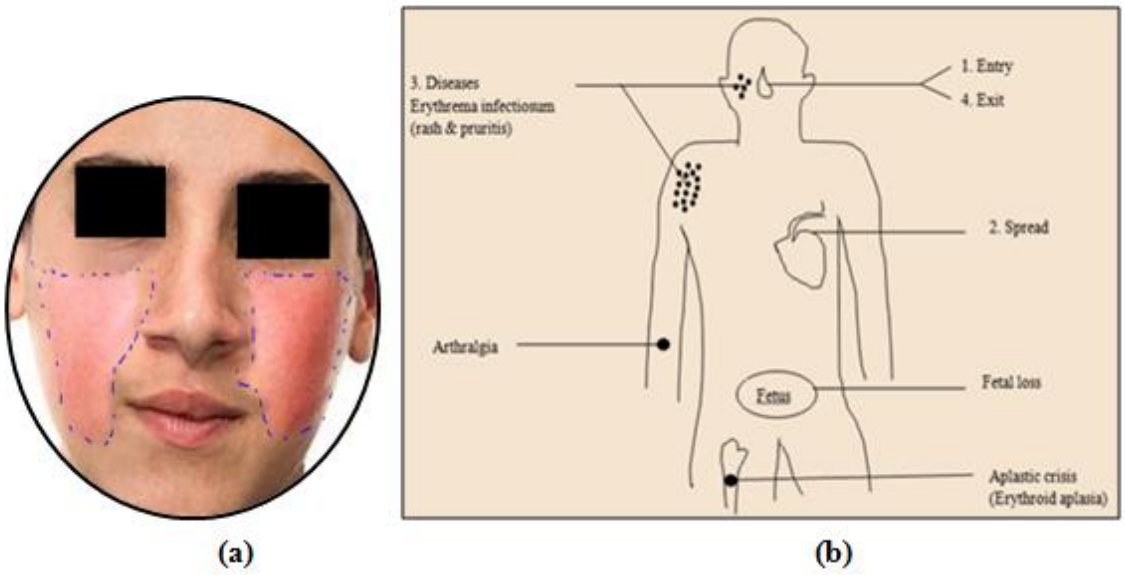

Figure 11: *Erythema Infectiosum - (a) Slap cheek appearance (b) Clinical presentation and pathogenesis of Parvo B19 (Kostolansky and Waymack, 2024)**:***

- **Human Bocavirus:** Causes respiratory infections in children.
- **Human Parvovirus 4 (PARV4):** Associated with blood-borne transmission, primarily in high-risk populations like injection drug users and HIV-infected.

RNA Viruses

1. **Picornavirus:** The picornavirus family (Figure 12) comprises numerous small RNA viruses that significantly affect both humans and livestock. This diverse family includes nine genera, causing diseases such as poliomyelitis, the common cold, hepatitis A, and foot-and-mouth disease (FMDV). Aphthovirus causes foot-and-mouth disease in cattle and cardiovirus causes encephalomyocarditis in mice.

2. **Enteroviruses:** Enteroviruses (Figure 13) infect higher vertebrates and can cause a wide range of diseases, from mild illnesses to severe conditions like central nervous system diseases, paralysis, and death. These non-enveloped viruses have icosahedral capsids about 30 nm in diameter, encasing a single-stranded RNA genome. They remain stable across a wide pH range, enabling them to stay infectious through the gastrointestinal tract.

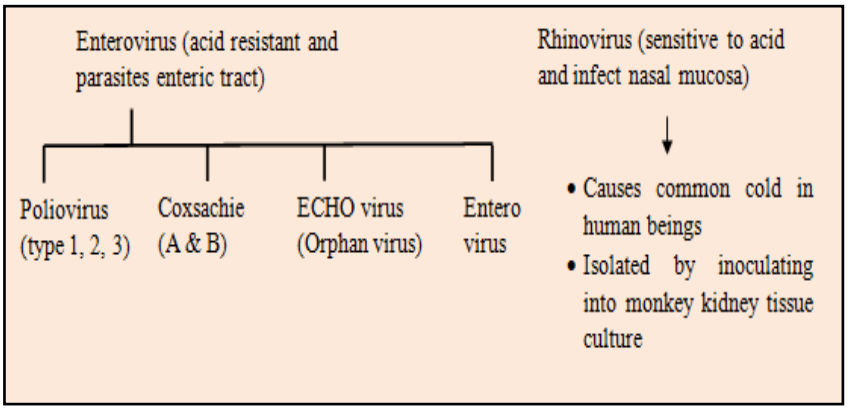

Figure 12: *Classificaion of picornaviruses*

3. **Enterovirus 71:** Enterovirus 71, closely related to coxsackievirus A16, causes skeletal myositis in suckling mice and paralysis in cynomolgus monkeys. It was first isolated in 1969 from young children with encephalitis and aseptic meningitis in California. Enterovirus 71 has since caused global outbreaks, particularly of hand, foot, and mouth (HFM) disease, often linked with severe CNS complications in young children. It is unique among non-polio enteroviruses for causing epidemic paralysis. Severe manifestations include brainstem encephalitis with high mortality, generalized maculopapular rash, interstitial pneumonia, and myocarditis. The virus is best isolated from vesicle swabs and cultured in African green monkey kidney cells. Treatment is primarily symptomatic and supportive, with significant recent epidemics in the Far East.

Classification of enteroviruses

Poliovirus- types 1, 2 and 3

Coxsachie virus-

- Group A- types 1-24
- Group B-types 1-6

ECHO virus- types 1-34

Enterovirus 70- causes conjunctivitis

Enterovirus 71- causes meningitis, encephalitis and paralysis

Enterovirus 72- hepatitis A virus

Figure 13: *Classification of enteroviruses*

4. **Poliovirus:** Paralytic disease in children, known since ancient times, saw a breakthrough in 1949 when Enders, Weller, and Robbins discovered that polioviruses could grow in non-neural cell cultures from human embryos, earning them a Nobel Prize. Polioviruses cause poliomyelitis, a systemic infection primarily affecting the CNS and leading to paralysis.

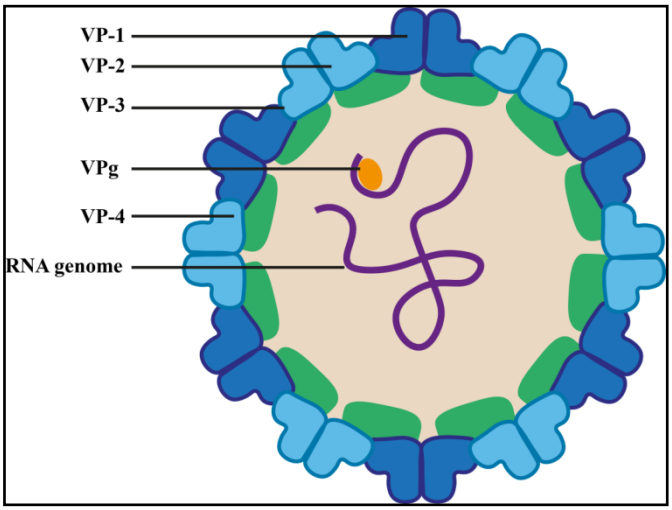

Figure 14: *Structure of poliovirus*

Structure: Poliovirus (Figure 14) is a positive-strand RNA virus in the Picornaviridae family, with a spherical 27 nm diameter virion containing 60 subunits arranged in icosahedral symmetry. The genome is a single strand of positive-sense RNA, about 7.4 kb long, directly translatable by host ribosomes. There are three serotypes: Brunhilde and Mahoney (type 1), Lansing and MEF1 (type 2), and Leon and Saukett (type 3) identified by their reactions with specific sera. Type 1 is most epidemic, type 2 causes endemic infections, and type 3 also causes epidemics.

Pathogenesis: Poliovirus infection involves two viremic phases. The virus spreads via the fecal-oral route, initially colonizing the nasopharynx and gastrointestinal tract, then entering the bloodstream. In a small number of cases, the virus reaches the CNS, causing paralysis by destroying neurons, particularly in the anterior horns of the spinal cord.

Epidemiology: Localized polio epidemics began around 1900 in the US, with significant outbreaks like the one in Brooklyn, New York, in 1916. The virus is transmitted fecal-orally, persisting in the environment. Infection is often asymptomatic, but certain factors like pregnancy and tonsillectomy increase paralysis risk.

Clinical Presentation: Poliomyelitis can range from asymptomatic infections to severe paralysis and death. Inapparent infections are common, while abortive poliomyelitis presents minor illness symptoms. Paralytic poliomyelitis occurs in 0.1% of infections, often with biphasic fever, meningitis, and asymmetric flaccid paralysis.

Laboratory Diagnosis: Diagnosis involves viral isolation from throat swabs, feces, blood, and CSF, with virus isolation in tissue culture being the preferred method. Serodiagnosis through antibody titer rise and molecular diagnosis using PCR and sequencing are also used.
Treatment: There is no specific antiviral treatment for poliomyelitis; management is supportive. Hospitalization, bed rest, pain relief, and physical therapy are essential. Immunoprophylaxis includes passive immunization with human gammaglobulin and active immunization with IPV and OPV (Table 6).

Table 6: Difference between IPV and OPV

Vaccine Difference	IPV (Salk's Vaccine)	OPV (Sabin's Vaccine)
Formulation	Inactivated (killed) poliovirus strains (types 1, 2, and 3).	Live, attenuated virus strains (types 1, 2, and 3).
Valency	Only trivalent, targeting all three serotypes.	Available as trivalent (tOPV), monovalent (mOPV1, mOPV3), or bivalent (bOPVs)
Pathogenesis	Generates humoral immunity, reducing virus replication, but does not provide gut immunity.	Induces a local immune response in the intestines, providing mucosal immunity.
Administration	Given intramuscularly (upper arm or anterolateral thigh), alone or combined with other vaccines.	Administered orally as drops.
Dosage	Two fractional dose at 6 and 14 weeks of age	OPV 0- at birth immediately. OPV 1, 2 & 3 - 6, 10 & 14 weeks (OPV cam be given till 5 years).
Safety	Virus is inactivated, no risk of disease from vaccine	Rarely, the vaccine virus can mutate and cause vaccine-derived poliovirus (VDPV) in immunocompromised
Efficacy	Highly effective in preventing paralytic polio and its transmission.	Highly effective in inducing mucosal immunity; beneficial in areas with poor sanitation.
Indication	Used in countries where wild poliovirus transmission has been interrupted or inactivated poliovirus outbreaks occur.	Historically used in global polio eradication efforts due to its ability to induce herd immunity.
Potential drawbacks	Requires trained healthcare professionals for administration, may not provide as robust mucosal immunity as OPV.	Risk of vaccine-associated paralytic polio (VAPP) in a very small number of vaccine recipients, especially in areas with low vaccination coverage and poor sanitation.

WHO Eradication and Containment Strategy: The strategy for polio eradication includes detecting and halting poliovirus transmission, strengthening routine immunization, and transitioning to inactivated polio vaccine (IPV) and bivalent oral polio vaccine (bOPV). It also involves implementing containment measures for wild poliovirus and preparing for the post-eradication phase through legacy planning.

Pulse Polio Program: In 1995, the Government of India initiated the Pulse Polio Immunization (PPI) program, aiming to vaccinate all children under five with OPV on designated national immunization days (NIDs). Despite initial successes, about 5-6% of children were missed, necessitating house-to-house searches for vaccination. In 1988, the World Health Assembly launched the Global Polio Eradication Initiative (GPEI) with the goal of eradicating polio worldwide by 2000.

India persisted with OPV despite its low efficacy, while IPV showed promise elsewhere but was not licensed in India until 2006. India achieved a significant milestone in 2012 when WHO declared it polio-free after sustained transmission interruption. However, global polio threats persist with wild poliovirus circulating in countries like Nigeria, Pakistan, Afghanistan, and Chad. True eradication requires transitioning from OPV to IPV to eliminate both wild and vaccine-derived polioviruses.

Vaccine-Induced Polio: In rare instances, the live poliovirus in OPV can mutate, regaining its ability to cause neurovirulence, resulting in paralysis similar to that caused by the wild poliovirus.

- **Vaccine-Associated Paralytic Poliomyelitis (VAPP):** Occurs when the virus mutates in a recently vaccinated individual, with an incidence of 0.09 to 25 cases per million OPV doses. VAPP in immunodeficient patients has distinct features such as a longer interval between OPV administration and disease onset, chronic meningitis, and a higher risk of mortality.
- **Vaccine-Derived Poliovirus (VDPV):** Arises from mutations over a longer period, resulting in a virus genetically similar to the vaccine strain. VDPVs circulate in under-immunized populations, acquiring properties similar to wild polioviruses.

5. **Coxsackievirus:** Coxsackieviruses are small (22–30 nm), non-enveloped, single-stranded RNA viruses. They are globally prevalent, peaking in summer and autumn in temperate regions. Primarily spread through oral contact with contaminated hands, water, or food and via aerosols. The virus multiplies in the throat, small intestine, and lymph nodes before spreading to target organs. Group A cause herpangina and hand, foot, and mouth disease (Herpetiform exanthems).. Group B cause epidemic myalgia, and are associated with juvenile diabetes. Virus isolation involves inoculating suckling mice and s hamsters. Coxsackie B viruses grow well in monkey kidney cell line, Coxsackie A21 grows in HeLa. There are no specific vaccines or antiviral agents, preventive measures focus on hygiene practices, with γ-globulins showing limited efficacy.

6. **Acute Hemorrhagic Conjunctivitis (AHC):** It is a highly contagious eye infection causing pain, eyelid swelling, and subconjunctival hemorrhage, usually resolving within a week, caused by enterovirus 70 and coxsackievirus A24. Outbreaks often occur in crowded, coastal regions. AHC transmits through direct contact.

7. **Echoviruses:** These small, non-enveloped RNA viruses initially termed "enteric cytopathogenic human orphan viruses," first identified in stool samples. They primarily spread via the fecal-oral route and are common in children under 5. Echovirus infections can be asymptomatic or cause aseptic meningitis, neonatal infections, respiratory and skin infections. No specific vaccine available.

8. **Rhinoviruses:** Rhinoviruses are the primary cause of upper respiratory tract (URT) infections globally, leading to significant economic burdens. Rhinoviruses are inactivated below pH 6 but stable at 20-37°C, surviving on surfaces for days. They primarily infect humans, attaching to ICAM-1 receptors on nasal epithelial cells, causing damage and sometimes secondary bacterial infections. Symptoms include common cold with runny

nose, rhinosinusitis in URT and coup, community acquired pneumonia (CAP) in lower respiratory tract (LRT). They spread through droplets, hand contact, and contaminated surfaces, peaking in early fall and spring. Diagnosis involves samples from the nasopharynx or LRT, with RT-PCR being the preferred method. Treatment is symptomatic, with no effective vaccines or antiviral agents, and preventive measures focus on hygiene and handwashing.

9. **Parechovirus:** Reclassified from echovirus serotypes 22 and 23 into a new picornavirus genus, differ from enteroviruses in capsid structure and cell membrane receptor usage. Transmission occurs through both fecal-oral and respiratory routes, with high viral loads in stool. Parechoviruses cause respiratory infections, exanthems, viral meningitis, encephalitis and myocarditis. In neonates, they cause encephalitis with white matter injury, presenting with fever, irritability, and poor feeding. A fatal pneumonia case linked to human parechovirus 1 has been reported in an elderly patient.

10. **Hepatovirus:** Hepatitis A (HAV), the most notable virus in the Hepatovirus genus of the Picornaviridae family, was identified in stool samples in 1973 by Feinstone and colleagues. There are five HAV genotypes, with I, II, and III affecting humans. It spreads via the fecal-oral route. HAV enters the liver via the portal vein, replicates, and excretes through bile ducts.

    Clinical infection progresses through three phases: a prodromal phase with flu-like symptoms, an icteric phase marked by jaundice and elevated liver enzymes, and a recovery phase with fatigue.. Higher mortality is seen in older individuals and those with liver disease. Diagnosis involves detecting specific antibodies (IgM for acute infection) and assessing liver function through blood tests. The inactivated vaccines, such as Havrix and VAQTA, are effective and administered in two doses.

11. **Astrovirus:** First identified in the feces of children with diarrhea, are enteric viruses recognizable by their star-like shape under electron microscopy. Genera include Mamastrovirus (infecting mammals) and Avastrovirus (infecting birds), astroviruses are now recognized as significant causes of gastroenteritis in both children and adults. They primarily spread via the fecal-oral route, with outbreaks linked to contaminated food, water, and shellfish. Astroviruses can be asymptomatic or cause mild gastroenteritis though they can also be associated with intussusception. Laboratory diagnosis is often accomplished using electron microscopy, enzyme immunoassays (EIA), or RT-PCR offering the highest sensitivity. Treatment usually involves fluid rehydration.

12. **Calcivirus:** Caliciviruses (Figure 15) including noroviruses, are significant causes of epidemic acute gastroenteritis. The prototype, Norwalk virus, was first identified during an outbreak in Norwalk, Ohio, in 1972. These viruses are known for their small, round structure and their association with gastroenteritis epidemics. They are transmitted via contaminated food and water. Sapoviruses cause milder gastroenteritis in children. Laboratory diagnosis of calicivirus infections, particularly norovirus, involves stool sample testing with RT-PCR or immunoassays. Treatment is mainly supportive, with hydration being crucial. No vaccine available.

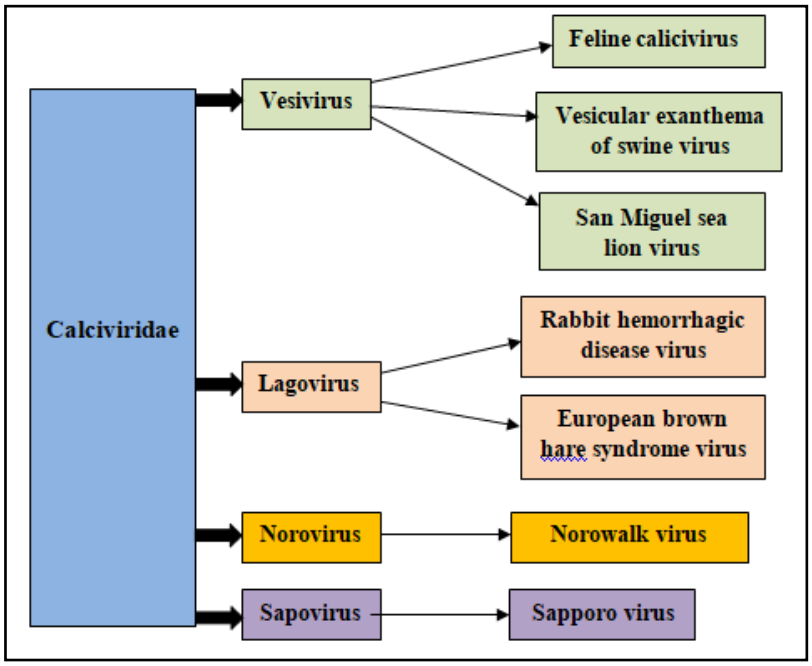

Figure 15: *Classification of calciviridae*

13. **Reovirus:** The Reoviridae family (Table 7) includes viruses that infect a broad spectrum of hosts. The name "Reoviridae" derives from early isolates that were respiratory and enteric but not linked to any known diseases, hence the term "respiratory, enteric orphanviruses."

Structure: Reoviruses are distinguished by their complex capsid architecture. Their virions have icosahedral symmetry and feature two or three layers. The innermost layer houses dsRNA segments and RNA synthesis machinery. Some reoviruses, such as those in the Rotavirus genus, have an additional protein layer with glycosylated spike proteins, resulting in a distinctive wheel-like appearance. Their genomes consist of 9 to 12 segments of linear dsRNA.

Table 7: Classification of Reoviruses

Genus	Rotavirus	Orbivirus	Orthoreovirus	Coltivirus
Subfamily	Sedoreovirinae	Sedoreovirinae	Spinareovirinae	Spinareovirinae
RNA segments	11	10	10	12
Capsid structure	3 layers	3 layers	2 layers	2 layers
Hosts	Vertebrates	Vertebrates, insects	Vertebrates	Vertebrates, insects

Replication: Reoviruses infect host cells by attaching through capsid proteins, such as rotavirus VP4 binding to histo blood group antigens (HBGAs) to aid viral entry. Once inside and uncoated, the viral core initiates mRNA synthesis, with translation occurring in the cytosol or on the rough endoplasmic reticulum (ER), where some proteins are glycosylated. The viral core assembles in viroplasms that support transcription and mRNA generation.

Rotavirus particles then assemble in the viroplasm, forming double-layered particles (DLPs) that bud into the ER lumen and shed a temporary envelope. High calcium ion concentrations are necessary for incorporating VP4 and VP7 into the outer capsid, and virions are released following host cell lysis.

VII. MAJOR GENERA OF REOVIRIDAE

1. **Rotavirus:** Rotavirus (Figure 16) causes gastrointestinal infections in humans and mammals, often leading to severe diarrhea and vomiting, especially in infants and young children. There are seven species (Groups A to G), with Group A being the most common cause of childhood gastroenteritis. Rotaviruses replicate in the small intestine, causing diarrhea through viral toxins and nutrient malabsorption, with severe symptoms linked to NSP4, which disrupts calcium levels and causes secretory diarrhea. The disease peaks in winter in temperate climates and during dry periods in tropical regions, with transmission primarily occurring via the fecal-oral route. High-risk areas include daycare centers and nursing homes. Diagnostic methods include ELISA and multiplexed RT-PCR, while cell culture is less sensitive. Treatment focuses on rehydration and electrolyte balance. Preventive vaccines, such as Rotarix and Rotateq, are crucial for reducing infection rates.

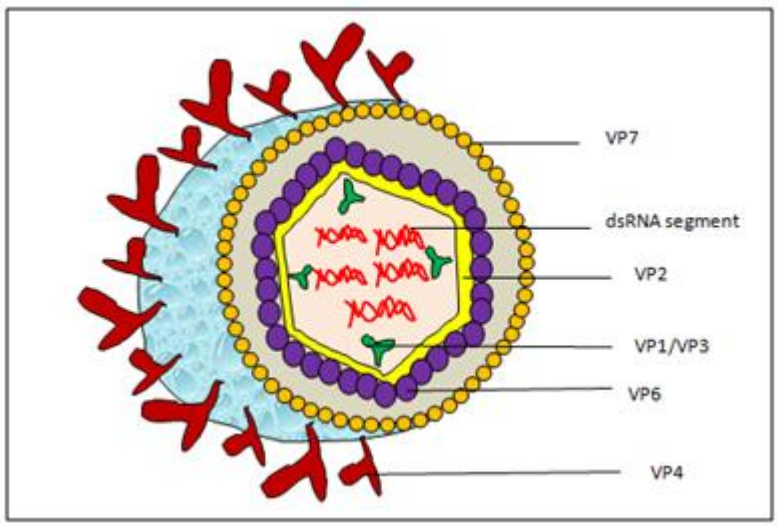

Figure 16: Structure of rotavirus

2. **Orthoreovirus:** Typically causes mild symptoms like upper respiratory infections and gastroenteritis. Orthoreoviruses are transmitted via fecal-oral and airborne routes and acts as oncolytic agents in cancer treatment.

3. **Orthoreovirus:** Typically causes mild symptoms like upper respiratory infections and gastroenteritis. Orthoreoviruses are transmitted via fecal-oral and airborne routes and acts as oncolytic agents in cancer treatment.

4. **Coltivirus:** Colorado tick fever virus, causes flu-like symptoms, transmitted by ticks and is most active in the spring and summer at high altitudes. Salmon river virus primarily affecting humans. Eyach virus is found in Ixodes ticks, associated with febrile illnesses and neurological conditions.

VIII. TOGAVIRUS

The name "Togaviridae" derives from the Latin word "toga," meaning "cloak" or "covering," referring to the virus's enveloped virion structure. This family (Figure 17) includes two genera: Alphavirus and Rubivirus.

A. Alphavirus

Alphaviruses are transmitted primarily by mosquitoes and have non-human hosts essential for their life cycles. Their RNA is encased in a nucleocapsid with glycoproteins E1 and E2 projecting from the lipid membrane, aiding in host cell entry via endocytosis.

1. Alphaviruses Causing Polyarthritis

- **Chikungunya Virus:** First identified in 1952 in Tanzania, the name "chikungunya" means "that which contorts," referring to the severe joint pain. The virus is widespread in sub-Saharan Africa, Saudi Arabia, the Indian subcontinent, and Southeast Asia. Potential vectors are-*Aedes aegypti* and *Aedes albopictus* mosquitoes, human and primates are reservoirs. It causes severe acute illness with symptoms such as high fever, severe joint pain, lymphadenopathy, conjunctivitis, and a maculopapular rash. Detection involves ELISA to identify IgM or IgG in serum samples or RT-PCR to detect viral RNA. There is no specific antiviral treatment or vaccine for chikungunya.

- **O'nyong-Nyong Virus:** First emerged in Uganda in 1959, with its name derived from a tribal word meaning "painful joints. The virus transmission occurs via *Anopheles funestus* and *Anopheles gambiae* mosquitoes. Clinical illnesses present milder fever and prominent cervical lymphadenopathy, with joint pain lasting several months.

- **Sindbis Virus:** Initially identified in Egypt, has since been found globally, including in Europe, Africa, Asia, and Australia. Birds serve as reservoirs, with mosquitoes, particularly *Aedes*, *Culiseta*, and *Culex*, acting as vectors. Clinical presentation includes joint pains, rash, fever, muscle pain, with recovery within weeks. Pogosta Disease, a sindbis variant, is characterized by arthritis and rash.

- **Ross River Virus:** First isolated from mosquitoes in northeastern Australia in 1966, has since been found in Papua New Guinea, Irian Jaya, and the Solomon Islands. Important mosquito vectors include *Aedes vigilax*, *Aedes camptorhynchus*, and *Culex annulirostris*. Joint pain persists for months or years. Most cases occur in individuals aged 20 to 60 years.

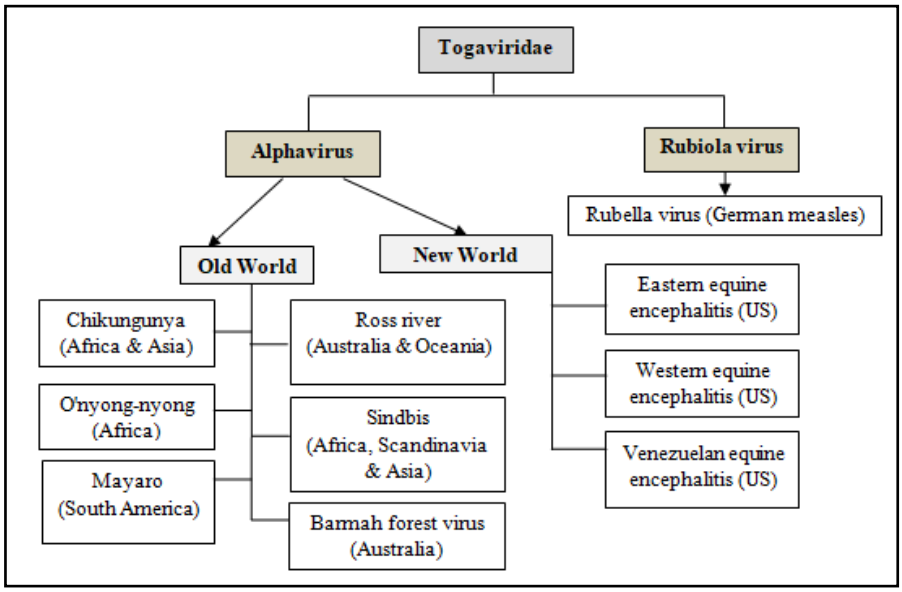

Figure 17: *Classification of Togaviridae*

- **Mayaro Virus:** First isolated from a forest worker in Trinidad in 1954, is prevalent in Central America, causes arthropathy. The virus is transmitted by forest-dwelling Haemagogus mosquitoes *Mansonia venezuelensis* and *Aedes aegypti*, maintaining a sylvatic cycle with wild vertebrates.

Other viruses are Bebaru, Cabassou, Semliki Forest virus and Barmah Forest virus.

2. Encephalitis Causing Alphaviruses

- **Eastern Equine Encephalitis:** First identified in 1933 from infected horses in Virginia and New Jersey, is primarily found in freshwater hardwood swamps across the Atlantic and Gulf Coast states. The virus is transmitted to humans and horses primarily by *Aedes*, *Coquillettidia*, and *Culex* mosquitoes. Symptoms appear 4-10 days post-infection and include fever, muscle pain and encephalitis, with brain imaging revealing edema and ischemia.

- **Western Equine Encephalitis:** Prevalent in North America, particularly west of the Mississippi River, transmitted by the *Culex tarsalis* mosquito and causes encephalomyelitis. Diagnosis involves MAC ELISA, RT-PCR and virus isolation.

- **Venezuelan Equine Encephalitis:** First isolated in 1938 from an infected animal in Venezuela, is prevalent in Central and South America. It is transmitted by *Melanoconion* mosquitoes between rodents and other mosquitoes, with epidemic cycles involving horses and humans. In children and immunocompromised it causes encephalitis with high fever, confusion, and seizures.

B. Rubella Virus (German Measles)

It was first isolated in 1962 and humans are the only natural hosts for rubella. The virus typically causes mild symptoms in postnatal infections, such as fever and rash, but can lead to severe complications like postinfectious encephalitis or arthritis in rare cases. Congenital rubella syndrome results from fetal infection, causing birth defects such as deafness, cataracts, and heart defects. The introduction of the live-attenuated rubella vaccine in 1969, can be administered alone or combined with measles and mumps as the MMR vaccine (RA 27/3 strain), has reduced its incidence. The first dose is administered to children between 12-15 months, with a second dose given at 4-6 years. In India, the MR (Measles-Rubella) vaccine campaign targets the elimination of measles and control of rubella, aiming to reach all children aged 9 months to 15 years.

Flavivirus: It is named after the Latin word "flavus" for yellow, encompass over 70 small, enveloped viruses. It has three structural (capsid, pre-membrane, and envelope) and seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5).

1. **Yellow Fever:** First recognized in the New World in 1648 and was a major epidemic threat until the early 20th century. Endemic to sub-Saharan Africa and South America, YF is transmitted by *Aedes aegypti*. Early infection stages show increased cytokine levels and viral replication in lymph nodes, spreading to the liver and kidneys. Symptoms range from mild flu-like symptoms to severe hemorrhagic fever, often resulting in death within 7-10 days. Prevention relies on the 17D vaccine, providing effective, long-lasting immunity.

2. **Dengue:** Described as "break-bone fever" in the 1780s, is caused by four serotypes of the dengue virus, primarily transmitted by *Aedes aegypti*. Dengue infections can range from mild to severe, with dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) being more severe forms. DHF involves vascular leakage and bleeding tendencies, while DSS is characterized by severe plasma leakage leading to circulatory failure. Clinical management focuses on supportive care, fluid replacement, and monitoring for complications.

3. **Japanese Encephalitis:** First isolated in Japan in 1934, has seen a rise in cases since the 1970s in Southeast Asia, India, Nepal, and Sri Lanka, likely due to agricultural changes JE is a major cause of epidemic viral encephalitis, with 10,000 to 15,000 deaths reported annually. The virus is transmitted by *Culex tritaeniorhynchus*, with humans as incidental hosts, peaking from March to October in subtropical regions. In India, JE was first identified in 1955, with endemic activity in Tamil Nadu and Andhra Pradesh, predominantly affecting children. Pathogenesis involves the virus causing inflammation and damage to the CNS, with fever and headache to severe cases leading to coma and death. Preventive measures include mosquito control and vaccination with formalin-inactivated or live attenuated vaccines.

    - **West Nile:** Primarily spreads through mosquito bites involving birds and is prevalent across Africa, southern Europe, the Middle East, Asia, Australia, and the Americas. The virus causes viremia and crosses the blood-brain barrier, leading to neuronal inflammation and damage.

- **Zika:** First identified in Uganda in 1947, and spread across the America. It is transmitted by *Aedes* mosquitoes, sexually and through body fluids. Symptoms in about 20% of cases include fever, rash, joint pain, and conjunctivitis, resolving within a week. Complications include congenital microcephaly and Guillain-Barre syndrome. Management involves supportive care, vector control, and safe sexual practices.

- **St. Louis Encephalitis:** It is prevalent in the U.S. especially among elders. The virus is transmitted by various *Culex* mosquitoes and infects birds in an enzootic cycle, with humans as incidental hosts. SLE causes febrile headaches, or severe encephalitis. Older adults and HIV-positives are at higher risk. No vaccine is available.

  Laboratory diagnosis (Figure 18) involves serological tests (IgM and IgG ELISA) and RT-PCR to detect viral RNA.

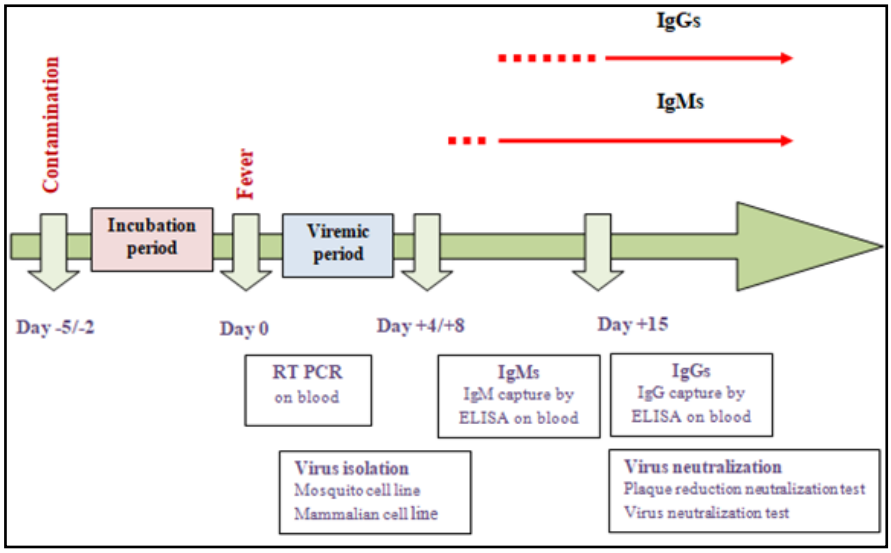

Figure 18: *Laboratory diagnosis of flavivirus*

- **Tick-Borne Encephalitis:** Initially described in Austria in the early 1930s and is caused by a virus with three subtypes—European, Siberian, and Far Eastern, known by various names such as Central European Encephalitis and Russian Spring-Summer Encephalitis. The virus is spread by Ixodes ticks in humid, forested environments and through unpasteurized milk. Clinical symptoms start with fever, headache, with meningitis and paralysis. Prevention involves supportive care and inactivated whole virus vaccine or a subunit vaccine, both requiring multiple doses.

IX. TICK-BORNE HEMORRHAGIC FEVERS

1. **Kyasanur Forest Disease (KFD):** Known as monkey fever, caused by KFD virus and primarily affects the Western Ghats of India. Transmitted through tick bites, KFD typically presents with a biphasic illness: an initial phase with flu-like symptoms, followed by a second phase with severe hemorrhagic and neurological symptoms. A formalin-inactivated vaccine is available for high-risk populations.

2. **Omsk Hemorrhagic Fever:** Omsk hemorrhagic fever, found in Russia and Romania, is clinically similar to KFD and caused by a related virus. *Dermacentor* ticks serve as the vector.

3. **Hepatitis C (HCV):** It is a spherical, enveloped positive-strand RNA virus, about 55 nm in diameter, classified under the genus Hepacivirus within the Flaviviridae family. The envelope glycoproteins E1 and E2 are crucial for viral entry, with E2 showing significant variability among isolates.HCV affects around 170 million people worldwide, identified by Houghton and Bradley. HCV primarily targets liver cells. Viremia peaks around 8-12 weeks post-infection but often persists. Chronic infection often presents with liver cirrhosis, and hepatocellular carcinoma. Diagnosis involves detecting HCV antibodies and RNA. Treatment has advanced with direct-acting antivirals (DAAs) achieving high cure rates.

X. CORONAVIRUS

Coronaviridae (Figure 19) is a virus family responsible for various illnesses in animals, including severe respiratory infections in humans. They are characterized by crown-like spikes, visible under an electron microscope. The first case in India was reported on January 21, 2020, involving a 20-year-old woman from Kerala who had traveled from Wuhan. Coronaviruses are classified into four genera: Alphacoronavirus (affecting humans and other mammals), Betacoronavirus (including those affecting bats and humans), Gammacoronavirus (primarily found in birds), and Deltacoronavirus (affecting both birds and mammals). Seven human coronaviruses have been identified, with HCoV-229E and HCoV-NL63 causing common colds and others like SARS-CoV and SARS-CoV-2 causing more severe diseases such as SARS and COVID-19. Diagnostic methods include RT-PCR, antibody tests, and imaging, while treatment and prevention strategies focus on vaccines and infection control measures.

A. Severe Acute Respiratory Syndrome (SARS)

The SARS epidemic began in Guangdong Province, China, in November 2002 and gained global attention in March 2003. Case-fatality rates ranged from 7% to 17%, spread through droplets, direct or fomite contacts causing acute respiratory distress syndrome (ARDS). The epidemic likely started with transmission from palm civets or other animals in Chinese wild game markets to humans,. Horseshoe bats are now considered the ultimate source of SARS-like viruses.

B. M**iddle East Respiratory Syndrome (MERS**)

MERS was first identified in Saudi Arabia in 2012. It is caused by the MERS-CoV and primarily affects the respiratory system. The virus is zoonotic, originating in bats and transmitted to humans through contacts with dromedary camels. It has high case-fatality rate of about 35%, causing fever, cough, and shortness of breath, often accompanied by diarrhea.

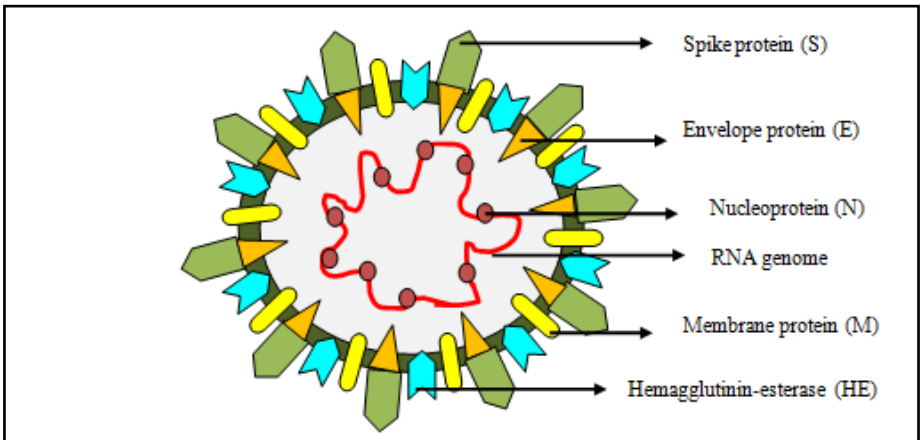

Figure 19: *Structure of coronaviridae*

C. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

SARS-CoV-2, the virus causing COVID-19, emerged in December 2019 in Wuhan, China. The virus rapidly spread worldwide, leading to a global pandemic declared by the World Health Organization in March 2020. The first case reported in India was on 21st January 2020 in a 20-year-old female from Kerala, Thrissur. SARS-CoV-2 primarily spreads through respiratory droplets from infected individuals. The pandemic has led to multiple waves of infection, with the extent and impact differing across regions due to factors like healthcare capacity, public health measures, and vaccination (Table 8) rates.

Table 8: WHO-EUA Qualified COVID-19 Vaccines

Vaccine	Type	Approved Schedule	Manufactured by
BNT162b2	mRNA	2 dosage, 21-28 days	Pfizer-BioNTech
mRNA-1273	mRNA	Two doses, 28 days apart	Moderna
AZD1222 Vaxzevria	Adenovirus (CHAdOx1) vector	2 doses, 4-12 weeks apart	AstraZeneca
COVISHIELD	Adenovirus (CHAdOx1) vector	2 doses, 4-12 weeks apart	Serum Institute of India
Ad26.COV2.5	Adenovirus type 26 vector	One dose	Janssen (Johnson & Johnson)
Covilo / BBIBPCorV	Whole inactivated Coronavirus	Two doses, 21-28 days apart	SinoPharm / Beijing Institute of Biological Products
CoronaVac	Whole inactivated virus	Two doses, 14-28 days apart	Sinovac
COVAXIN	Whole inactivated virus	Two doses, 28 days apart	Bharat Biotech, India
NVX-CoV2373 / Nuvaxovid	Protein subunit	2 doses, 21-28 days apart	Novavax
NVX-	Protein subunit	Two doses, 21-28	Serum Institute of India

CoV2373 / Covovax		days apart	
Ad5-nCoV	Adenovirus Type 5 vector	One dose	CanSinoBio

Retrovirus: The Retroviridae family comprises seven genera (Table 9), primarily infecting mammals.

Table 9: Classification of Retroviridae

Genus	Morphology	Disease	Examples
Alpharetrovrus	C type	Tumors in various avian species	Avian leukosis virus , Rous sarcoma virus
Betaretrovirus	B and D type	Mammary tumors in mice, latent infection	Mouse mammary tumor virus, Mason-Pfizer monkey virus, Jaagsiekte sheep retrovirus
Gammaretrovirus	C type	Leukemia and lymphoma in mice	Murine leukemia virus, Feline leukemia virus
Deltaretrovirus	-	T-cell leukemia, bovine leukemia; Transmission occurs mainly through bodily fluids; diagnosis involves serological or PCR-based tests	Human T-cell lymphotropic virus (HTLV) 1–2 , Bovine leukemia virus, Simian T-cell lymphotropic virus 1-3
Epsilonretrovirus	-	Skin tumors in walleye, spread horizontally among fish populations	Walleye dermal sarcoma virus
Lentivirus	Rod/cone core	HIV leads to AIDS by depleting CD4+ T cells,; immunodeficiency in cats and primates; transmissions through bodily fluids	Human immunodeficiency virus type 1 &2, Simian Immunodeficiency viruses, Equine infectious encephalitis virus
Spumavirus/ foamy virus	Immature	Foamy appearance under electron microscopy; In humans, they are found in blood, saliva, and urine but are not linked to specific diseases.	Human foamy virus (HFV)

Human Immunodeficiency Virus (HIV): The earliest known case of HIV-1 in humans dates to 1959 (Table 10), discovered from a blood sample in Kinshasa, Democratic Republic

of Congo. The virus was isolated in 1983 in Paris, using specific serums to culture T lymphocytes, a discovery credited to Robert Gallo and Luc Montagnier.

Table 10: Major Differences between HIV-1 and HIV-2

Feature	HIV-1	HIV-2
Discovery	Discovered earlier (1983)	Discovered later (1986)
Source	Zoonosis, from chimpanzee	Sooty Mangabey Monkey from West Africa
Global distribution	Widespread	Predominantly found in West Africa and parts of Central Africa
Genotype	Groups M, N and O; M has subtypes of A-K except I	None
Phenotype	Syncytium Inducing (use CXCR4, called as X4 virus), Non-syncytium inducing (use CCR5, called as R5 virus)	None
Viral load	Higher viral load	Lower viral load
Envelope protein	Contains Vpu	Contains Vpx
Drug susceptibility	Generally sensitive to standard antiretrovirals	Less sensitive to some antiretrovirals

Structure: The structural proteins (Figure 20) include gag, pol, and env. The gag protein is a precursor cleaved into p15, p18, and p24 (capsid), p17 (matrix), p7 (nucleocapsid), and p6 (late domain). The pol protein encodes polymerase reverse transcriptase for converting ssRNA to dsDNA, protease for cleaving viral polyproteins into functional proteins, and integrase for integrating viral DNA into the host genome. The env protein encodes gp140, which is cleaved into gp120 for viral attachment to host cells and gp41 for membrane fusion. The HIV genome is around 10 kilobases, and contains structural genes (gag, pol, env) and regulatory genes (tat, rev, nef).

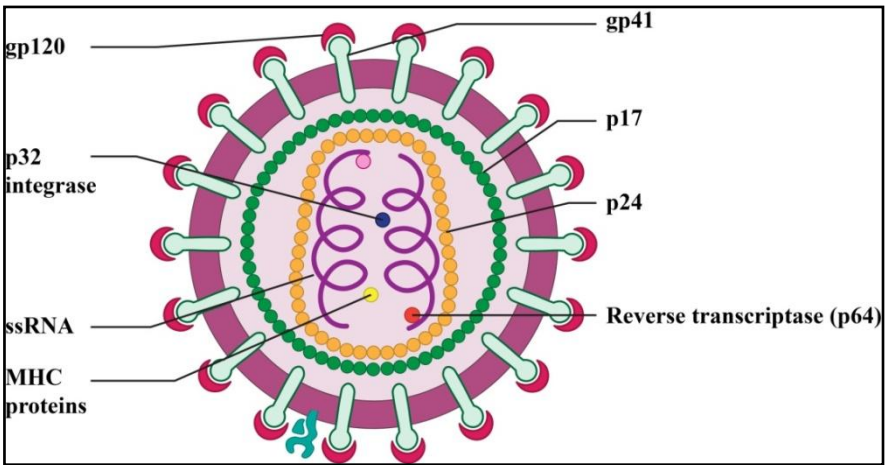

Figure 20: *Structure of HIV*

Classification: HIV-1 is classified into different groups, subtypes, and circulating recombinant forms (CRFs) with Group M (subtypes A to K except I) being the main cause of

the global pandemic. Subtypes within Group M have distinct geographical distributions, with Subtype C being the most prevalent in India. Groups O and N are less common and are confined mainly to Africa. HIV infection (Figure 21) damages CD4+ T lymphocytes, reversing the T4 cell ratio and compromising both cell-mediated and humoral immunity. This makes individuals susceptible to opportunistic infections and certain cancers, such as Kaposi's sarcoma, not caused directly by HIV but due to immune suppression.

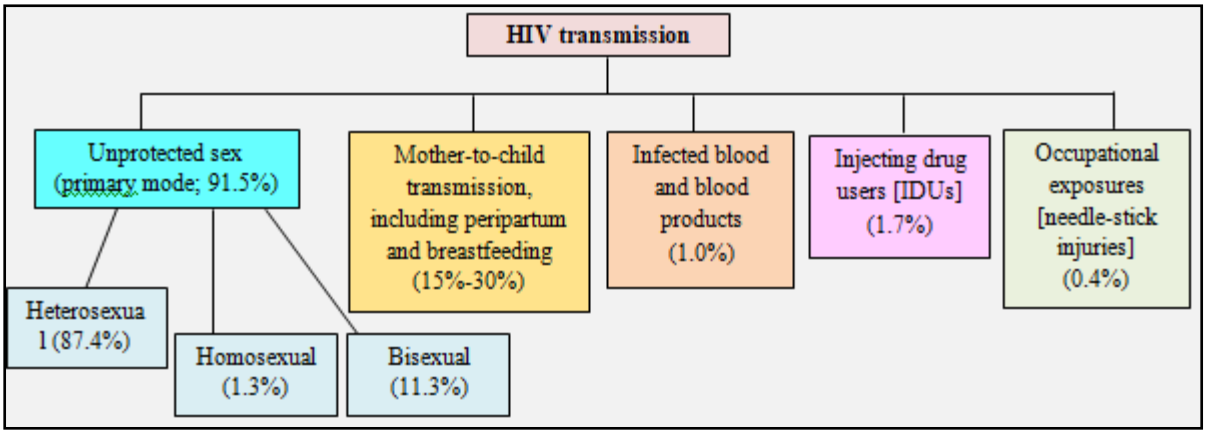

Figure 21: *Transmission of HIV Virus*

WHO HIV Clinical Stages

- **Stage 1 (CD4 Count ≥500 cells/mm³):** Asymptomatic or Persistent Generalized Lymphadenopathy (PGL).
- **Stage 2 (CD4 Count 350-499 cells/mm³):** Mild symptoms such as unexplained weight loss (<10%), sinusitis, herpes zoster, fungal nail infections).
- **Stage 3 (CD4 Count 200-349 cells/mm³)**: Moderate symptoms including weight loss (>10%), prolonged diarrhea (>1 month), pulmonary tuberculosis, severe bacterial infections, oral candidiasis, oral hairy leukoplakia, pneumonia.
- **Stage 4 (CD4 Count <200 cells/mm³)**: Severe symptoms (AIDS) such as HIV wasting syndrome, Pneumocystis pneumonia (PCP), recurrent severe bacterial pneumonia, extrapulmonary tuberculosis, Kaposi's sarcoma.

Diagnosis: HIV diagnosis (Figure 22) involves antigen detection, virus isolation, PCR, and serological tests (ELISA, Western Blot). Rapid tests offer quick screening results. Antibodies appear 2-8 weeks to months post-infection. In infants, antibody tests aren't diagnostic until after 18 months due to maternal antibodies. The p24 antigen can be detected in blood about two weeks post-infection using the p24 antigen capture assay (ELISA).

Treatment: WHO recommended TLD (Tenofovir disoproxil fumarate + Lamivudine + Dolutegravir) for HIV treatment, a regimen including Tenofovir, Lamivudine, and Efavirenz for mothers and Nevirapine or Zidovudine for newborns from HIV-infected mothers.

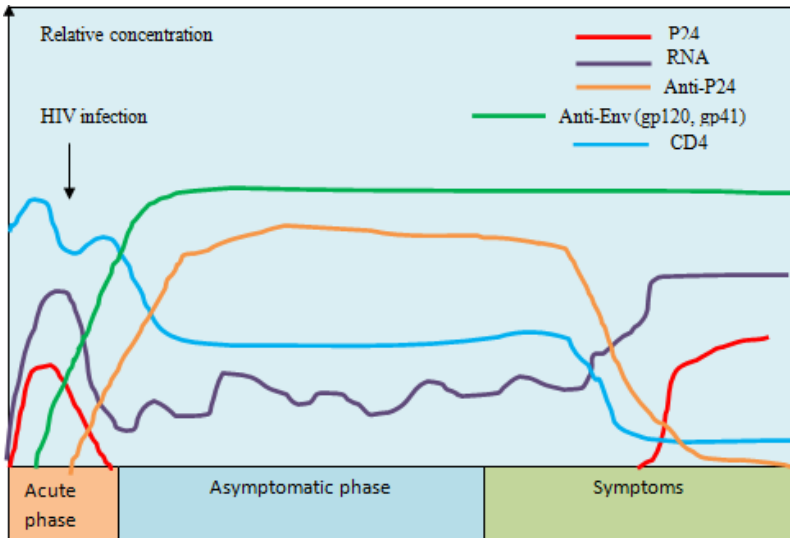

Figure 22: *Laboratory diagnosis of HIV*

Prophylaxis: Primarily a combination of tenofovir and emtricitabine are recommended for pre-exposure prophylaxis (PrEP). Post-exposure prophylaxis (PEP) must start within 72 hours of HIV exposure, requiring a 28-day course of tenofovir, emtricitabine, and either raltegravir or dolutegravir. HIV vaccine development faces significant challenges due to the virus's high mutation rate, latent reservoirs, immune evasion, and strain diversity.

Arenavirus: Arenaviruses are a family (Table 11) of viruses that affect rodents but can also infect humans

Table 11: Details of Arenaviruses

Virus	Description
Lassa Fever	Endemic in West Africa; primary reservoir is Natal multimammate mouse; infection occurs through direct contact with rodent excreta; onset within 10-14 days after exposure; causes arthralgia; abortion
Lujo Hemorrhagic Fever	Causes bleeding gum, confusion and disseminated intravascular coagulation; unknown reservoir; death due to multi-organ failure
Lymphocytic Choriomeningitis	Primary host is house mouse; transmission via close contact, organ transplantation or congenital infection; meningoencephalitis with CSF pleocytosis; fetal abnormalities (hydrocephalus and chorioretinitis)
South American hemorrhagic fevers **(causes headache, myalgia, epigastric pain, anorexia and fetal abortion)**	**Argentinian Hemorrhagic Fever-** Endemic to Argentina's Pampas region; primary reservoir is drylands *Calomys musculinus* rodent
	Bolivian Hemorrhagic Fever -Seen among young children and the elderly; caused by Machupo virus ; primary reservoir is *Calomys callosus* rodent; caused by Junin virus; infections occur during agricultural activities
	Venezuelan Hemorrhagic Fever -Focal to specific regions in Venezuela and primarily affects agricultural workers; caused by

	Guanarito virus; short-tailed *Zygodontomys brevicauda* is primary reservoir
	Brazilian hemorrhagic fever- Caused by Sabia virus

Filovirus: Filoviruses (Table 12) cause severe hemorrhagic fevers in humans and nonhuman primates.

Table 12: Details of Filoviruses

Virus	Subtypes	First Isolated	Geographical Distribution	Clinical Presesntation
Ebola	Zaire (EBOV)	1976 in Yambuku, Democratic republic of Congo (DRC)	Central Africa (DRC, Gabon)	Severe hemorrhagic fever, high fatality rate
	Sudan (SUDV)	1976 in Nzara, Sudan	East Africa (Sudan, Uganda)	Hemorrhagic fever, lower fatality rate than EBOV
	Reston (RESTV)	1989 in Reston, Virginia, USA (from monkeys)	Asia (Philippines)	Asymptomatic in humans, pathogenic in monkeys
	Ivory Coast (TAFV)	1994 in Tai Forest, Ivory Coast	West Africa (Ivory Coast)	Hemorrhagic fever, similar to EBOV
	Bundibugyo (BDBV)	2007 in Bundibugyo, Uganda	East Africa (Uganda, DRC)	Hemorrhagic fever, intermediate fatality rate
Marburg	Marburg (MARV)	1967 in Marburg and Frankfurt, Germany (from monkeys imported from Uganda)	East Africa (Uganda, Kenya), Southern Africa (Angola)	Severe hemorrhagic fever, high fatality rate
	Ravn (RAVV)	1987 in Kenya	East Africa (Kenya)	Severe hemorrhagic fever, similar to MARV

XI. ORTHOMYXOVIRUS

The Orthomyxoviridae family (Figure 23) includes segmented, ssRNA viruses with five genera: Influenzavirus A, Influenzavirus B, Influenzavirus C, Isavirus, and Thogotovirus. Their name reflects their ability to attach to mucous proteins on cell surfaces ("myxo" meaning mucous).

1. **Thogotovirus:** Transmitted by arthropods (ticks), and can infect both humans and animals Isavirus. Eg: infectious salmon anemia virus.

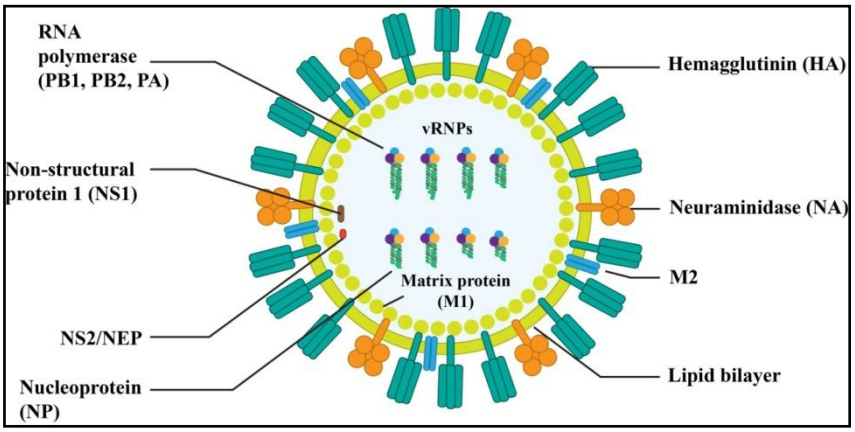

Figure 23: *Structure of orthomyxovirus*

2. **Influenza:** Influenza A and B cause regular epidemics (eg: 1918 "Spanish Flu"), while Influenza C typically results in mild infections. Influenza viruses are spherical or pleomorphic, with segmented (A & B-8 ; C-7) negative-strand RNA genomes. Genetic diversity arises from antigenic drift and shift, with drift causing gradual changes and shift leading to new strains through genome reassortment. Influenza strains are classified by their hemagglutinin (HA) and neuraminidase (NA) proteins.

   Influenza spreads primarily through respiratory secretions. Influenza has an incubation period of 1 to 3 days, with symptoms ranging from mild, cold-like symptoms to severe, rapidly progressing fatal pneumonia. Type B is linked to Reye syndrome in children and "gastric flu". Laboratory diagnosis includes immunofluorescence, virus isolation, serological tests, and PCR. Treatments include antiviral drugs like oseltamivir, with live or inactivated vaccination. Influenza vaccines are updated regularly to match circulating strains, but challenging due to virus evolution.

Paramyxovirus: They are (Table 13) enveloped, single-stranded, negative-sense RNA viruses that replicate in the cytoplasm. The details are-

Table 13: Details of Paramyxoviruses

Property	Measles	Mumps	Respiratory Syncytial Virus	Parainfluenza 1-4
Genus	Morbillivirus	Rubulavirus	Pneumovirus	Human Parainfluenza Virus
Clinical illness	**Prodromal Stage (**fever with Koplik spots on the buccal mucosa) **Eruptive Phase:** erythematous	Swelling of the parotid glands, incubation period- 12 to 25 days	Bronchiolitis and pneumonia	Croup (types 1 and 2), bronchitis, bronchiolitis, and pneumonia (type 3). minor respiratory issues and parotitis (type 4).

	rash appears on the head and spreads downward.			
Surface Glycoproteins	Hemagglutinin (H) and Fusion (F)	Hemagglutinin-Neuraminidase (HN) and Fusion (F)	Fusion (F) and Glycoprotein (G)	Hemagglutinin-Neuraminidase (HN) and Fusion (F)
Attachment Protein (G/HN)	Hemagglutinin (H)	Hemagglutinin-Neuraminidase (HN)	Glycoprotein (G)	Hemagglutinin-Neuraminidase (HN)
Intracellular Inclusions	Cytoplasm (C)	Cytoplasm (C)	Nucleus (N) and Cytoplasm (C)	Cytoplasm (C)
Diameter of Nucleocapsid (nm)	18	18	18	13
Hemolysin	+	+	+	-

Bunyavirus: The Bunyaviridae family, encompassing over 350 arthropod-borne viruses, can cause mild fevers to severe conditions like encephalitis, hemorrhagic fever, and acute respiratory illnesses.

In India, viruses such as Ingwavuma and Thottapalayam have been identified.

- **Orthobunyavirus:** Transmitted by mosquitoes and midges, causing diseases like California encephalitis and La Crosse virus encephalitis.
- **Hantavirus:** Known for hemorrhagic fevers with renal syndrome and hantavirus pulmonary syndrome, transmitted mainly by rodents.
- **Nairovirus:** Tick-borne, causing diseases such as Crimean-Congo hemorrhagic fever
- **Phlebovirus:** Spread by sandflies, associated with Rift Valley fever and sandfly fever.
- **Tospovirus:** Plant pathogens transmitted by thrips, with no known human disease.

Rhabdovirus: Rhabdoviruses (Table 14) are bullet-shaped, enveloped viruses with a ssRNA genome. The Rhabdoviridae family, named from the Greek word "rhabdos" meaning rod.

Table 14: Classification of Rhabdoviruses Causing Human Infections

Genus	Notable Viruses`	Host	Clinical Illness	Geographical Distribution
Lyssavirus	Rabies virus (RABV)	Mammals (including humans), bats	Rabies: fatal encephalitis, hydrophobia	Worldwide, especially in low- and middle-income countries
	Duvenhage virus (DUVV)	Bats, humans	Encephalitis	Southern and Eastern Africa

	Irkut virus (IRKV)	Murina leucogaster bats	Rabies-like illness	China, Russia
Ledantevirus	Le Dantec virus (LEDV)	Unknown, possibly bats	Febrile illness, rash, delirium, parkinsonism	West Africa, possible wider African distribution
	Kumasi virus (KURV)	Fruit bat (*Eidolon helvum*)	Mild febrile illness	Ghana
Tibrovirus	Bas-Congo virus (BASV)	Unknown	Hemorrhagic fever	Democratic Republic of the Congo (DRC)
	Ekpoma viruses (EKV-1, EKV-2)	Unknown	Mild febrile illness	Nigeria, detected in a Chinese worker from Angola
Vesiculovirus	Vesicular stomatitis virus (VSV)	Cattle, horses, pigs, humans	Vesicular stomatitis: flu-like symptoms, vesicles	Americas (primarily in the USA, Central, and South America)
	Chandipura virus (CHPV)	Humans, sandflies	Encephalitis-like illness, febrile illness	India, Africa

Rabies Virus: The term "rabies" originates from the Latin word for "madness," derived from the Sanskrit "rabhas" meaning "violence," Rabies transmission typically occurs through bites from infected mammals, with rare cases of aerosol and organ transplant transmission. Once transmitted, the virus remains near the entry site during an incubation period lasting weeks to months. It binds to nicotinic acetylcholine receptors at neuromuscular junctions, facilitating its concentration and subsequent uptake into peripheral motor neurons (Figure 24). From there, it spreads through axons of peripheral nerves via retrograde fast axonal transport, initially infecting local dorsal root ganglia and causing neurologic symptoms such as paresthesias and pain.

Clinical Presentation: Human rabies progression includes four stages:

- **Prodrome:** Characterized by non-specific symptoms such as fever, headache, malaise, with early neurological symptoms like pain or tingling at the site of virus entry.
- **Acute Encephalitic Phase:** Encephalitic rabies involves hyperexcitability, autonomic dysfunction, and characteristic hydrophobia. It progresses to coma and widespread organ failure.
- **Paralytic Rabies:** Begins with weakness in the bitten area and spreads to quadriparesis and facial weakness.
- **Coma and Death:** Some patients progress into a comatose state, typically resulting in death within 1-6 days after symptom onset.

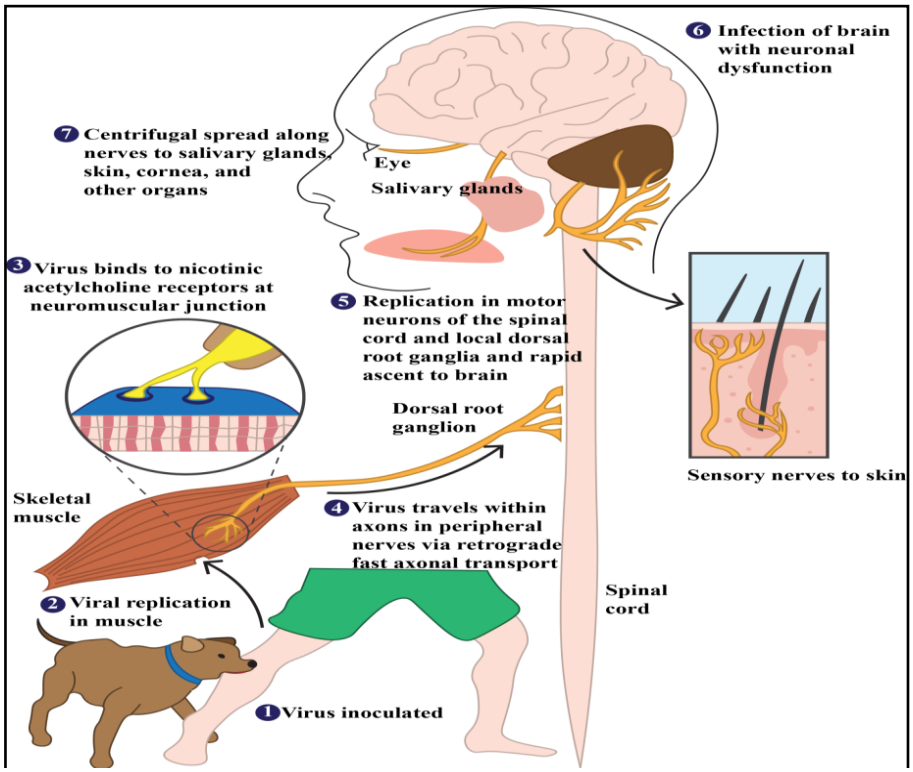

Figure 24: *Pathogenesis of rabies*

Rabies in Dogs Includes three Stages:

- **Prodrome:** Behavioral changes such as restlessness, snapping at imaginary objects, and licking or gnawing at the site of the bite.
- **Furious Rabies:** Characterized by aggressive behavior, drooling saliva, and experiencing paralysis and convulsions before death.
- **Dumb Rabies:** Involves paralysis with dogs appearing huddled and unable to feed. Though they may not exhibit aggression, they are still infectious.

Prophylaxis: Prophylaxis includes wound cleansing, administering a modern cell culture rabies vaccine, and injecting human rabies immune globulin into and around the wound. Wound management involves thorough flushing and washing with soap and water, followed by the application of povidone-iodine or an antiseptic with virucidal activity. There are different types of rabies vaccines, including neural and non-neural vaccines. Neural vaccines include the Semple vaccine (developed in 1911 in India), Beta Propiolactone vaccine. Non-neural vaccines, like human diploid cell (WI-38 and MRC-5) vaccines, are highly antigenic and safe but costly.

Prion Disease: Prion diseases arise from the misfolding of the prion protein (PrP), which exists in two forms: the normal cellular form (PrPC) and the pathogenic misfolded form (PrPSc). The PRNP gene encodes PrP, which plays roles in neuroprotection.

1. Prion Diseases in Humans

- **Kuru:** Kuru is a transmissible spongiform encephalopathy akin to scrapie in sheep, Clinical stages include ambulant, sedentary, and terminal phases with symptoms like ataxia, tremors, and cognitive decline.

- **Sporadic Creutzfeldt-Jakob Disease:** Creutzfeldt-Jakob disease (CJD) is a rare transmissible spongiform encephalopathy affecting humans, primarily as sporadic cases.

- **Variant CJD:** It was identified in Britain from 1996, raised concerns about BSE transmission through contaminated beef. Initially affecting younger individuals (aged 16-39 years), causing agitation and depression.

2. Prion Diseases in Animals

- **Scrapie:** Scrapie, a historical form of transmissible spongiform encephalopathies (TSEs), affects sheep, goats, and moufflons. Clinical symptoms including behavioral changes, blindness, ataxia, and intense pruritus. PrPSc is detectable in various tissues and secretions, contributing to horizontal transmission among animals.

- **Transmissible Mink Encephalopathy:** It is a rare transmissible spongiform encephalopathy affecting farmed mink, primarily for fur production.

- **Chronic Wasting Disease:** It is a neurological disorder affecting deer family members since 1967, spreading across states, provinces, and South Korea.

- **Bovine Spongiform Encephalopathy:** "Mad Cow disease," is a fatal neurodegenerative disease in cattle, characterized by tremors, ataxia, and aggressive behaviour. PrPSc accumulates in the brain.

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REFERENCES

[1] Abduljalil, J.M., Abduljalil, B.M., 2020. Epidemiology, genome, and clinical features of the pandemic SARS-CoV-2: a recent view. New Microbes and New Infections 35, 100672. https://doi.org/10.1016/j.nmni.2020.100672
[2] Agarwala, P., Bhargava, A., Gahwai, D.K., Negi, S.S., Shukla, P., Dayama, S., 2022. Epidemiological Characteristics of the COVID-19 Pandemic During the First and Second Waves in Chhattisgarh, Central India: A Comparative Analysis. Cureus. https://doi.org/10.7759/cureus.24131
[3] Badri, T., Gandhi, G.R., 2024. Molluscum Contagiosum, in: StatPearls. StatPearls Publishing, Treasure Island (FL).
[4] Baxby, D., 1996. Poxviruses, in: Baron, S. (Ed.), Medical Microbiology. University of Texas Medical Branch at Galveston, Galveston (TX).
[5] Cloyd, M.W., 1996. Human Retroviruses, in: Baron, S. (Ed.), Medical Microbiology.
[6] University of Texas Medical Branch at Galveston, Galveston (TX).

[7] Couch, R.B., 1996. Orthomyxoviruses, in: Baron, S. (Ed.), Medical Microbiology. University of Texas Medical Branch at Galveston, Galveston (TX).
[8] Desselberger, U., 2019. Caliciviridae Other Than Noroviruses. Viruses 11, 286. https://doi.org/10.3390/v11030286
[9] Enders, G., 1996. Paramyxoviruses, in: Baron, S. (Ed.), Medical Microbiology. University of Texas Medical Branch at Galveston, Galveston (TX). Hurisa, T.T., Jia, H., Chen, G., Xiang, F.Y., He, X.-B., Wang, X. oxia, Jing, Z., 2019.
[10] Methodical Review on Poxvirus Replication, Genes Responsible for the Development of Infection and Host Immune Response Against the Disease. Archives of Microbiology & Immunology 3, 3–19.
[11] Imran, M., Mahmood, S., 2011a. An overview of animal prion diseases. Virology Journal 8, 493. https://doi.org/10.1186/1743-422X-8-493
[12] Imran, M., Mahmood, S., 2011b. An overview of human prion diseases. Virol J 8, 559.
[13] Kostolansky, S., Waymack, J.R., 2024. Erythema Infectiosum, in: StatPearls. StatPearls Publishing, Treasure Island (FL).
[14] Jacobs, S.E., Lamson, D.M., St. George, K., Walsh, T.J., 2013. Human Rhinoviruses. Clin Microbiol Rev 26, 135–162. https://doi.org/10.1128/CMR.00077-12
[15] John, T.J., Vashishtha, V.M., 2013. Eradicating poliomyelitis:India's journey from hyperendemic to polio-free status. Indian J Med Res 137, 881–894.
[16] Joseph P. Lynch, I.I.I., Kajon, A.E., 2016. Respiratory Viral Infections: Adenovirus: Epidemiology, Global Spread of Novel Serotypes, and Advances in Treatment and Prevention. Seminars in Respiratory and Critical Care Medicine 37, 586. https://doi.org/10.1055/s-0036-1584923
[17] Li, H.-C., 2015. Hepatitis C virus: Virology, diagnosis and treatment. WJH 7, 1377.
[18] https://doi.org/10.4254/wjh.v7.i10.1377
[19] Luria, L., Cardoza-Favarato, G., 2024. Human Papillomavirus, in: StatPearls. StatPearls Publishing, Treasure Island (FL).
[20] Mehndiratta, M.M., Mehndiratta, P., Pande, R., 2014. Poliomyelitis: Historical Facts, Epidemiology, and Current Challenges in Eradication. The Neurohospitalist 4, 223–229. https://doi.org/10.1177/1941874414533352
[21] Moser, L., Schultz-Cherry, S., 2008. Astroviruses, in: Encyclopedia of Virology. Elsevier, pp. 204–210. https://doi.org/10.1016/B978-012374410-4.00348-4
[22] Nair, P.A., Patel, B.C., 2024. Herpes Zoster, in: StatPearls. StatPearls Publishing, Treasure Island (FL).
[23] Pattison, J.R., Patou, G., 1996. Parvoviruses, in: Baron, S. (Ed.), Medical Microbiology. University of Texas Medical Branch at Galveston, Galveston (TX).
[24] Payne, S., 2017. Family Reoviridae, in: Viruses. Elsevier, pp. 219–226. https://doi.org/10.1016/B978-0-12-803109-4.00026-X
[25] Payne, S., 2017. Family Bornaviridae, in: Viruses. Elsevier, pp. 191–196. https://doi.org/10.1016/B978-0-12-803109-4.00022-2
[26] Pozzetto, B., Gaudin, O.G., 1999. COXSACKIEVIRUSES (PICORNAVIRIDAE).
[27] Encyclopedia of Virology 305–311. https://doi.org/10.1006/rwvi.1999.0057
[28] Radoshitzky, S.R., De La Torre, J.C., 2019. Human Pathogenic Arenaviruses (Arenaviridae), in: Encyclopedia of Virology. Elsevier, pp. 507–517. https://doi.org/10.1016/B978-0- 12-814515- 9.00014-X
[29] Romero, J.R., Selvarangan, R., 2011. The Human Parechoviruses: An Overview. Advances in Pediatrics 58, 65–85. https://doi.org/10.1016/j.yapd.2011.03.008
[30] Salahshoori, I., Mobaraki-Asl, N., Seyfaee, A., Mirzaei Nasirabad, N., Dehghan, Z., Faraji, M., Ganjkhani, M., Babapoor, A., Shadmehr, S., Hamrang, A., 2021. Overview of
[31] COVID-19 Disease: Virology, Epidemiology, Prevention Diagnosis, Treatment, and Vaccines. Biologics 1, 2–40. https://doi.org/10.3390/biologics1010002
[32] Shim, B.-S., Stadler, K., Nguyen, H.H., Yun, C.-H., Kim, D.W., Chang, J., Czerkinsky, C., Song, M.K., 2012. Sublingual immunization with recombinant adenovirus encoding SARS-CoV spike protein induces systemic and mucosal immunity without redirection of the virus to the brain. Virol J 9, 215. https://doi.org/10.1186/1743-422X-9-215
[33] Shepherd, J.G., Davis, C., Streicker, D.G., Thomson, E.C., 2023. Emerging Rhabdoviruses and Human Infection. Biology 12, 878. https://doi.org/10.3390/biology12060878
[34] Shope, R.E., 1996. Bunyaviruses, in: Baron, S. (Ed.), Medical Microbiology. University of Texas Medical Branch at Galveston, Galveston (TX).
[35] Sinclair, W., Omar, M., 2024. Enterovirus, in: StatPearls. StatPearls Publishing, Treasure Island (FL).

[36] Smith, D.W., Mackenzie, J.S., Lindsay, M.D.A., 2008. Togaviruses Causing Rash and Fever in:Encyclopedia of Virology. Elsevier, pp. 83–91. https://doi.org/10.1016/B978-012374410- 4.00631-2
[37] Sun, L., Chen, J., Yang, K., Zhang, L., Ma, Z., Chen, X., Li, M., Zhou, X., Li, P., Zhao, H., Xiao, J., Qi, L., Wang, P., 2022. Cytomegalovirus cell tropism and clinicopathological characteristics in gastrointestinal tract of patients with HIV/AIDS. Diagnostic Pathology 17, 9. https://doi.org/10.1186/s13000-022-01193-9
[38] Usman, N., Suarez, M., 2023. Adenoviruses, in: StatPearls [Internet]. StatPearls Publishing.
[39] Wahl-Jensen, V., Feldmann, H., Sanchez, A., Zaki, S.R., Rollin, P., Peters, C.J., 1997.
[40] Filovirus Infections, in: Tropical Infectious Diseases. Elsevier, pp. 784–796. https://doi.org/10.1016/B978-0-443-06668-9.50075-2
[41] Zhao, R., Wang, M., Cao, Jing, Shen, J., Zhou, X., Wang, D., Cao, Jimin, 2021. Flavivirus: From Structure to Therapeutics Development. Life 11, 615. https://doi.org/10.3390/life11070615
[42] Zuckerman, A.J., 1996. Hepatitis Viruses, in: Medical Microbiology. 4th Edition. University of Texas Medical Branch at Galveston.

