RNA non-enveloped viruses

1- Poliovirus, the causative agent of polio (also known as poliomyelitis), is a serotype of the species *Enterovirus C*, in the family of *Picornaviridae*.

Poliovirus is composed of an RNA genome and a protein capsid. The genome is a single-stranded positive-sense RNA genome with icosahedral symmetry. Because of its short genome and its simple composition—only RNA and a nonenveloped icosahedral protein coat that encapsulates it,

Poliovirus is an enterovirus. Infection occurs via the fecal–oral route, meaning that one ingests the virus and viral replication occurs in the alimentary tract. Virus is shed in the feces of infected individuals. In 95% of cases only a primary, transient presence of viremia (virus in the bloodstream) occurs, and the poliovirus infection is asymptomatic. In about 5% of cases, the virus spreads and replicates in other sites such as brown fat, reticuloendothelial tissue, and muscle. The sustained viral replication causes secondary viremia and leads to the development of minor symptoms such as fever, headache, and sore throat. Paralytic poliomyelitis occurs in less than 1% of poliovirus infections. Paralytic disease occurs when the virus enters the central nervous system (CNS) and replicates in motor neurons within the spinal cord, brain stem, or motor cortex, resulting in the selective destruction of motor neurons leading to temporary or permanent paralysis. This is a very rare event in babies, who still have anti-poliovirus antibodies acquired from their mothers. In rare cases, paralytic poliomyelitis leads to respiratory arrest and death. In cases of paralytic disease, muscle pain and spasms are frequently observed prior to onset of weakness and paralysis. Paralysis typically persists from days to weeks prior to recovery.

- **Poliovirus is very contagious and spreads through person-to-person contact.**
- **It lives in an infected person's throat and intestines.**

Poliovirus only infects people. It enters the body through the mouth and spreads through:

- Contact with the feces (poop) of an infected person.
- Droplets from a sneeze or cough of an infected person (less common).

Pathogenesis:-

Poliomyelitis is a disease of the central nervous system. However, CD155 is believed to be present on the surface of most or all human cells. Therefore, receptor expression does not explain why poliovirus preferentially infects certain tissues. This suggests that tissue tropism is determined after cellular infection. Recent work has suggested that the type I interferon response (specifically that of interferon alpha and beta) is an important factor that defines which types of cells support poliovirus replication. In mice expressing CD155 (through genetic engineering) but lacking the type I interferon receptor, poliovirus not only replicates in an expanded repertoire of tissue types, but these mice are also able to be infected orally with the virus.

Poliovirus uses two key mechanisms to evade the immune system. First, it is capable of surviving the highly acidic conditions of the stomach, allowing the virus to infect the host and spread throughout the body via the lymphatic system. Second, because it can replicate very quickly, the virus overwhelms the host organs before an immune response can be mounted. If detail is given at the attachment phase; poliovirus with canyons on the virion surface have virus attachment sites located in pockets at the canyon bases. The canyons are too narrow for access by antibodies, so the virus attachment sites are protected from the host's immune surveillance, while the remainder of the virion surface can mutate to avoid the host's immune response.

Individuals who are exposed to poliovirus, either through infection or by immunization with poliovaccine,develop immunity.

In immune individuals, antibodies against poliovirus are present in the tonsils and gastrointestinal tract (specifically IgA antibodies) and are able to block poliovirus replication; IgG and IgM antibodies against poliovirus can prevent the spread of the virus to motor neurons of the central nervous system. Infection with one serotype of poliovirus does not provide immunity against the other serotypes; however, second attacks within the same individual are extremely rare.

Symptoms:-

Most people who get infected with poliovirus (about 72 out of 100) **will not have any visible symptoms.**

About **1 out of 4 people** with poliovirus infection **will have flu-like symptoms** that may include:

- Sore throat
- Fever
- Tiredness
- Nausea
- Headache
- Stomach pain

These symptoms usually last 2 to 5 days, then go away on their own.

A smaller proportion of people with poliovirus infection **will develop other, more serious symptoms** that affect the brain and spinal cord:

- **Paresthesia** (feeling of pins and needles in the legs)
- **Meningitis** (infection of the covering of the spinal cord and/or brain) occurs in about 1 out of 25 people with poliovirus infection

- **Paralysis** (can't move parts of the body) or weakness in the arms, legs, or both, occurs in about 1 out of 200 people with poliovirus infection

Paralysis is the most severe symptom associated with polio, because it can lead to permanent disability and death. Between 2 and 10 out of 100 people who have paralysis from poliovirus infection die, because the virus affects the muscles that help them breathe.

Even children who seem to fully recover can develop new muscle pain, weakness, or paralysis as adults, 15 to 40 years later. This is called post-polio syndrome.

Prevention & Treatment

There are two types of vaccine that can prevent polio:

Inactivated poliovirus vaccine (IPV) given as an injection in the leg or arm, depending on the patient's age. Oral poliovirus vaccine (OPV) is still used throughout much of the world.

Polio vaccine protects children by preparing their bodies to fight the poliovirus. Almost all children (99 children out of 100) who get all the recommended doses of the inactivated polio vaccine will be protected from polio.

2-Rotavirus is a genus of double-stranded RNA viruses in the family *Reoviridae*. Rotaviruses are the most common cause of diarrhoeal disease among infants and young children. Nearly every child in the world is infected with a rotavirus at least once by the age of five. Immunity develops with each infection, so subsequent infections are less severe; adults are rarely affected. There are nine species of the genus, referred to as A, B, C, D, F, G, H, I and J. **Rotavirus A**, the most common species, causes more than 90% of rotavirus infections in humans. **Rotavirus E**, which is seen in pigs, has not been confirmed as a distinct species.

The virus is transmitted by the faecal-oral route. It infects and damages the cells that line the small intestine and causes gastroenteritis (which is often called "stomach flu" despite having no relation to influenza).

Structure:-

The genome of rotaviruses consists of 11 unique double helix molecules of RNA (dsRNA). Each helix, or segment, is a gene, numbered 1 to 11 by decreasing size. Each gene codes for one protein, except genes 9, which codes for two. The RNA is surrounded by a three-layered icosahedral protein capsid. Viral particles are are not enveloped.

Transmition:-

Rotaviruses are transmitted by the faecal-oral route, via contact with contaminated hands, surfaces and objects, and possibly by the respiratory route. Viral diarrhoea is highly contagious.

Rotaviruses are stable in the environment. The viruses survive between 9 and 19 days. Sanitary measures adequate for eliminating bacteria and parasites seem to be ineffective in control of rotavirus, as the incidence of rotavirus infection in countries with high and low health standards is similar.

Sign and Symptom:-

Rotaviral enteritis is a mild to severe disease characterised by nausea, vomiting, watery diarrhoea and low-grade fever. Once a child is infected by the virus, there is an incubation period of about two days before symptoms appear. The period of illness is acute. Symptoms often start with vomiting followed by four to eight days of profuse diarrhoea. Dehydration is more common in rotavirus infection than in most of those caused by bacterial pathogens, and is the most common cause of death related to rotavirus infection.

Rotavirus A infections can occur throughout life: the first usually produces symptoms, but subsequent infections are typically mild or asymptomatic, as the immune system provides

some protection. Consequently, symptomatic infection rates are highest in children under two years of age and decrease progressively towards 45 years of age. The most severe symptoms tend to occur in children six months to two years of age, the elderly, and those with immunodeficiency. Due to immunity acquired in childhood, most adults are not susceptible to rotavirus; gastroenteritis in adults usually has a cause other than rotavirus, but asymptomatic infections in adults may maintain the transmission of infection in the community. There is some evidence to suggest blood group secretor status and the predominant bacteria in the gut can impact on the susceptibility to infection by rotaviruses.

Disease:-

Rotaviruses replicate mainly in the gut, and infect enterocytes of the villi of the small intestine, leading to structural and functional changes of the epithelium. There is evidence in humans, and particularly in animal models of extraintestinal dissemination of infectious virus to other organs and macrophages.

The diarrhoea is caused by multiple activities of the virus. Malabsorption occurs because of the destruction of gut cells called enterocytes. The toxic rotavirus protein NSP4 induces age- and calcium ion-dependent chloride secretion, disrupts SGLT1 (sodium/glucose cotransporter 2) transporter-mediated reabsorption of water, apparently reduces activity of brush-border membrane disaccharidases, and activates the calcium ion-dependent secretory reflexes of the enteric nervous system. The elevated concentrations of calcium ions in the cytosol (which are required for the assembly of the progeny viruses) is achieved by NSP4 acting as a viroporin. This increase in calcium ions leads to autophagy (self destruction) of the infected enterocytes.

NSP4 is also secreted. This extracellular form, which is modified by protease enzymes in the gut, is an enterotoxin which acts on uninfected cells via integrin receptors, which in turn cause and increase in intracellular calcium ion concentrations, secretory diarrhoea and autophagy. The vomiting, which is a characteristic of rotaviral enteritis, is caused by the virus infecting the enterochromaffin cells on the lining of the digestive tract.

Treatment of acute rotavirus infection is nonspecific and involves management of symptoms and, most importantly, management of dehydration. If untreated, children can die from the resulting severe dehydration. Depending on the severity of diarrhoea, treatment consists of oral rehydration therapy, during which the child is given extra water to drink that contains specific amounts of salt and sugar. The World Health Organisation (WHO) recommended the use of low-osmolarity oral rehydration solution and zinc supplementation as a two-pronged treatment of acute diarrhoea.

Probiotics have been shown to reduce the duration of rotavirus diarrhoea,

Human immunodeficiency virus infection and acquired immune deficiency syndrome (**HIV/AIDS**) is a spectrum of conditions caused by infection with the human immunodeficiency virus (HIV). Following initial infection a person may not notice any symptoms, or may experience a brief period of influenza-like illness. Typically, this is followed by a prolonged period with no symptoms. If the infection progresses, it interferes more with the immune system, increasing the risk of developing common infections such as tuberculosis, as well as other opportunistic infections, and tumors which are otherwise rare in people who have normal immune function. These late symptoms of infection are referred to as acquired immunodeficiency syndrome (AIDS).

HIV is spread primarily by sexual contact , contaminated blood transfusions, hypodermic needles, and from mother to child during pregnancy, delivery, or breastfeeding.

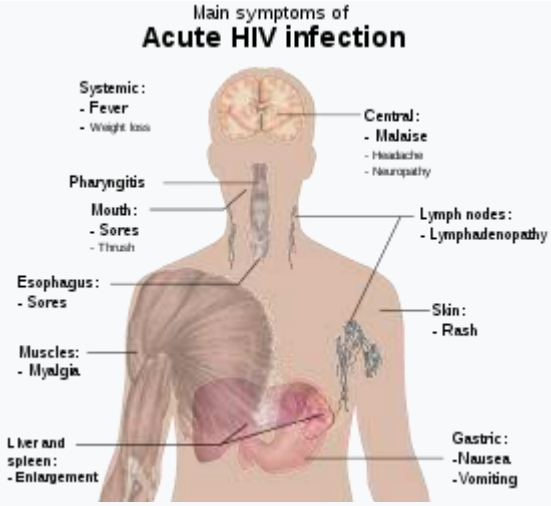
HIV is a member of the group of viruses known as retroviruses.

Methods of prevention include safe sex, needle exchange programs, treating those who are infected, and pre- & post-exposure prophylaxis. Disease in a baby can often be prevented by giving both the mother and child antiretroviral medication. There is no cure or vaccine; however, antiretroviral treatment can slow the course of the disease and may lead to a near-normal life expectancy. Treatment is recommended as soon as the diagnosis is made. Without treatment, the average survival time after infection is 11 years.

Signs and Symptoms:-

There are three main stages of HIV infection: acute infection, clinical latency, and AIDS.

Acute infection



Main symptoms of acute HIV infection

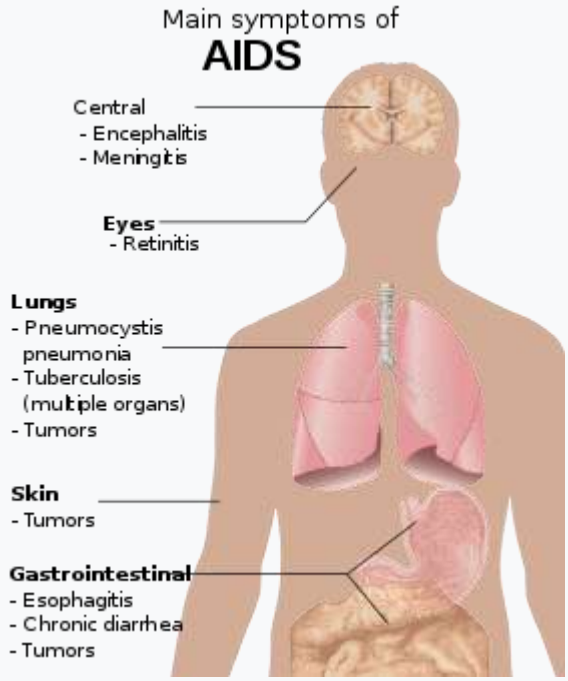
The initial period following the contraction of HIV is called acute HIV, primary HIV or acute retroviral syndrome. Many individuals develop an influenza-like illness or a mononucleosis-like illness 2–4 weeks after exposure while others have no significant symptoms. Symptoms occur in 40–90% of cases and most commonly include fever, large tender lymph nodes, throat inflammation, a rash, headache, tiredness, and/or sores of the mouth and genitals. The rash, which occurs in 20–50% of cases, presents itself on the trunk and is maculopapular, classically. Some people also develop opportunistic infections at this stage. Gastrointestinal symptoms, such as vomiting or diarrhea may occur. Neurological symptoms of peripheral neuropathy or Guillain–Barré syndrome also occurs. The duration of the symptoms varies, but is usually one or two weeks.

Clinical latency

The initial symptoms are followed by a stage called clinical latency, asymptomatic HIV, or chronic HIV. Without treatment, this second stage of the natural history of HIV infection can last from about three years to over 20 years (on average, about eight years). While typically there are few or no symptoms at first, near the end of this stage many

people experience fever, weight loss, gastrointestinal problems and muscle pains. Between 50% and 70% of people also develop persistent generalized lymphadenopathy, characterized by unexplained, non-painful enlargement of more than one group of lymph nodes (other than in the groin) for over three to six months.

Acquired immunodeficiency syndrome



Main symptoms of AIDS.

Acquired immunodeficiency syndrome (AIDS) is defined as an HIV infection with either a $CD4^+$ T cell count below 200 cells per µL or the occurrence of specific diseases associated with HIV infection. In the absence of specific treatment, around half of people infected with HIV develop AIDS within ten years. The most common initial conditions that alert to the presence of AIDS are pneumocystis pneumonia (40%), cachexia in the form of HIV wasting syndrome (20%), and esophageal candidiasis. Other common signs include recurrent respiratory tract infections.

Opportunistic infections may be caused by bacteria, viruses, fungi, and parasites that are normally controlled by the immune system. Which infections occur depends partly on what organisms are common in the person's environment. These infections may affect nearly every organ system.

People with AIDS have an increased risk of developing various viral-induced cancers, including Kaposi's sarcoma, Burkitt's lymphoma, primary central nervous system lymphoma, and cervical cancer. Kaposi's sarcoma is the most common cancer, occurring in 10% to 20% of people with HIV.

Transmission:-

HIV is spread by three main routes: sexual contact, significant exposure to infected body fluids or tissues, and from mother to child during pregnancy, delivery, or breastfeeding (known as vertical transmission). There is no risk of acquiring HIV if exposed to feces, nasal secretions, saliva, sputum, sweat, tears, urine, or vomit unless these are contaminated with blood. It is also possible to be co-infected by more than one strain of HIV—a condition known as HIV superinfection.

Structure:-

The viral RNA genome is converted (reverse transcribed) into double-stranded DNA by a virally encoded reverse transcriptase that is transported along with the viral genome in the virus particle. The resulting viral DNA is then imported into the cell nucleus and integrated into the cellular DNA by a virally encoded integrase and host co-factors. Once integrated, the virus may become latent, allowing the virus and its host cell to avoid detection by the immune system.

Diagnosis:-

Days after exposure needed for the test to be accurate	
Blood test	**Days**
Antibody test (rapid test, ELISA 3rd gen)	23–90
Antibody and p24 antigen test (ELISA 4th gen)	18–45
PCR	10–33

HIV/AIDS is diagnosed via laboratory testing and then staged based on the presence of certain signs or symptoms.

HIV testing

HIV Rapid Test being administered

Oraquick

Most people infected with HIV develop specific antibodies (i.e. seroconvert) within three to twelve weeks after the initial infection. Diagnosis of primary HIV before seroconversion is done by measuring HIV-RNA or p24 antigen. Positive results obtained by antibody or PCR testing are confirmed either by a different antibody or by PCR.

Antibody tests in children younger than 18 months are typically inaccurate, due to the continued presence of maternal antibodies.

Vaccination:-

Currently there is no licensed vaccine for HIV or AIDS. The most effective vaccine trial to date, RV 144, was published in 2009; it found a partial reduction in the risk of transmission of roughly 30%, stimulating some hope in the research community of developing a truly effective vaccine. Further trials of the RV 144 vaccine are ongoing.

Treatment:-

There is currently no cure, nor an effective HIV vaccine. Treatment consists of highly active antiretroviral therapy (HAART) which slows progression of the disease. Treatment also includes preventive and active treatment of opportunistic infections. Rapid initiation of anti-retroviral therapy within one week of diagnosis appear to improve treatment outcomes in low and medium-income settings.

Antiviral therapy

Current HAART options are combinations (or "cocktails") consisting of at least three medications belonging to at least two types, or "classes", of antiretroviral agents. Initially, treatment is typically a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside analog reverse transcriptase inhibitors (NRTIs). Typical NRTIs include: zidovudine (AZT) or tenofovir (TDF) and lamivudine (3TC) or emtricitabine (FTC).

Oncogenic Viruses

Introduction:-

- Viruses are the intracellular pathogens that reproduce only in the living cell and manipulate the cellular machinery to produce more viruses.
- Viral replications can affect cellular genes of the host in multiple cancerous ways.
- An oncovirus is a virus that can cause cancer.
- Viruses account for about 20% of total human cancer cases.
- Although many viruses can cause various tumors in animals, only seven of them are associated with human cancers and are currently considered oncogenic viruses.
- These viruses include hepatitis B virus (HBV), hepatitis C virus (HCV), human papillomavirus (HPV), Epstein Barr virus (EBV), human herpes virus 8 (HHV8), Merkel cell polyomavirus (MCPyV), and HTLV-1.
- HBV and HCV cause approximately 80% of hepatocellular carcinoma (HCC), the most common cancer of the liver.
- High-risk HPV strains are the major causes of cervical cancer and other ano-genital neoplasms as well as a significant proportion of head and neck tumors.
- EBV is associated with nasopharyngeal carcinoma, Hodgkin's lymphoma, and Burkitt's lymphoma.
- HHV8 (also called Kaposi's sarcoma-associated herpesvirus, KSHV) is responsible for Kaposi's sarcoma often found in patients with acquired immunodeficiency syndrome (AIDS).
- MCPyV causes Merkel cell carcinoma and HTLV-1 is the causative agent of adult T-cell lymphoma.

Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV)

- HBV and HCV can cause a liver infection that can sometimes lead to liver cancer.
- Medication doesn't cure HBV, but it can lower the chance of liver damage and liver cancer.

- There's a vaccine to prevent HBV, but not HCV. Those with higher chances of getting HBV should get vaccinated. That includes people who have HIV, inject illicit drugs, or are health care workers.

Kaposi Sarcoma-Associated Herpesvirus (KSHV)

- KSHV is a herpes virus that can cause Kaposi sarcoma, a cancer of the blood vessels, as well as two types of lymphoma.
- The virus can be spread during sex, and also through blood and saliva.

Merkel Cell Polyomavirus (MCV)

- MCV is a common virus that infects the skin.
- It usually doesn't cause symptoms or lead to cancer. But in some people, MCV causes a rare skin cancer called Merkel cell carcinoma.

Human Papillomavirus (HPV)

- HPV is a group of more than 200 viruses, and at least a dozen of them can cause cancer.
- HPV spreads during vaginal or anal sex.
- HPV often goes away on its own and doesn't cause any health problems. Some people stay infected, though.
- If they have the HPV that causes cancer, it can lead to cancers of the cervix, vulva, vagina, penis, anus, tonsils, or tongue.
- HPV vaccines can keep you from getting infected with the virus. Health officials recommend them for young women through age 26 and young men through age 21.

Human T-Cell Lymphotropic Virus Type 1 (HTLV-1)

- HTLV-1 infects T cells, which are a type of white blood cell. It can cause leukemia and lymphoma.
- HTLV-1 spreads several ways, including: From mother to child during birth or through breastfeeding, sharing needles with infected people, organ transplant, unsafe sex, etc.

- About 2% to 5% of people who have the virus get adult T-cell leukemia or other health conditions. It's not clear why some people get leukemia and others don't. Symptoms and how it develops are different for each person.
- There isn't a cure or treatment for HTLV-1. It's a lifelong condition. But regular checkups can lower your chances of cancer.

Epstein-Barr Virus (EBV)

- EBV is a common virus. Most people get infected with it at some point in their lives. Most of the time, people with EBV stay healthy and don't have symptoms.
- For others, EBV can cause mononucleosis and other more serious conditions, from viral meningitis to pneumonia.

Several cancers are linked with EBV as well:

- Burkitt's lymphoma
- Nasopharyngeal carcinoma (cancer of the upper throat)
- Hodgkin's and non-Hodgkin's lymphoma
- T-cell lymphomas
- Post-transplant lymphoproliferative disorder (too many white blood cells)
- Leiomyosarcoma (cancer in the soft tissue)
- There's no vaccine for EBV, but you can help protect yourself by not kissing or sharing drinks, food, or personal items with someone who has the virus.
- There's no specific treatment if you have EVB, but you can ease symptoms if you drink plenty of fluids, get rest, and take medicines for pain and fever.

Mechanisms of Viral Oncogenesis

The molecular mechanisms of viral oncogenesis are complex and may involve:

1. Induction of chronic inflammation
2. Disruption of host genetic and epigenetic integrity and homeostasis
3. Interference with cellular DNA repair mechanisms resulting in genome instability
4. Cell cycle dysregulation.

5. Oncogenic DNA viruses can also insert their genomic DNA into cellular chromosomes, resulting in genetic abnormity.

6. Viral 'oncoproteins' can activate cellular signaling pathways, alter the expression of cellular genes and microRNAs either transcriptionally or post-transcriptionally, and destabilize or inactivate tumor suppressor proteins and proteins that regulate cell polarity, signal transduction, immune response, and apoptosis.

7. Genetic and epigenetic alterations induced by infection and replication of oncogenic viruses may lead to the appearance and proliferation of cancer stem cells, which are important for the initiation, progression, metastasis, relapse, and chemotherapy resistance of cancers.

The importance and underlying molecular mechanisms of specific cellular genes and signaling pathways in viral oncogenesis are subjects of intense research efforts.

References

1. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4731227

2. https://www.ncbi.nlm.nih.gov/pubmed/27830995

3. https://www.asm.org/Articles/2019/January/The-Seven-Viruses-that-Cause-Human-Cancers

References: From

Jawetz, R., J.L. Melnick, and E.A. Adelberg, Review of Medical Microbiology, 16th Edition.

Dr. Margaret Hunt., University of South Carolina School of MedicineBASIC VIROLOGY: DEFINITIONS, CLASSIFICATION, MORPHOLOGY AND CHEMISTRY