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REVIEW REPORT ON STUDY OF HUMAN VIRAL DISEASES

Swati Karande*, Shirish S. Patil, Dr Suresh G. Killedar

Assistant Professor of Pharmacology, Sant Gajanan Maharaj College of Pharmacy, Mahagaone.

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***Corresponding Author**
Swati Karande
Assistant Professor of Pharmacology, Sant Gajanan Maharaj College of Pharmacy, Mahagaone.

ABSTRACT

Understanding the molecular events accompanying virus replication is essential for the proper understanding and control of all virus diseases. The virus replication cycle generates new viral genomes and proteins in sufficient quantities to ensure propagation of the viral genome; this requires that the extracellular viral genome is protected from enzymatic degradation and can be introduced into further target cells for further rounds of replication. The initial recognition between virus and host is more complex than originally supposed and may involve more than one cellular receptor. A critical first intracellular step is the generation of viral mRNA by one of a limited number of strategies first described by David Baltimore. Lacking ribosomes, viruses have no means of producing protein and are reliant on the host cell for protein synthesis. Viral proteins are often modified by host cell glycosylation during or after virus assembly. Temporal regulation of intracellular events is critical in all but the very simplest of viruses, and someform ofsuppression of the hos tinnateimmuneres ponseiscommontonearly all human viruses. Infected cells often produce non-infectious particles with incomplete genomes, and these defective interfering particles may play a role in pathogenesis. Understanding these processes will open up a range of targets for the development of novel therapies. Here we review the current concepts in viral pathogenesis, clinical signs and symptoms, diagnosis, treatment, prevention and control in humans.

KEYWORDS: Virus, Antiviral Drugs, Zika Virus, HIV.

INTRODUCTION

A virus, in the words of one eminent scientist, can be thought of as "a piece of bad news wrapped in protein." Unlike bacteria and fungi, viruses are not living organisms; rather, they consist in essence of a length of nucleic acid-their genetic material-that is surrounded and protected by a protein coat. The genetic material of viruses is com posed of one type of nucleic acid, which may be either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA).

Viruses carry out no independent metabolism: they do not respiration, they do not process nutrients, they don otgeneratewasteproducts,andtheyrelyonlivingcellsoftheh ostfortheir reproduction. A virus outside a cell is an inert bit of particulate matter; once inside, however, the virus sizes common and of the cell's biosynthetic machinery, converting the cell in to a" high- tech" factory for the production of new virus particles.

Many viruses eventually kill their host cells, resulting in disease and provoking an assault by the immune response of the host. Sometimes, this response goes away, so that the harmful effects of the immune response are actually more serious than those of the viral disease itself Other viruses provoke little, if any, reaction, and some can remain dormant, or latent, in the host for years.

The vast majority of all virus infections appear to be asymptomatic in nature that is, the infections are so mild and the host response so effective that clinical signs of disease never develop.

Definition of Virus

An infective agent that typically consists of a nucleic acid molecule in a protein coat, is too small to be seen by light microscopy and is able to multiply only within living host cells.

Definition of viral diseases

A **viral disease** (or **viral** infection, or infectious **disease**) occurs when an organism's body is invaded by pathogenic **viruses**, and infectious **virus** particles (viroid) attach to and enter susceptible cells.

Components of a Viral cell

Virus particles (known as viroid) consist of two or three parts: the genetic material made from either DNA or RNA, long molecules that carry genetic information; a protein coat that protects these genes; and in some cases an envelope of lipids that surrounds the protein coat when they are outside a cell. The shapes of viruses range from simple helical and icosahedral forms to more complex structures. The average virus is about one one-hundredth the size of the average bacterium.

Steps Of Viral Infection

A virus must use cell processes to replicate. The viral replication cycle can produce dramatic biochemical and structural changes in the host cell, which may cause cell damage. These changes, called cytoplasm (causing cell damage) effects, can change cell functions or even destroy the cell. Some infected cells, such as those infected by the common cold virus known as rhinovirus, die through lysosome (bursting) or apoptosis (programmed cell death or "cell suicide"),releasing all progeny viroid at once. The symptoms of viral diseases result from the immune response to the virus, which attempts to control and eliminate the virus from the body and from cell damage caused by the virus. Many animal viruses, such as HIV (Human Immunodeficiency Virus), leave the infected cells of the immune system by a process known as budding, where Virus leave the cell individually. During the budding process, the cell does not undergo so some and is not immediately killed. However, the damage to the cells that the virus infects may make it impossible for the cells to function normally, even though the cells remain alive for a period of time. Most productive viral infections follow similar steps in the virus replication cycle: attachment, penetration, uncoated replication, assembly, and release.

A virus must undergo the process of replication to create new, infectious viroid that is able to infect other cells of the body or subsequent hosts. After gaining entry into the body, a virus makes physical contact with and crosses the plasma membrane of a target cell. Inside, it releases and replicates its genome while facilitating the manufacture of its proteins by host ribosomes. Virus particles are assembled from these newly synthesized biological molecules and become infectious Virus. Finally, the Virus is released from the cell to continue the process of infection.

The seven stages of virus replication are categorized as follows:

1. Attachment/Adsorption
2. Penetration
3. Uncoated
4. Replication
5. Assembly
6. Maturation
7. Release

Attachment

A virus attaches to a specific receptor site on the host cell membrane through attachment proteins in the capsid or via glyco proteins embedded in the viral envelope. The specificity of this interaction determines the host (and the cells within the host) that can be infected by a particular virus. This can be illustrated by thinking of several keys and several locks where each key will fit only one specific lock.

Penetration/ Entry

The nucleic acid of bacterio phages enters the host cell naked, leaving the capsid outside the cell. Plant and animal viruses can enter through endocytosis, in which the cell membrane surrounds and engulfs the entire virus. Some enveloped viruses enter the cell when the viral envelope fuses directly with the cell membrane. Once inside the cell, the viral capsid is degraded and the viral nucleic acid is released, which then becomes available for replication and transcription.

Penetration is characterized in three phases:

- Direct penetration
- Receptor mediated endocytosis
- Fusion

Uncoated

Coat is lost and nucleic acid is exposed which is non infectious.

Replication and Assembly

The replication mechanism depends on the viral genome. DNA viruses usually use host cell proteins and enzymes to make additional DNA that is transcribed to messenger RNA (mRNA), which is then used to direct protein synthesis. RNA viruses usually use the RNA coreas a template for synthesis of viral genomic RNA and mRNA. The viral mRNA directs the host cell to synthesize viral enzymes and capsid proteins, and to assemble new viroid Of course, there are exceptions to this pattern. If a host cell does not provide the enzymes necessary for viral replication, viral genes supply the information to direct synthesis of the missing proteins.

Retroviruses, such as HIV, have an RNA genome that must be reverse transcribed into DNA, which then is incorporated into the host cell genome.

To convert RNA into DNA, retroviruses must contain genes that encode the virus-specific enzyme reverse transcriptase, which transcribes an RNA template to DNA. Reverse transcription never occurs in uninfected host cells; the needed enzyme, reverse transcriptase, is only derived from the expression of viral genes within the infected host cells. The fact that HIV produces some of its own enzymes not found in the host has allowed researchers to develop drugs that inhibit these enzymes. These drugs, including the reverse transcriptase inhibitor AZT, inhibit HIV replication by reducing the activity of the enzyme without affecting the host's metabolism. This approach has led to the development of a variety of drugs used to treat HIV and has been effective at reducing the number of infectious viroid (copies of viral RNA) in the blood to non-detectable levels in many HIV-infected individuals.

Maturation

Maturation of new Virus takes place inside the host cell.

Release

The last stage of viral replication is the release of the new Virus produced in the host organism. They are then

able to infect adjacent cells and repeat the replication cycle. As you have learned, some viruses are released when the host cell dies, while other viruses can leave infected cells by budding through the membrane without directly killing the cell.

Release takes place either by cleavage of cell membrane or by budding.

Spreading of viruses

Viruses spread in many ways; viruses in plants are often transmitted from plant to plant by insects that feed on the sap of plants, such as aphids; viruses in animals can be carried by blood-sucking insects. These disease-bearing organisms are known asvectors.

Influenza viruses are spread by coughing and sneezing. Nor virus and rotavirus common causes of viral gastroenteritis, are transmitted by the – oral route and are passed from person to person by contact, entering the body in food or water. HIV is one of several viruses transmitted through sexual contact and by exposure to infected blood. The range of host cells that a virus can infect is called its "host range". This can be narrow or, as when a virus is capable of infecting many species, broad.

Viral infections in animals provoke an immune response that usually eliminates the infecting virus. Immune responses can also be produced by vaccines, which confer an artificially acquired immunity to the specific viral infection. However, some viruses including those causing AIDS and viral hepatitis evade these immune responses and result in chronic infections.

Antibiotics have no effect on viruses, but several antiviral Viral diseases are extremely wide spread infections caused by viruses, a type of microorganism. There are many types of viruses that cause a wide variety of viral diseases. The most common type of viral disease is the common cold, which is caused by a viral infection of the upper respiratory tract (nose and throat). Other common viral diseases include:

- Chickenpox
- Flu(influenza)
- Herpes
- Human immunodeficiency virus(HIV/AIDS)
- Human papilloma virus (HPV)
- Infectious mononucleosis
- Mumps, measles andrubella
- Shingles
- Viral gastroenteritis (stomach flu)
- Viral hepatitis
- Viral meningitis
- Viral pneumonia drugs have been developed.

Viral diseases

About These Diseases

Viral diseases are contagious and spread from person to person when a virus enters the body and begins to multiply. Common ways that viruses spread from person to person include:

- Breathing in air-borne droplets contaminated with a virus.
- Eating food or drinking water contaminated with a virus.
- Having sexual contact with a person who is infected with a sexually transmitted virus.
- Indirect transmission from person to person by a virus host, such as a mosquito, tick, or field mouse.
- Touching surfaces or body fluids contaminated with a virus.

In some cases, viral diseases can lead to serious, possibly life-threatening complications, such as dehydration, bacterial pneumonia, and other secondary bacterial infections. People at risk for complications include those who have a chronic disease or a suppressed or compromised immune system, and the very young and very old. In addition, certain types of sexually transmitted viral infections, such as HIV/AIDS and HPV, can lead to serious complications and death. Seek prompt medical care if you think you have a viral disease, especially if you are at risk for complications, or if you believe you have been exposed to a sexually transmitted disease.

General treatment and diagnosis

Viral disease is usually detected by clinical presentation, for instance severe muscle and joint pains preceding fever, or skin rash and swollen lymph glands. Laboratory investigation is not directly effective in detecting viral infections, because they do not themselves increase the cell count. Laboratory investigation may be useful in diagnosing associated bacterial infections, however. Viral infections are commonly of limited duration, so treatment usually consists in reducing the symptoms antipyretic and analgesic drugs are commonly prescribe.

Treatment

Antiviral Drugs Definition

An agent that kills a virus or that suppresses its ability to replicate and, hence, inhibits its capability to multiply and reproduce.

For **example**, amantadine (Symmetry) is a synthetic **antiviral**. It acts by inhibiting the multiplication of the influenza A virus.

Use Of Antiviral Drugs

✓ Anti-Herps Virus

Idoxuridine, Trifluridine, Acyclovir.

✓ Anti-Influenza Virus

Amantadine, Rimantadine.

✓ Anti-Hepatitis Virus

Lamivudine, Ribavirin.

✓ Anti-Retrovirus

Nucleoside reverse transcriptase inhibitors (NRTIs)
Zidovudine (AZT), Didanosine, Lamivudine, Tenofovir.

Nonnucleoside reverse transcriptase inhibitors
Nevirapine, Delavirdine, Efavirenz.

Protease inhibitors
Ed. Indinavir, Nelfinavir, Amprenavir, Lopinavir, Atazanavir.

Prevention of Human Rhinovirus infections
Human rhinovirus (HRV) causes over 80% of the common cold in the fall. Developing vaccines against HRV is unfeasible because HRVs have at least 115 antigenically distinct serotypes. One of the proven methods to prevent and inhibit viral infections is to block host cell receptors that are used by viruses to gain cell entry. Receptor blockage is commonly achieved via application of MAbs that bind to specific epitopes on the receptor molecules. A plethora a of in vitro studies have reported effective viral inhibition by receptor-blocking MAbs. However, these works have not yielded yet any approved drug on the markers.

High avidity is achieved by multivalency. To improve avidity of HRV receptor blocking antibody, a novel tetravalent recombinant antibody, CFY196, has been generated against ICAM-1. CFY196 is composed of Fab fragment of a humanized version of MAb1A6 fused with a linker derived from human immunoglobulin D (IgD) hinge and a tetramerization domain derived from the coiled-coil sequence of human transcription factor ATFα. CFY196 is expressed in bacteria and purified as a homogenous tetrameric molecular complex. CFY196 exhibited almost two-orders-of-magnitude improvement in functional affinity compared with its bivalent counterpart based on the kinetic parameters measured by BIAcore analysis. Such kinetic improvement also directly leads to functional superiorities of CFY196. In vitro assays, CFY196 consistently and significantly outpaced the best commercial anti- ICAM-1 MAbs in preventing HRV infection as measured by reduction of cytopathic effects and HRV viral titers. The preclinical findings of CFY196 bode well its efficacy in human since MAb 1A6, from which CFY196 is derived, has already exhibited positive effects in a human trial. Moreover, to prevent possible immunogenicity, CFY196 is humanized. Biochemical Prevention and Treatment via targeting on viral mRNA.

Targeting viral mRNA is one of the most active areas of research and development. Several strategies have emerged over the years and are being tested pre-clinically and clinically. They include: antisense-oligonucleotides (AS-ONs), ribozymes, and recently, RNA interference (RNAi).

1. Human Immunodeficiency Virus Infection

1.1. Introduction

HIV stands for human immunodeficiency virus. AIDS stands for acquired immunodeficiency syndrome. HIVH-It infects only human beings and also transmitted between humans not from animals. It is not transmitted from bites of mosquitoes, batsorany other species. The body has immune system whose function is to protectour body from germs, infections etc. But a person suffering from HIV has inability to fight against diseases. However, immune system becomes deficient. Virus is a small, simplest thing which is in inactive form outside the body and becomes active when it goes inside human body. AIDS It is not inherited means it cannot be transmit from one generation to another. It is transmitted to healthy person by infected person. It weakens the immune system. Creates a deficiency of CD4+ cells in the immune system.

It is a collection of diseases. HIV is a virus that causes AIDS. Normally, our body has immune system that attack viruses and bacteria. Immune system has white blood cells which protectus from infections. White blood cells contain CD4+ cells which is also known as helper cells or T cells. A person who is infected will be able to develop. These infections take advantage of body's immune system. These infections cause several health problems and even lead to death ofaperson.HIV has in ability to protect against diseases and count of CD4 cells also decreases in HIV. There is no cure of AIDS but there are certain medicines which are use to slow down the diseases so you stay healthier for long time. There is no medicine to get rid of diseases. HIV is a virus that causes AIDS. Normally, our body has immune system that attack viruses and bacteria. Immune system has white blood cells which protect us from infections. White blood cells contain CD4+cellswhichis also known as helper cells or Tcells. A person who is infected will be able to develop. These infections take advantage of body's immune system. These infections cause several health problems and even lead to death of a person. HIV has inability to protect against diseases and count of CD4 cells also decreases in HIV. There is no cure of AIDS but there are certain medicines which are use to slow down the diseases so you stay healthier for long time. There is no medicine to get rid of diseases.

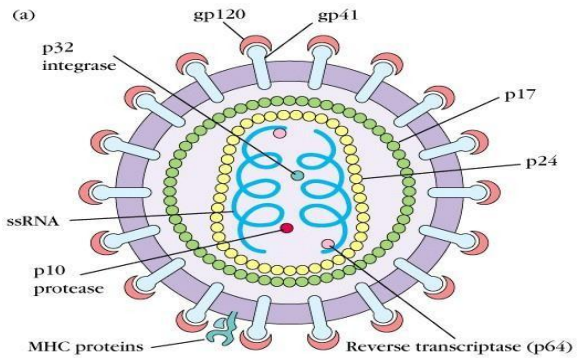

Figure 1: Structure of HIV virus.

1.2. Transmission

Transmission HIV is transmitted principally in three ways: By sexual contact, by blood through transfusion,

blood products or contaminated needles or by passage from mother to child. Although homosexual contac tremain samajorsource of HIVwithinthe UnitedStates,"hetero sexual transmission is the most important means of HIV spread worldwide today." Treatment of blood products and donor screening has essentially eliminated the risk of HIV from contaminated blood products in developed countries, but its spread continues among intravenous drug users who share needles. In developing countries, contaminated blood and contaminated needles remain important means of infection. Thirteen to thirty-five percent of pregnant women infected with HIV will pass the infection on to their babies; transmission occurs before as well as during birth. Breast milk from infected mothers has been shown to containhighlevelsofthevirusalso.HIVisnotspreadbythefecal-oralroute;aerosols;insects; or casual contact, such as sharing household items or hugging. The risk to health care workers is primarily from direct inoculation by needle sticks. Although saliva can contain small quantities of the virus, the virus cannot be spread by kissing. HIV can be transmitted from an infected person to another through:[2]

- Blood (including menstrual blood)
- Semen
- Vaginal secretions
- Breast milk.
- Unprotected sexual contact
- Direct blood contact, including injection drug needles, blood transfusions, accidents in health care settings or certain health care products. Mother to baby (before or during birth).

HIV is known to be transmitted only through:

- Contact of infected blood, semen, or vaginal and cervical secretions with mucous membranes.
- Injection of infected blood or blood products.
- Vertical transmission (that is, from infected mother to fetus) and from mother to infant via breast milk.[3]

Contact of Sexual Fluids or Blood with Mucous Membranes

The virus cannot pass through undamaged skin. HIV can enter the body through the mucous membranes that line the vagina, rectum, urethra, and possibly, on rare occasions, the mouth. Damage to a mucous membrane may increase the risk of transmission of HIV but is not necessary for transmission to occur. Injection of Infected Blood: HIV can be transmitted by infected blood getting directly into the bloodstream through intravenous, intramuscular, or subcutaneous injection. Blood-to-blood transmission occurs in the following ways:-

- Transfusion of contaminated blood and blood products and other blood recipients
- Sharing of unsterilized hypodermic needles and syringes.

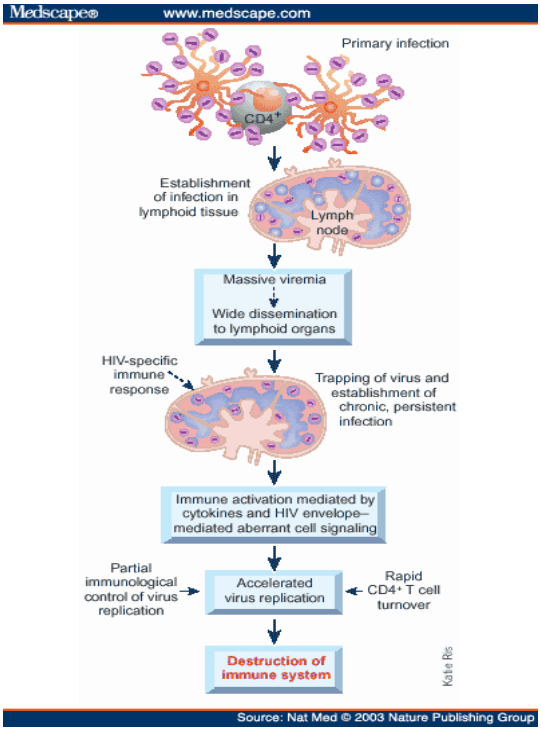

Figure 2: Pathogenesis of HIV

1.3. Symptoms

Many people who are living with HIV have no obvious signs and symptoms at all. Recent evidences how's that between 70% to 90% of people who become infected with HIV experience flu-like symptoms within a few weeks after infection. The most common symptoms are a fever, arash and a severe sore throat all occurring at the same time. These symptoms in another wise healthy person may indicate recent HIV infection. HIV infected patients may get yeast infections (oral or vaginal) that do not go away or that occur often. Frequent and severe herpes infections that cause mouth, genital, or anal sores are also common. Herpes zoster (shingles) is more likely to occur in infected patients. Other pulmonary infections (pneumonia) or so called atypical mycobacterial infections can be serious for your loved one. Women may get pelvic inflammatory disease that does not respond to treatment. The virus may attack the nervous system (nerves, spinal cord or brain)and produce a variety of symptoms ranging from tingling in the feet and trouble walking to memory disturbances. Symptoms large lymph nodes or "swollen lands "that may been larged, for more than three months, frequent fevers and sweats skin rashes or flaky skin that does not go away, short-term memory loss, slow growth or frequent illness in children, cough and shortness of breath, seizures and lack of coordination, difficult or painful swallowing, confusion and forgetfulness nausea, cramps, diarrhoea or vomiting that do not go away, vision loss, Unexplained weight loss. (Fried land, 1987).[3]

1.4. Primary infection (Acute HIV)

SomepeopleinfectedbyHIVdevelopaflu-likeillnesswithintwotofourweeksafterthevirus enters the body. This illness, known as primary (acute) HIV

infection, may last for a few weeks. Possible signs and symptoms include:

- Fever
- Headache
- Muscle aches and joint pain
- Rash
- Sore throat and painful mouth sores
- Swollen lymph glands, mainly on the neck
- Diarrhoea
- Weight loss
- Cough
- Night sweats

These symptoms can be so mild that you might not even notice them. However, the amount of virus in your blood stream (viral load) is quite high at this time. As a result, the infection spreads more easily during primary infection than during the next stage.

Clinical latent infection (Chronic HIV)

In this stage of infection, HIV is still present in the body and in white blood cells. However, many people may not have any symptoms or infections during this time.

This stage can last for many years if you're not receiving antiretroviral therapy (ART). Some people develop more severe disease much sooner.

Symptomatic HIV infection

As the virus continues to multiply and destroy your immune cells—the cells in your body that help fight off germs — you may develop mild infections or chronic signs and symptoms such as:

- Fever
- Fatigue
- Swollen lymph nodes — often one of the first signs of HIV infection
- Diarrhoea
- Weight loss
- Oral yeast infection(thrush)
- Shingles (herpes zoster)
- Pneumonia

1.4. Progression to AIDS

Thanks to better antiviral treatments, most people with HIV in the U.S. Today don't develop AIDS. Untreated, HIV typically turns into AIDS in about 8 to 10years.

When AIDS occurs, your immune system has been severely damaged. You'll be more likely to develop opportunistic infections or opportunistic cancers — diseases that wouldn't usually cause illness in a person with a healthy immune system.

The signs and symptoms of some of these infections may include

- Sweats
- Chills
- Recurring fever
- Chronic diarrhoea
- Swollen lymph glands
- Persistent white spots or unusual lesions on your tongue or in your mouth
- Persistent, unexplained fatigue
- Weakness
- Weight loss
- Skin rashes or bumps

When to see a doctor

If you think you may have been infected with HIV or are at risk of contracting the virus, see a doctor as soon as possible.

1.5. Life Cycle of HIV Virus

Entry to human cells HIV is the only viruses which make new copies of itself inside the human cells. This process begins when this virus enters into cell that carries on its surface a protein that is cd4. The HIV virus sticks to the cd4 receptor and allow them to fuse. HIV mainly infect immune cells i.e. T-helper cells that forms the body immune system. HIV infects more cells, therefore immunes stem becomes weak. Reverse transcription there is an enzyme reverse transcriptase which helps in reverse Transcription. The main function of reverse transcriptase is conversion of viral RNA into DNA. After that DNA is transported to cell's nucleus where insertion of DNA is done by enzyme integrase. Transcription and translation now, transcription takes place. HIV virus converts HIV virus into messenger RNA. Assembly, budding and maturation Copies of HIV gather together with newly made HIV protein and enzymes to form new viral particle which are then bud off from the original CD4 cell. The enzyme protease breaks the long chains of HIV protein into smaller pieces. These newly virus has ability to target and infect other CD4 cells.

1.6. Diagnosis

Diagnosis HIV is most commonly diagnosed by testing your blood or saliva for antibodies to the virus. Unfortunately it takes time for your body to develop these antibodies-usually up to 12 week. A newer type of test that checks for HIV antigen, a protein produced by the virus immediately after infection, can quickly confirm a diagnosis soon after infection.

These tests include

CD4 count CD4 cells are a type of white blood cell that's specifically targeted and destroyed by HIV. Viral load this test measures the amount of virus in your blood. Studies have shown that people with higher viral loads generally fare more poorly than do those with a lower viral load.

1.7. Treatment

Treatment Antiretroviral drugs are used to treat HIV. These are the drugs active against human immunodeficiency virus (HIV) which is a retrovirus. They are useful in prolonging and improving a quality of life. Antiretroviral drugs are classified as following:

- Nucleoside reverse transcriptase inhibitors (NRTIs): Zidovudine (AZT), Didanosine, Lamivudine, Tenofovir.
- Nonnucleoside reverse transcriptaseinhibitors:
- Nevirapine, Delavirdine, Efavirenz. Protease inhibitors: Indinavir, Nelfinavir, Amprenavir, Lopinavir, Atazanavir.
- Nucleoside analogue reverse transcriptase inhibitors(NRTIs):

NRTIs were the first type of drug available to treat HIV infection in 1987. When HIV infects a cell, it copies its own genetic code into the cell's DNA, and the cell is then programmed to create new copies of HIV. To reproduce, HIV must first convert its RNA into DNA using the enzyme reverse transcriptase. These inhibitors act like false building blocks and compete with the cell's nucleosides, thereby preventing DNA synthesis.

✓ Non nucleoside reverse transcriptase inhibitors (NNRTIs)

NNRTIs started to be approved in 1997. These also interfere with HIV's ability to infect cells by targeting reverse transcriptase. In contrast to nucleoside analogue reverse transcriptase inhibitors, non nucleosides bind directly to the enzyme.

1.8. HAART

It is **Highly Active Antiretroviral Therapy.**

HIV can also be treated by HAART. It is a combination of three drugs.

Complications In HIV

HIV infection weakens your immune system, making you much more likely to develop many infections and certain types of cancers.

1.9. Infections common to HIV/AIDS

Pneumocystis pneumonia (PCP)

This fungal infection can cause severe illness. Although it's declined significantly with current treatments for HIV/AIDS, in the U.S. PCP is still the most common cause of pneumonia in people infected with HIV.

Candidiasis (thrush)

CanddiasisisacommonHIV-relatedinfection.Itcausesinflammationandathick,white coating on your mouth, tongue, oesophagus or vagina.

Tuberculosis (TB)

In resource-limited nations, TB is the most common opportunistic infection associated with HIV. It's a leading cause of death among people with AIDS.

Cytomegalovirus

This common herpes virus is transmitted in body fluids such as saliva, blood, urine, semen and breast milk. A healthy immune system inactivates the virus, and it remains dormant in your body. If your immune system weakens, the virus resurfaces — causing damage to your eyes, digestive tract, lungs or other organs.

Cryptococcal meningitis

Meningitis is an inflammation of the membranes and fluid surrounding your brain and spinal cord (meninges). Cryptococcal meningitis is a common central nervous system infection associated with HIV, caused by a fungus found in soil.

Toxoplasmosis

This potentially deadly infection is caused by Toxoplasmagondii, a parasite spread primarily by cats. Infected cats pass the parasites in their stools, which may then spread to other animals and humans. Toxoplasmosis can cause heart disease, and seizures occur when it spreads to the brain.

1.10. Cancers common to HIV/AIDS

Lymphoma

This cancer starts in the white blood cells. The most common early sign is painless swelling of the lymph nodes in your neck, armpit or groin.

Kaposi's sarcoma

A tumor of the blood vessel walls, Kaposi's sarcoma usually appears as pink, red or purple lesions on the skin and mouth. In people with darker skin, the lesions may look dark brown or black. Kaposi's sarcoma can also affect the internal organs, including the digestive tract and lungs.

Other complications

Wasting syndrome

Untreated HIV/AIDS can cause significant weight loss, often accompanied by diarrhoea, chronic weakness and fever.

Neurological complications

HIV can cause neurological symptoms such as confusion, forgetfulness, depression, anxiety and difficulty walking. HIV-associated neurocognitive disorders (HAND) can range from mild symptoms of behavioral changes and reduced mental functioning to severe dementia causing weakness and inability to function.

Kidney disease

HIV-associated nephropathy (HIVAN) is an inflammation of the tiny filters in your kidneys that remove excess fluid and was tesfromyourbloodandpassthemtoyoururine. It most often affects black or Hispanic people.

Liver disease

Liver disease is also a major complication, especially in people who also have hepatitis B.

2. ZikaVirus Infection

2.1. Introduction

The genus Flavivirus of the family Flaviviridae comprises around 70 viruses such as: dengue (DEN), Japanese encephalitis (JE), St. Louis encephalitis (SLE), and yellow fever (YF), which are important human pathogens. The difficulty encountered with Flavivirus classification partly erives from the extensive geographic distribution and the diversity of the arthropod vectors or vertebrate hosts associated with biological transmission of these viruses. In this genus is found the Zika Virus (ZIKV), an emerging arthropod-borne virus (arbovirus) isolated in 1947 from a rhesus monkey in the Zika Forest.

ZIK virus has been isolated from Ae. Africans, Ae. apicoargenteus, Ae. luteocephalus, Ae. aegypti, Ae.vitattus, andAe. furcifermosquitoesandthemostcommonclinicalmanifestations in patients with Zika infections included high fever, malaise, stomach ache, diarrohea, conjunctivitis, dizziness, and anorexia; other less frequent manifestations included myalgia, headache, retro-orbital pain, oedema, and vomiting.[4]

2.2 Transmission

Although a ZIK virus entrance mechanism into the cell is poor understood, it is known that flaviviruses mechanism is mediated by the E glycoprotein and cell surface receptors13. The initial contact between flaviviruses and the host cell is mediated by glycosaminoglycans (GAGs), such as heparin sulphate proteoglycans or syndecans. GAGs are long, unbranched, sulphated polysaccharides normally found linked to core proteins attached to cellular surfaces (proteoglycans). (Kuno G., 1998).[5]

2.3. Genetic aspects of Zika virus

Zika virus like other members of the Flavivirus genus contains a positive single stranded genomic RNA, containing 10,794 nucleotides encoding 3,419 amino acids, giving a poly protein that is processed into three structural proteins. The capsid (C), the precursor of membrane (prM) and the envelope (E), and non structural proteins NS1 to NS5 (Table 1) 4 Virus replication occurs in the cellular cytoplasm.[6]

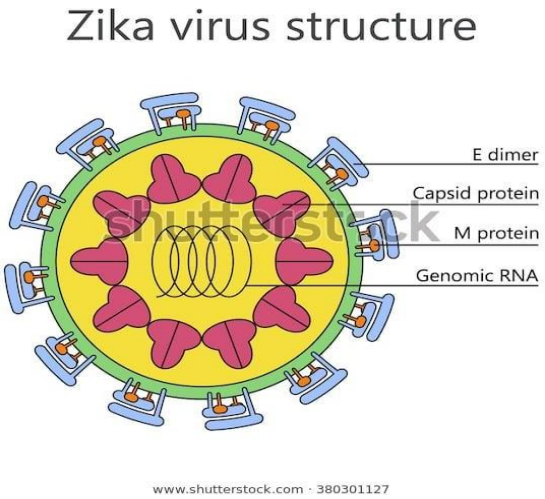

Figure 3: ZIKA virus.

2.4. Diagnosis

ZIKV specific IgM/IgG antibodies can be detected by ELISA and immune fluorescence assays in serum specimens, usually from day five or six of symptomatic illness. Interpretation of serological results should be considered very carefully as false positive dengue IgM cross reactivity both by indirect immune fluorescence assay and rapid test has been reported in both primary Zika virus infected patients and also those with a probable history of other prior flavi viral infection. There are no commercially available serological assays for the detection of Zika virus-specific antibodies.[7]

Incubation Period

The incubation period (the time from exposure to symptoms) of Zika virus disease is estimated to be 3–14 days. The majority of people infected with Zika virus do not develop symptoms.

2.5. Symptoms

- Rash
- Itching all over the body
- High temperature or hepatitis C.
- Headache
- Muscle pain
- Red eyes
- Lower back pain

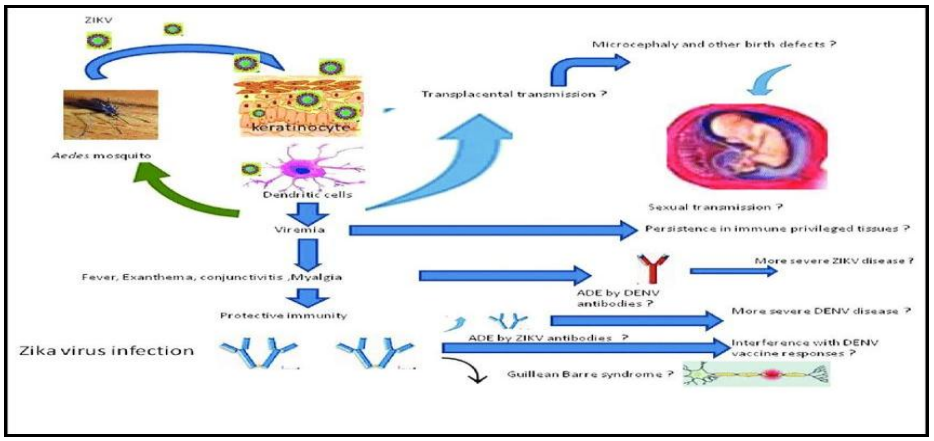

Figure 4: Pathogenesis of Zika virus.

2.6. Prevention

Arboviruses present a high capability of adaptation reflected by the fact of being transmitted by arthropods (mosquitoes, ticks, sand flies, midges, bug) and vertebrates during the lifecycle of the virus (approximately 300 types of mosquito can transmit arboviruses). This diversity of species and the wide distribution of these transmission vectors explain why arboviruses are so successful in dispersing globally via the mechanisms highlighted earlier. A high proportion of arboviruses associated with human and animal disease circulate in tropical and subtropical regions, where mosquitoes and other flying insects tend to be abundant.

However, many arboviruses also circulate amongst wildlife species in temperate parts of the world.

Currently, advances in both antiviral molecules and vaccine development have help to control diseases in patients with viral infections such as AIDS, Swine influenza, etc. But considering the eradication of RNA viruses is not that simple, because of their high mutation rate and particularly the case of arboviruses, it has been reported that mosquitoes carry large numbers of known and unknown viruses that infect humans, primates, mammals, birds, insects, and plants. Preventing or reducing arboviruses transmission depends entirely on control of the mosquito vectors or interruption of human– vector contact.

Mosquito Bites

Protection against mosquito bites during the day and early evening is a key measure to prevent zika virus infection. Special attention should be given to prevention of mosquito bites among pregnant women, women of reproductive age, and young children.

Personal protection measures include wearing clothing (preferably light-coloured) that covers as much of the body as possible; using physical barriers such as window screens and closed doors and windows; and applying insect repellent to skin or clothing that contains DEET, IR3535 or icaridin according to the product label instructions.

Young children and pregnant women should sleep under mosquito nets if sleeping during the day or early evening. Travellers and those living in affected areas should take the same basic precautions described above to protect themselves from mosquito bites.

Aedes mosquitoes breed in small collections of water around homes, schools, and work sites. It is important to eliminate these mosquito breeding sites, including: covering water storage containers, removing standing water in flower pots, and cleaning up trash and used tires. Community initiatives are essential to support local government and public health programs to reduce mosquito breeding sites. Health authorities may also advise use of larvicides and insecticides to reduce mosquito populations and disease spread.

No vaccine is yet available for the prevention or treatment of Zika virus infection. Development of a Zika vaccine remains an active area of research.

2.7. Treatment

No specific treatment for ZIKA virus is available yet. Treatment is aimed at relieving pain with rest and fluid.

Medication such as Acetaminophen (Tylenol) can be given to relieve pain and fever. No vaccines are available yet though several vaccines are currently under clinical trials.

3. Smallpox Viral Infection

Introduction 3.1

Variola is a member of the virus genus Orthopox virus and family Poxviridae and is characterized as a double stranded DNA virus. Viruses similar to variola include cowpox and monkeypox. The virus measures approximately 300 ×250 ×200 nm and is characterized by a large, brick-shaped appearance on electron micrograph. Variola replicates in the cytoplasm of an infected cell and invades the epithelium of the dermal layer. Variola only infects humans andcannotbeacquiredfromanotherspecies.Pastoutbreaksw eremorecommonduringwinter and early spring since the aerosolized variola survives longer in low humidity and low temperature environments.

Two forms of variola virus exist: minor and major. Smallpox secondary to variola major is implicated in 90% of the cases. Variola minor may affect only 2% of unvaccinated persons, but may present in up to 25% of vaccinated hosts.[8]

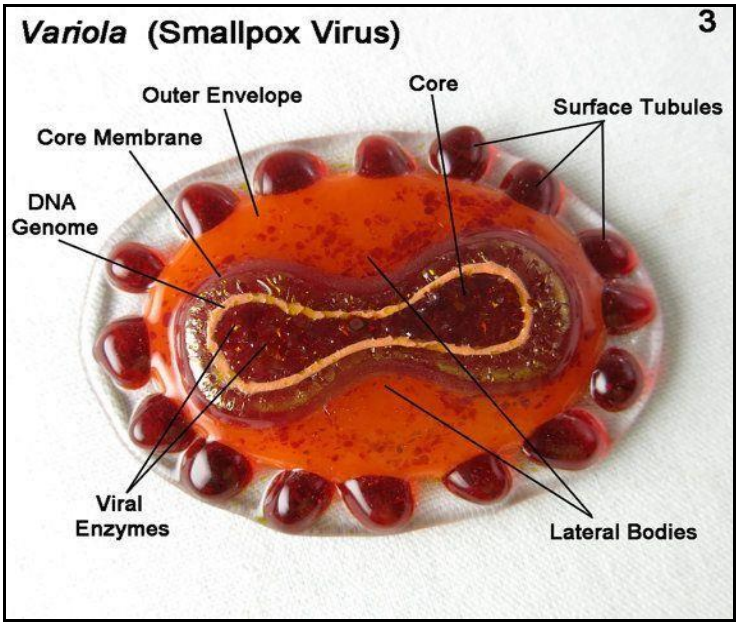

Figure 5: Smallpox virus.

3.2. Pathogenesis

Smallpox is a serious, contagious, and sometimes fatal infectious disease. Exposure to an infected individual by direct contact, body fluid contact, and aerosolized inhalation begins the pathogenesis of the disease process. Manifestations of the disease usually appear within 7–17 days (average incubation 12 days) after exposure, beginning with high fever, myalgia, and headache. A maculopapular rash erupts, often beginning on the face and neck of the infected person. The lesions spread throughout the epidermis and appear simultaneously. After 1–2 days, the rash papules become vesicular and pustular. Vesicles appear round and firm with dermal involvement and measure 2–5 mm in diameter. Crusting and scabs appear 9–10 days after initial exposure. Pitting scars are common following small pox resolution. The disease can be spread by airborne droplets until the skin scabs fall off. Some patients may experience a temperature spike 3–5 days following initiation of the prodrome, which may indicate secondary bacterial infection, a marker of increased mortality. In most cases, death secondary to smallpox is a result of toxemia, pneumonia, or bacteria. Mortality rates differ depending upon the strain of variola involved. Variola minor, more common among patients previously vaccinated for smallpox, has a mortality rate of approximately 1%. On the other hand, variola major may be lethal in up to 30% of cases. Much higher mortality rates are seen with hemorrhagic and malignant forms of variola, characterized by a shorter incubation period, severe prodromal illness, and petechiae, as well as cutaneous and mucosal hemorrhage. Morbidity following smallpox infection is common. Pockmarks are noticeable in up to 80% of smallpox survivors and blindness from viral keratitis occurs in approximately 1% of affected patients. The incidence of arthritis among smallpox survivors who were afflicted with the disease as a child is estimated at about 2%.Althoughveryuncommon, encephalitis can occur in patient infected with smallpox, possibly resulting

3.3 Diagnosis

Confirmation of smallpox is problematic as it may be confused with chickenpox or other dermal conditions. Quick diagnosis is imperative to prevent spread of the disease to other persons and overall mortality. In order to systematically assess possible smallpox, the CDC has created a method for diagnosis based on major and minor criteria. The risk of smallpox infection is based upon characteristics that a patient exhibits during the prodrome. Patients at high risk of having variola infection must meet all 3 major criteria. Moderate-risk individuals have a typical prodrome and must meet at least one of the major criteria or ≥4 minor criteria. Low-risk patients have ≥4 minor criteria with or without a febrile prodrome. Differential diagnosis should involve testing for varicella zoster virus and other viral infections that resemble smallpox manifestations.3 Prior vaccination against chickenpox, round rather than oval lesions, and centrifugal rather than central distribution so frash and lesions on the patients' soles and palms suggest smallpox. The rash of human monkeypox appears like smallpox clinically, but patients with monkeypox often have lymphadenopathy. Coxsackie virus or measles virus can cause morbilli form rash on the face and can be confused with early smallpox. The use of electron microscopy greatly enhances confirmation of smallpox diagnosis, as does the use of polymerase chain reaction (PCR) technology. Using primer pairs, a specific diagnosis of variola infection can be made quickly in virtually all hospitals using commercially available PCR assay. Methods of diagnosis using immunoglobulin M responses may increase the sensitivity and specificity of a diagnosis when using other diagnostic tools. A suspected case of smallpox is a public health and medical emergency and should be reported immediately to the

local and/or state health department. Following notification, samples of pustules, skin lesions, vesicles, blood, and tonsillar swabs must be sent to the CDC for further investigation.

3.5. Symptoms

Signs and symptoms of smallpox may include:

- Sudden onset of high fever which may berecurrent
- Malaise (general feeling of unwellness)
- Widespread skin rash – flat spots which change into raised bumps then firm fluid filled blisters which then scab (see image)
- Severe headache
- Backache
- Abdominal pain
- Vomiting
- Diarrhoea.

In 30 to 50% of unvaccinated people with variola major the disease progressed with bleeding, low blood pressure, multi-organ failure and death.

Incubation period

(Time between becoming infected and developing symptoms) From 7 to 19 days, usually 10 to 14 days.

Infectious period

- (Time during which an infected person can infect others*)*
- From the start of the fever until all scabs have fallen off. People are most contagious during the early skin rash.

3.6. Treatment

Successful smallpox management involves isolation of the infected person(s), preferably in a negative-pressure room. Isolation of the infected person is critical during treatment and should last for at least 17 days. Healthcare workers should wear appropriate airborne and contact precaution garments (disposable gloves, gowns, shoe covers, properly fitted masks) to prevent spread of this highly contagious disease. There is no smallpox treatment approved by the Food and Drug Administration (FDA). Most of the medical care provided is supportive and, in patients with suspected secondary bacterial infection, broad-spectrum antibiotics with β- lactamase inhibition should be administered. Cidofovir, approved for treatment of cytomegalovirus-induced retinitis, may be of use in the treatment and prevention of smallpox. In vitro, cidofovir has shown efficacy against various poxviruses including vaccinia, camel pox, and monkeypox. In animals with cowpox, treatment with cidofovir decreased mortality by 60–100%.18 Although the treatment is unproven, cidofovir may prove useful, especially in persons with contraindications to the vaccinia-derived vaccine. Ophthalmic keratitis may be treated with idoxuridine.

Vaccination

Vaccination remains the primary method in reducing smallpox incidence in the case of a in retardation or death.[9]

Vaccination has not been routine among American civilians since 1972, although the military continued to vaccinate until 1985. Since vaccination is believed to offer protection for only 5–10 years to the majority of the population, virtually everyone in the US is susceptible to variola. 4, 19, 20 Vaccination using vaccinia is believed to create a cytotoxic T-cell and B-cell response, resulting in antibody formation. Subsequent exposure to variola should result in minor or no response. There commended means of vaccination is to 15 needle pricks to the skin, usually in the deltoid region of the arm, in a circular motion using abifurcated needle dipped in to the vaccine. If the vaccination is administered properly, a small amount of blood should appear at the vaccination site. If blood is not present, the procedure must be repeated. Following administration, the CDC recommends placing a semipermeable membrane bandage over the area vaccinated until the underlying skin has healed.21 The bandage should be changed every 1–3 days. Also, at least one layer of clothing should cover the applied bandage. A primary reaction, or erythema, at the vaccination site should occur by day one. If the primary reaction does not occur, the person should be revaccinated. Six to 8 days following successful vaccination, a greyish pustule 1–2 cm in diameter should appear. The pustule will spread peripherally, then crust 3–5 days later. A dark crust with local oedema results and will last for approximately 3 weeks. The appearance of the palpable pustule for 6– 8 days confirms successful vaccination. Revaccination should occur at least every 5 years in persons needing protection from smallpox.

3.7. Prevention

- Exclude people with smallpox from childcare, preschool, school and work from the start of the illness until all scabs have disappeared and they have been advised by the Chief Quarantine Officer in SA Health that they may return.
- A vaccine is available. Vaccination against smallpox is not routinely recommended in Australia and is not on the National Immunisation Program schedule. Vaccination is recommended for laboratory staff who routinely work with vacciniapox viruses (unless contraindicated).
- There is a small risk that smallpox could be released intentionally as a bioweapon and health departments around the world are planning for this possibility, including South Australia.
- Promptly isolate suspected and confirmed cases of smallpox until no longer infectious administer

4. Ebola viral Infection

4.1. Introduction

Ebola disease is a severe, often fatal illness in humans.

- Thevirusistransmittedtopeoplefromwildanimalsandthenspreadsinthehumanpopulation through human-to-human transmission.

- The average Ebola case fatality rate is around 50%. Early supportive care with rehydration, symptomatic treatment improvessur vival.
- Five species of Ebola virus have been identified. Among them, Bundibugyo ebola virus, Zaïre ebola virus, and Sudan ebola virus have been associated with large outbreaks in Africa. [10]

4.2. Clinical features

- The incubation period is 2 – 21days.
- Human are not infectious until they develop symptoms.
- Initial symptoms are sudden onset of fever and fatigue, muscle pain, headach eandsore throat.
- Usually followed by: vomiting, diarrhoea, rash, impaired kidney and liver function, spontaneous bleeding internally and externally (in somecases). (F. Shuaib)

4.3 Diagnosis

- Differential diagnosis includes other viral haemorrhagic fevers, yellow fever, malaria, typhoid fever, shigellosis, and other viral and bacterial diseases.
- Patient history is essential and should include: Contact with a dead or sick animal, contact with a suspected, probable or confirmed Ebola patient.

Laboratory diagnosis

- Reverse transcriptase polymerase chain reaction (RT-PCR)assay
- IgG and IgM antibodies with enzyme-linked immune sorbent assay(ELISA)
- Antigen detection tests virus.

Isolation by cell culture

4.4.Symptoms

- Pain in abdomen, chest, joints or muscles
- Fever, fatigue and chills
- Dehydration
- Loss of appetite
- Coughing up blood
- Diarrhoea or vomiting

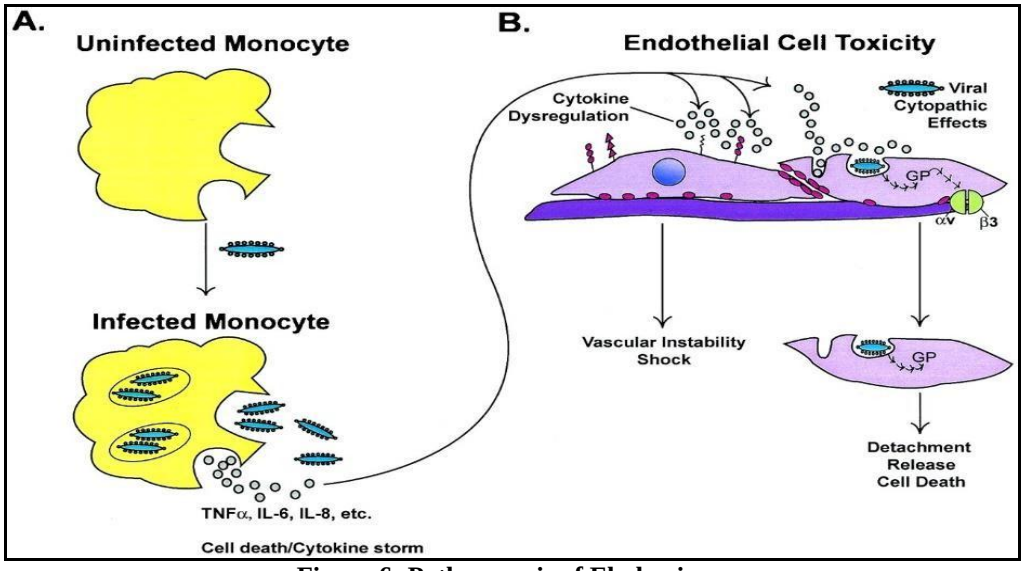

Figure 6: Pathogenesis of Ebola virus.

4.5. Treatment

Providing fluids and electrolytes through infusion into the vein. Offering oxygen therapy to maintain oxygen status.

Using medication to support blood pressure, reduce vomiting and diarrhoea and to manage fever and pain. Treating other infections, if they occur.

5. Polio Virus Infection

5.1 Introduction

Polio virus (PV) is the causal agent of paralytic poliomyelitis, an acute disease of the central nervous system (CNS) resulting in flaccid paralysis. In addition, another neuromuscular pathology, called the post-polio syndrome, affects some poliomyelitis survivors several decades after the most severe forms of the acute disease.

PV is anentero virus belonging to the Picorna viridae family that is one of the most important groups of human and animal pathogens. This family also includes human hepatitis A virus, human rhinoviruses, the agents of the common cold, and foot-and-mouth disease virus. PV is classified into three serotypes (PV-1, PV-2, and PV-3). Because of its very simple structure, PV has been used as a model for studying non retroviral RNA viruses, and consequently PV is now one of the best characterized animal viruses. The development of new animal and cell models, together with the identification of the virus receptor CD155, has all owed the key steps of the pathogenesis of poliomyelitis to be investigated at the molecular level. In particular, the involvement of PV-

induced apoptosis in CNS injury has been studied.[11]

5.2. Structure of the Virion

The PV is composed of a single-stranded RNA genome of positive polarity surrounded by a no enveloped icosahedral protein capsid. The mature virion is approximately 30 nm in diameter and the three-dimensional structures of the three serotypes of PV have been determined by X-ray crystallography. The capsid consists of 60 copies of each of the four viral structural proteins, VP1 toVP4.

A deep surface depression, called the "can yon", surround search five fold axis of symmetry and contains the site for cell receptor binding. The PV RNA genome is about 7,500 nucleotides long.Itispoly-adenylatedatits30-terminus and covalently linked to a small viral protein, VPg (3B), at its 50-terminus. It contains a long 50 non coding region (NCR) followed by a single large open reading frame (ORF) and a short 30 NCR that includes the poly (A) tail. The ORF is translated to produce a 247-kDa poly protein that is processed into three large precursors of structural (P1) and non-structural (P2 and P3) proteins.

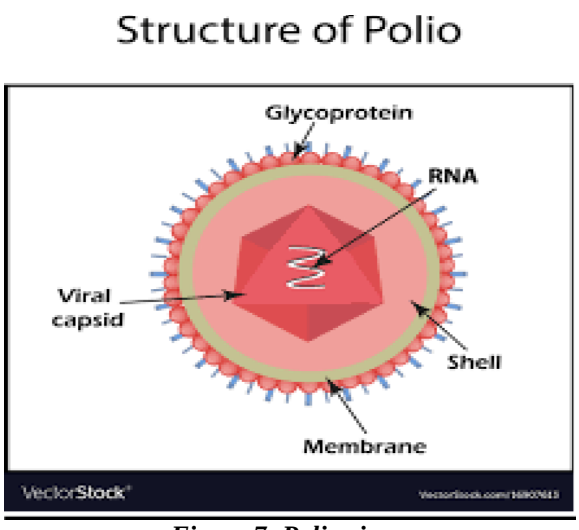

Figure 7: Polio virus.

5.3. Diagnosis

Doctors often recognize polio by symptoms, such as neck and back stiffness, abnormal reflexes and difficulty in swallowing and breathing.

To confirm the diagnosis, a sample of throat secretions, stool or colour less fluid that surrounds the brain and spinal cord (cerebro spinal fluid) is checked for poliovirus.

5.4. Symptoms

Polio, in its most severe forms, can cause paralysis and death. However, most people with polio do not display any symptoms or become noticeably sick. When symptoms do appear, they differ depending on the type of polio.

Symptomatic polio can be broken down further into a mild form, called non-paralytic or abortive polio, and a severe form called paralytic polio that occurs in around 1percent of cases.

Many people with non-paralytic polio make a full recovery. Unfortunately, those with paralytic polio generally develop permanent paralysis.

Non-paralytic polio symptoms

Non-paralytic polio, also called abortive poliomyelitis, leads to flu-like symptoms that last for a few days or weeks. These include:

- Fever
- Sore throat
- Headache
- Vomiting
- Fatigue
- Back and neck pain
- Arm and leg stiffness
- Muscle tenderness and spasms
- Meningitis, an infection of the membranes surrounding the brain

Paralytic polio symptoms

Paralytic polio affects only a small percentage of those invaded by the polio virus. In these cases, the virus enters motor neurons where it replicates and destroys the cells. These cells are in the spinal cord, brain stem, or motor cortex, which is an area of the brain important in controlling movements.

Symptoms of paralytic polio often start in a similar way to non-paralytic polio, but later progress to more serious symptoms such as:

- A loss of muscle reflexes
- Severe muscle pain and spasms
- Loose or floppy limbs that are often worse on one side of the body

5.5. Treatment

Because no cure for polio exists, the focus is on increasing comfort, speeding recovery and preventing complication. Supportive treatment includes:

- Pain relievers
- Portable ventilators to assist breathing
- Moderate exercise (physical therapy) to prevent deformity and loss of muscle function. (Adams JM)

5.6. Signs and symptoms include

- Muscle and joint pain and weakness that slowly progresses
- Muscle atrophy or shrinkage
- Exhaustion for no reason
- Swallowing and breathing difficulties
- Suffering in colder temperatures
- Sleep-related problems, such asapnea
- Concentration and memory difficulties
- Mood swings and depression

Post-polio syndrome is a slow, progressive disease. There is no cure, but it is not infectious or contagious.

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