



## AN OVERVIEW ON EMERGING OF VIRAL DISEASES IN INDIA AND FUTURE PROSPECTIVES ON THEIR TREATMENT

D. Nagavalli<sup>1</sup>, S. Shoba<sup>2</sup>, F. Nishvanth<sup>3\*</sup>

<sup>1</sup>Principal and Head, Dept. of Pharmaceutical Chemistry, Adhiparasakthi College of Pharmacy, Melmaruvathur -603319, (Affiliated to The Tamilnadu Dr. M. G. R. Medical University, Chennai) Tamilnadu, India.

<sup>2</sup>Professor and Head, Dept. of Pharmacology, Adhiparasakthi College of Pharmacy, Melmaruvathur -603319, (Affiliated to The Tamilnadu Dr. M. G. R. Medical University, Chennai) Tamilnadu, India.

<sup>3\*</sup> Assistant Professor cum Ph.D research scholar, Dept. of Pharmacology, Adhiparasakthi College of Pharmacy, Melmaruvathur -603319, (Affiliated to The Tamilnadu Dr. M. G. R. Medical University, Chennai) Tamilnadu, India.

### Abstract:

*A virus is comprised of nucleic acid, either DNA or RNA, surrounded by a protein coat. It requires to multiply a living cell. A viral infection can lead to a spectrum of symptoms from asymptomatic to severe disease. A virus is a small infectious organism—much smaller than a fungus or bacterium—that must invade a living cell to reproduce (replicate). The virus attaches to a cell (called the host cell), enters the cell, and releases its DNA or RNA inside the cell. The virus's DNA or RNA is the genetic material containing the information needed to replicate the virus. The virus's genetic material takes control of the host cell and forces it to replicate the virus. The infected cell usually dies because the virus keeps it from performing its normal functions. When the infected host cell dies, it releases new viruses, which go on to infect other cells. People may get viruses by swallowing or inhaling them, by being bitten by insects, through sexual contact, or congenitally (passed by a pregnant person to the fetus). Most commonly, viral infections involve the nose, throat, and upper airways, or systems such as the nervous, gastrointestinal, and reproductive systems. Doctors may base the diagnose on symptoms, blood tests and cultures were examined. Antiviral drugs may interfere and affect the reproduction of viruses or strengthen the host cell immune response to the viral infection.*

**Key words:** Virus, Avian Influenza virus, Nipah Virus, Sars- Cov 19 (Covid-19), Zika Virus, Monkey Pox Virus and Chandipura Virus

### Corresponding author:

**F. Nishvanth,**

Assistant Professor cum Ph.D research scholar,  
Dept. of Pharmacology, Adhiparasakthi College of Pharmacy,  
Melmaruvathur -603319, (Affiliated to The Tamilnadu Dr. M. G. R. Medical University, Chennai) Tamilnadu, India.

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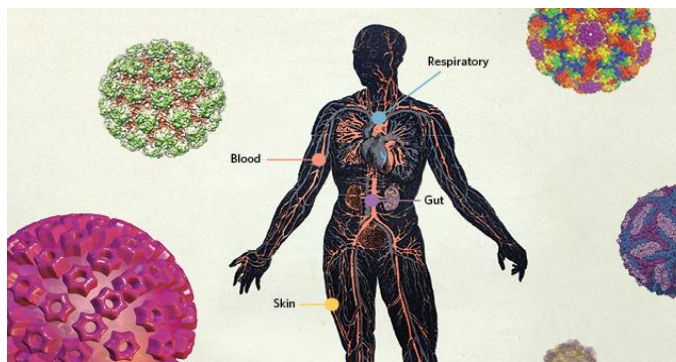
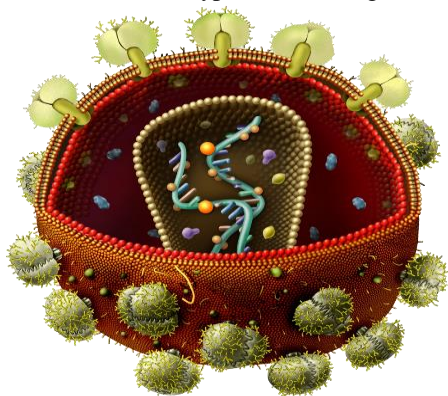


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**INTRODUCTION:**

A virus is a sub microscopic infectious agent that replicates only inside the living cells of an organism.[1] Viruses infect all life forms, from animals and plants to microorganisms, including bacteria and archaea[2,3]. Viruses are found in almost every ecosystem on Earth and are the most numerous type of biological entity.[4,5]

Since Dmitri Ivanovsky's 1892 article describing a non-bacterial pathogen infecting tobacco plants and the discovery of the tobacco mosaic virus by Martinus Beijerinck in 1898,<sup>[6]</sup> more than 11,000 of the millions of virus species have been described in detail [7,8]. The study of viruses is known as virology, a subspeciality of microbiology.



**Figure 1: Virus**

**Types of viruses:**

Viruses are grouped based on size and shape, chemical composition and structure of the genome, and mode of replication. The genome of a virus may consist of DNA or RNA, which may be single stranded (ss) or double stranded (ds), linear or circular [9,10].

Table :1 Types of viruses based on shape

S.No	Viral Shapes	Example
1.	Polyhedral	Adenovirus
2.	Spherical	Influenza virus
3.	Helical	Tobacco mosaic virus
4.	Complex	Bacteriophage

Table :2 Types of viruses based on size

S.No	Viral size (nm)	Example
1.	80-120	Influenza virus
2.	200	Herpes simplex virus
3.	300	Tobacco mosaic virus
4.	400-800	Polyphagia mimic virus

Table :3 Types of viruses based on viral composition

S.No	Viral composition	Example
1.	DNA virus	Herpes virus and small pox virus
2.	RNA virus	Rabies virus and retro virus

Table :4 Types of viruses based on viral genomic structure

S.No	Genomic structure of virus	Example
1.	Non-segmented genome consists of single segment of genetic material	Parainfluenza virus
2.	Segmented genome is divided into multiple segments	Influenza virus

Table :5 Types of viruses based on virus replication

S.No	Replication of virus	Example
1.	RNA virus - Replicate using RNA-to-RNA transcription	Influenza virus and Hepatitis-C virus
2.	DNA virus- Replicate using DNA-to-DNA transcription	small pox virus
3.	Reverse transcribing virus- Replicate using reverse transcription (DNA from RNA template).	Hepatitis B virus
4.	Replicate in bacteria	Bacteriophages

**Structure of virus:**

Viruses come in two main shapes as seen from electron micrographs: spherical, or rod-shaped. Some viruses are naked, while others have a lipid envelope around them, often derived from the host cell. In some cases, viruses approach the shape of regular solids. In some of these viruses, 20 replicas of the same proteins make up the capsid. This can be a single protein, or three or many proteins, which interact spontaneously when in contact through template domains at their edges. The bonds between the capsid proteins are angled so that the complete structure acquires the form of a regular icosahedron. Spherical viruses exist in two classes: non-enveloped but may have attachments to the vertices (corners) of the icosahedron (see figure of adenovirus); or enveloped.

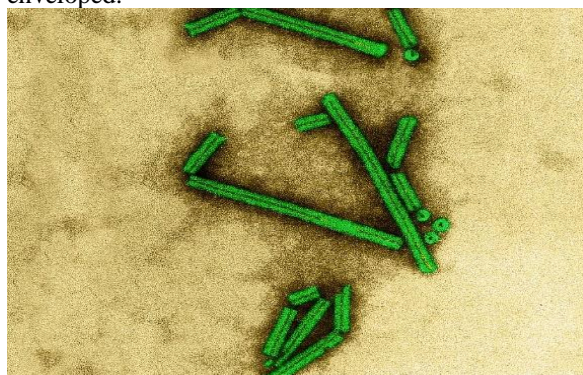


Figure: 2 Rod shape and spherical shape virus  
All mammalian living cells are covered by a membrane—the viability of the cell depends on the

integrity of this membrane. Enveloped viruses leaving the cell must, therefore, allow this membrane to remain intact if the cell is to survive, or even if the cell eventually dies. This is achieved by the budding of the viral nucleocapsid through the membrane, during which the virus becomes coated in a lipid envelope derived from the host cell membrane or modified membrane. Some viruses are rod-shaped, as illustrated by the tobacco mosaic virus (TMV) and vesicular stomatitis virus (VSV). In the case of TMV this rod is made up of repeating units of a single coat protein enclosing the nucleic acid.

In most cases, viruses undergo self-assembly. Apart from a few bacteriophages in which a scaffolding protein exists, viral proteins interact with each other or with the nucleic acid almost as if they have magnetic properties to spontaneously form a stable structure. The ability to undergo self-assembly is influenced by both pH (acidity or basic conditions) and salt concentrations. Poliovirus capsids will undergo self-assembly in the test tube from sub-viral particles. Classical experiments have shown that mixing RNA of Holmes' ribgrass virus and the tobacco mosaic virus protein will give rise to a viable virus. The species propagated will depend on the source of the RNA, in this case, RNA from Holmes' ribgrass virus. The ability to undergo self-assembly makes it easy to reconstruct viruses in the test tube, and has been done for polio and other viruses.

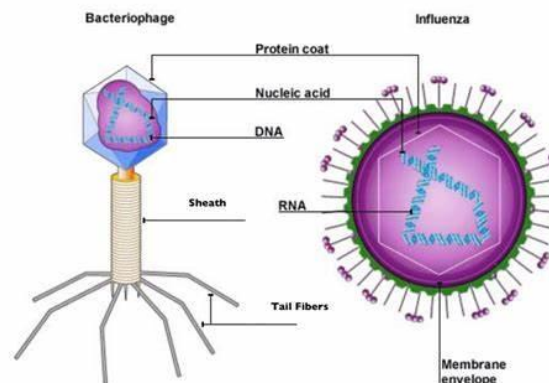


Figure:3 Structure of virus



The single virus is referred to as the “virion.” It consists of an outer shell (protein capsid, or membrane), the function of which is to protect the genetic information from physical, chemical, or enzymatic damage, and a nucleocapsid containing the genetic information and any required replicating enzymes. The outer surface of the virus is also responsible for recognition of and attachment to the host cell. Initially, this takes the form of binding of a virus-attachment protein to a cellular receptor molecule. Once the virus attaches to the cell, it is engulfed through the cellular membrane and the viral coat removed in small cellular vesicles, releasing the viral nucleic acid into the cytoplasm for replication. In the case of bacteriophage, the viral coat is not taken into the cell, but the genetic material is injected into the bacterial cell as if through a syringe, with the bacteriophage proteins remaining attached through their tails [11-18].

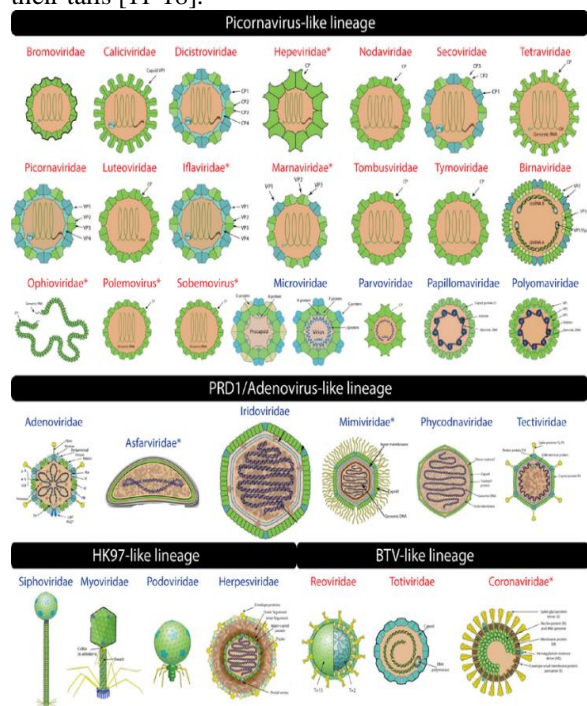


Figure:4 Various types of virions

#### Viral infections:

Upper respiratory infections (infections of the nose, throat, upper airways, and lungs) are likely the most common viral infections. Upper respiratory infections include sore throat, sinusitis, and the common cold. Other viral respiratory infections include influenza, pneumonia, and coronaviruses, including SARS-CoV-2 (the virus that causes COVID-19).

In small children, viruses also commonly cause croup (which is inflammation of the upper and lower airways, called laryngotracheobronchitis) or

lower airways (bronchiolitis). Respiratory infections are more likely to cause severe symptoms in infants, older people, and people with a lung or heart disorder. Respiratory viruses are typically spread from person to person by contact with infected respiratory droplets [19].

Other viruses infect other specific parts of the body:

- **Gastrointestinal tract:** Infections of the gastrointestinal tract, such as gastroenteritis, are commonly caused by viruses, such as noroviruses and rotaviruses.
- **Liver:** These infections result in hepatitis.
- **Nervous system:** Some viruses, such as the rabies virus and the West Nile virus, infect the brain, causing encephalitis. Others infect the layers of tissue that cover the brain and spinal cord (meninges), causing meningitis.
- **Skin:** Viral infections that affect only the skin sometimes result in warts or other blemishes. Many viruses that affect other parts of the body, such as chickenpox, also cause a rash.
- **Placenta and fetus:** Some viruses, such as the Zika virus, the rubella virus, and cytomegalovirus, can infect the placenta and fetus in pregnant women.

Some viruses typically affect many body systems. Such viruses include enteroviruses (such as coxsackieviruses and echoviruses) and cytomegaloviruses.

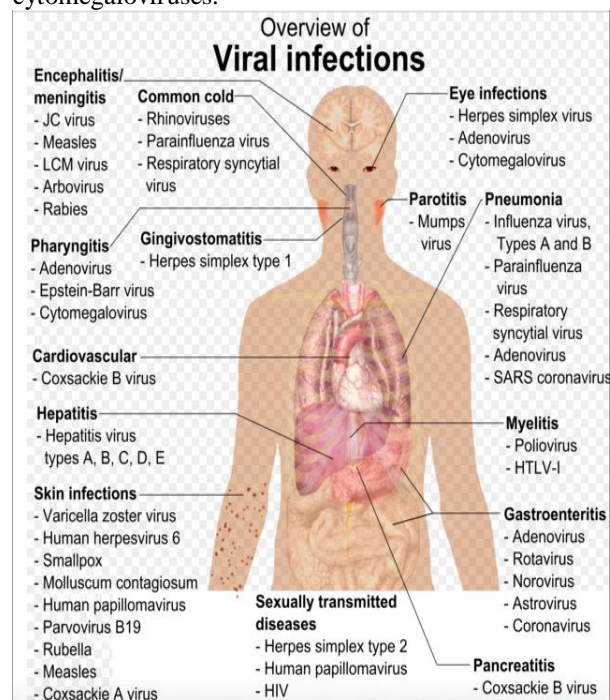


Figure: 5 Overview of viral infections

### Emerging and Re-emerging Viral diseases in India:

The emergence of novel human pathogens and re-emergence of several diseases are of particular concerns in the current decade. At a basic level, emerging infections can be defined as those diseases whose incidence has been found to be increased within recent decades or which have threatened to increase in the future [20]. Estimates indicate that about 60 per cent of infectious diseases and 70 per cent of emerging infections of humans are zoonotic in origin, with two-thirds originating in wildlife [21].

Respiratory viral infections, arboviral infections and bat-borne viral infections represent three major categories of emerging viral infections in India. Infectious aerosols of the tracheobronchial tree represent efficient means for spread of viral pathogens affecting the respiratory tract [22]. Pandemic influenza H1N1pdm09, highly pathogenic avian influenza (AI) infection (H5N1) and the Middle East respiratory syndrome coronaviruses (MERS-CoV) represent three pathogens posing severe threat in this category. Arthropod-borne viruses have consistently been the reason of emerging and re-emerging diseases in the Indian subcontinent, including Crimean-Congo haemorrhagic fever (CCHF), dengue, chikungunya, Japanese encephalitis and Kyasanur forest disease (KFD) [23].

### AVIAN INFLUENZA VIRUS-A:

Avian influenza, also known as avian flu or bird flu, is a disease caused by the influenza A virus, which primarily affects birds but can sometimes affect mammals including humans [24]. Humans and other mammals can only become infected with avian influenza after prolonged close contact with infected birds [25]. In mammals including humans, infection with avian influenza (whether LPAI or HPAI) is rare. Symptoms of infection vary from mild to severe, including fever, diarrhoea, and cough [26].

### Virology:

Avian influenza is caused by the *influenza A virus* which principally affects birds but can also infect humans and other mammals. Influenza A is an RNA virus with a genome comprising a negative-sense, RNA segmented genome that encodes for 11 viral genes. The virus particle (also called the virion) is 80–120 nanometres in diameter and elliptical or filamentous in shape. There is evidence that the virus can survive for long periods in freshwater after being excreted in feces by its avian host, and can withstand prolonged freezing.

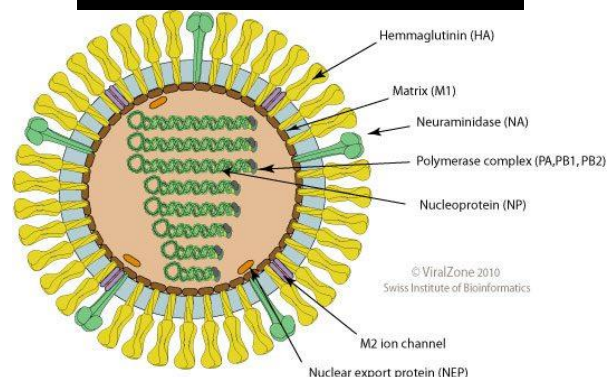
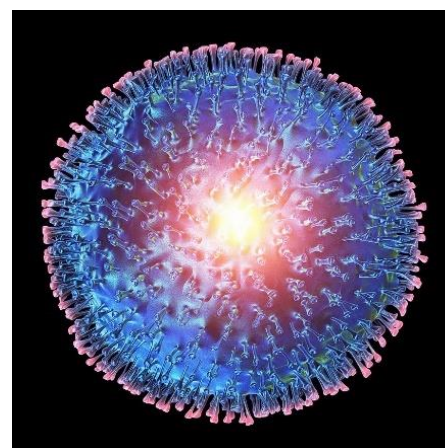


Figure:6 Structure of Avian Influenza Virus

There are two proteins on the surface of the viral envelope; hemagglutinin and neuraminidase. These are the major antigens of the virus against which neutralizing antibodies are produced. Influenza virus epidemics and epizootics are associated with changes in their antigenic structure.

Hemagglutinin (H) is an antigenic glycoprotein which allows the virus to bind to and enter the host cell. Neuraminidase (N) is an antigenic glycosylated enzyme which facilitates the release of progeny viruses from infected cells. There are 18 known types of hemagglutinin, of which H1 thru H16 have been found in birds, and 11 types of neuraminidases [27-34].

### Outbreaks of Avian Influenza Virus in India:

- During January 2003–February 3, 2022, there were 862 reported cases of human infection with avian influenza A(H5N1) virus in 18 countries, resulting in a 53% case-fatality rate.
- The first outbreak of highly pathogenic avian influenza H5N1 in poultry in India, which occurred in January 2006 in Maharashtra.

- On March 15, 2019, a human case of low-pathogenicity avian influenza A(H9N2) was detected in India.
- To date, 371 H5N1 and H5N8 avian influenza outbreaks in domestic or wild birds have been recorded in 15 of 28 states in India.

- The first outbreaks of highly pathogenic avian influenza H5N8 in Europe were reported in August 2020 and since have been reported in poultry and wild birds in several countries in Europe, Asia, and Africa [41,42]

#### Pathophysiology:

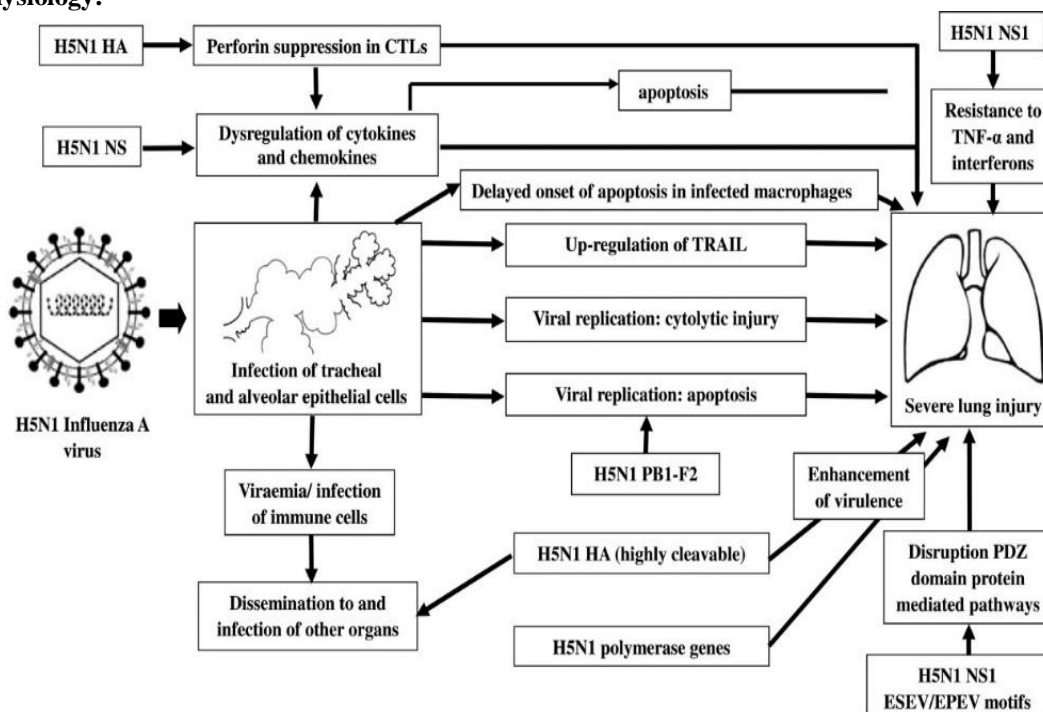


Figure:7 Pathology of Avian Influenza virus

For mammals, A(H5N5) was reported for the first time in Europe, while goat kids in the United States of America represented the first natural A(H5N1) infection in ruminants. Since the last report and as of 12 March 2024, five human avian influenza A(H5N1) infections, including one death, three of which were clade 2.3.2.1c viruses, have been reported by Cambodia [36]. China has reported two human infections, including one fatal case, with avian influenza A(H5N6), four human infections with avian influenza A(H9N2) and one fatal case with co-infection of seasonal influenza A(H3N2) and avian influenza A(H10N5). The latter case was the first documented human infection with avian influenza A(H10N5). Human infections with avian influenza remain rare and no sustained human-to-human infection has been observed [37].

On 22 May 2024, the International Health Regulations (IHR) National Focal Point (NFP) for India reported to WHO a case of human infection with avian influenza A(H9N2) virus detected in a child resident of West Bengal state in India. This is the second human infection of avian influenza A(H9N2) notified to WHO from India, with the first in 2019. The child has recovered and was discharged from hospital. According to the IHR (2005), a human infection caused by a novel influenza A virus subtype is an event that has the potential for high public health impact and must be notified to the WHO. Most human cases of infection with avian influenza A(H9N2) viruses are exposed to the virus through contact with infected poultry or contaminated environments. Human infection tends to result in mild clinical illness [37,38].



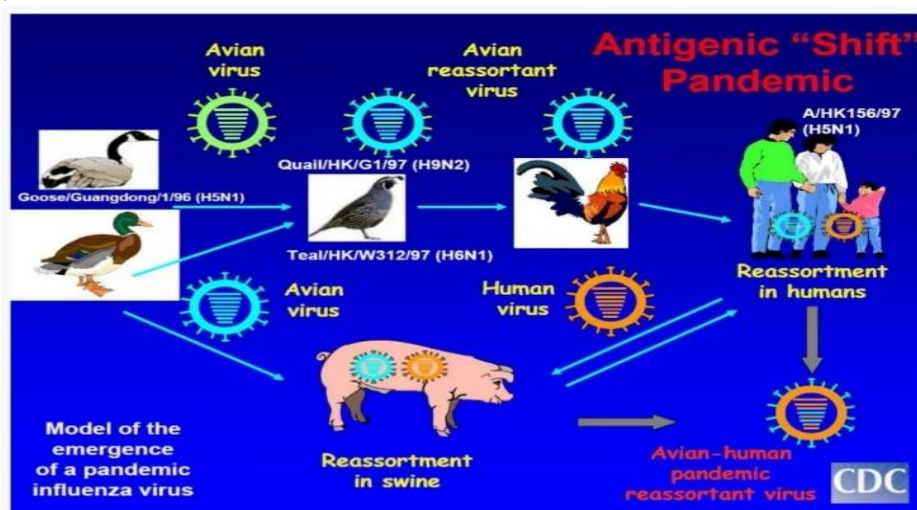
**Transmission:**

Figure:8 Transmission of Avian Influenza Virus

**Diagnosis:**

- Detection of viral RNA by means of conventional or real-time reverse-transcriptase polymerase chain reaction remains the best method for the initial diagnosis of influenza A.
- Diagnostic yields are higher with throat specimens than with nasal swabs because of higher viral loads of influenza A (H5N1) in the throat. However, nasal swabs are useful for detecting human influenza viruses, so collection of both specimens is recommended.
- rapid antigen tests have similar analytic sensitivity for detecting human and avian influenza A (H5N1) viruses, they require 1000 times higher levels of virus than viral cultures to be positive.
- The detection of anti-H5 antibodies is essential for epidemiologic investigations and may provide retrospective diagnostic confirmation in patients.
- Microneutralization assays are the most reliable methods for detecting antibodies to avian viruses, but they are labor-intensive and require biosafety level 3 facilities and appropriate strains of influenza A (H5N1) viruses [39-42].

**Medication and Treatment:****Table: 6 Treatment of Avian Influenza Infection**

S.No	Category	Treatment	Medication
1.	Allopathy	Anti-viral agents [43-47]	Oseltamivir -150mg twice daily in adults for 10 days Others – Zanamivir, Peramivir and Amantadine. Prophylactic therapy – Corticosteroids Vaccines – Egg based, cell-culture and recombinant.
2.	Ayurvedic	Active against pre and post IBV infection [48-53]	Natural plants - <i>Thymus vulgaris</i> , <i>Mentha piperita</i> , <i>Desmodium canadense</i> and <i>Sambucus nigra</i> <i>Hypericum perforatum</i> - hypericin (HY), quercetin, pseudohypericin, quercitrin and polycyclic quinone <i>Camellia sinensis</i> (green tea) -Catechins (phenolic compounds)

**Future prospective:**

- A new project aiming to accelerate the development and accessibility of human avian influenza (H5N1) messenger RNA (mRNA) vaccine candidates for manufacturers in low- and middle-income countries has been launched 29 July 2024.
- The World Health Organization announced Monday a new project to accelerate the development in poorer countries of vaccines for human bird flu infections using cutting-edge messenger RNA technology.
- Baloxavir marboxil use for critical human infection of avian influenza A H5N6 virus. A new class of inhibitors for the influenza virus cap-dependent endonuclease, has been confirmed in vitro, but it has not yet been fully characterized [54,55].

**NIPAH VIRUS:****Introduction:**

A Nipah virus infection is a viral infection caused by the Nipah virus. Symptoms from infection vary from none to fever, cough, headache, shortness of breath, and confusion. This may worsen into a coma over a day or two, and 50 to 75% of those infected die. Complications can include inflammation of the brain and seizures following recovery [56].

The Nipah virus (NiV) is a type of RNA virus in the genus *Henipavirus*, which normally circulates among fruit bats of the genus *Pteropus*. Spread typically requires direct contact with an infected source; it can both spread between people and from other animals to people. Diagnosis is based on symptoms and confirmed by laboratory testing [57].

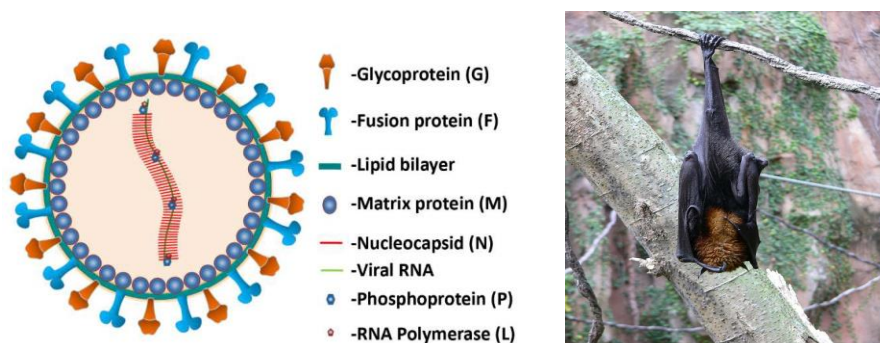


Figure: 9 Structure of Nipah Virus

The disease was first identified in 1998 by a team of researchers at the Faculty of Medicine, University of Malaya during an outbreak in Malaysia [58]. The majority of the patients in Malaysia diagnosed with the disease were referred to and treated at the University of Malaya Medical Centre. The virus was isolated and identified in 1999. The disease is named after a village in Malaysia, Sungai Nipah. Pigs may also be infected, and millions were killed by Malaysian authorities in 1999 to stop the spread of disease, a measure which proved to be successful.

**Signs and Symptoms:**

- Acute respiratory infection,
- Seizures
- Fatal encephalitis. This illness typically initially presents as 3-14 days
- Fever and headache, often accompanied by a cough, sore throat, difficulty breathing, and other signs of respiratory illness.
- Dizziness, drowsiness, altered consciousness, and neurological signs that indicate acute encephalitis.,
- Coma within 24 to 48 hours [57].



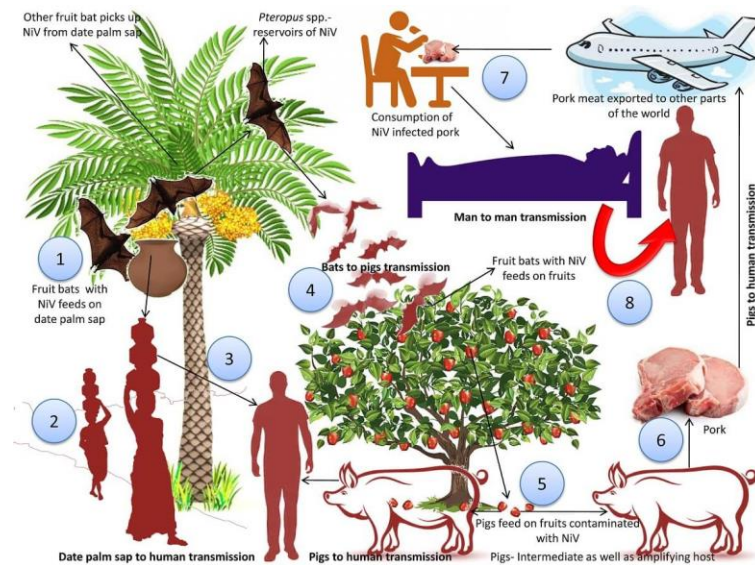


Figure:10 Transmission of Nipah Virus infection

Death occurs in 40-75% of cases, and some long-term side effects of infection include persistent convulsions and personality changes. Most survivors make a full recovery, although some are left with residual neurological conditions after acute encephalitis. Some cases of relapse have been reported.

#### Pathophysiology:

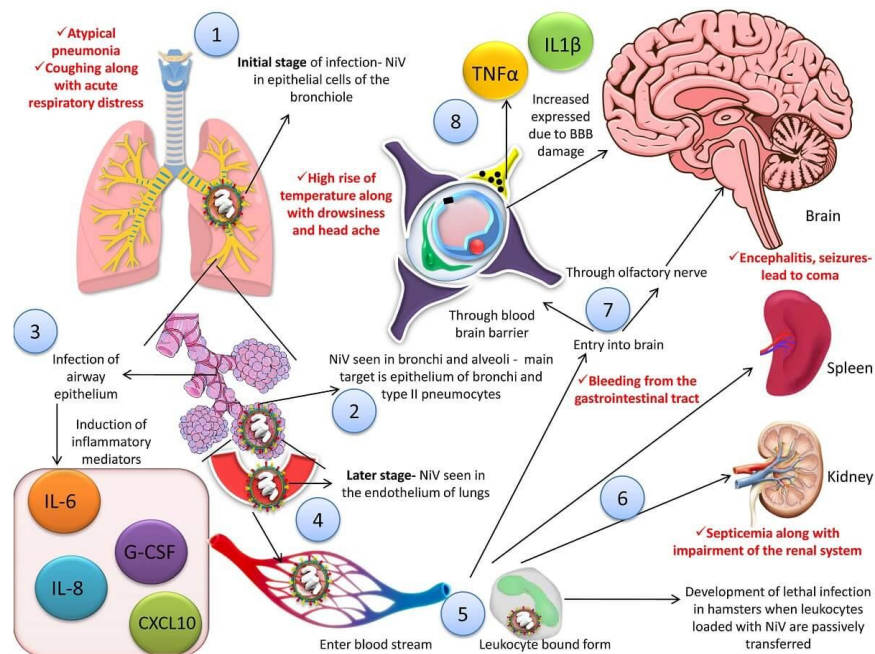


Figure:11 Pathology of Nipah virus

#### Outbreaks of Nipah Virus in India:

- 2021: September: 12-year-old boy, a native of Chathamangalam village was admitted to a hospital at Kozhikode in Kerala on September 1. He died from the virus four days after admission. Two healthcare workers who came into contact with the victim were already showing symptoms of Nipah infection by Monday.

- 2023: Since 4 January 2023 and as of 13 February 2023, 11 cases (10 confirmed and one probable) including eight deaths (Case Fatality Rate (CFR) 73%) have been reported in Bangladesh. WHO assesses the ongoing risk as high at the national level.
- 2023: September: Kozhikode district, Kerala, India: As of 14 September 2023, five cases, including two deaths, were confirmed in Kozhikode district in Kerala. The government has prepared a contact list of over 700 people linked to the two deaths, of whom two family members and a healthcare worker tested positive for the virus.
- 2024 :July: One person died and 60 were identified as at risk of infection in Malappuram district, Kerala, India [59-62].

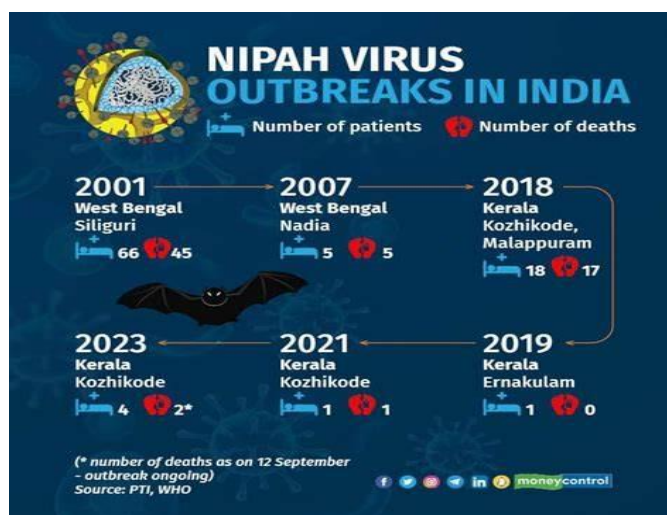


Figure:12 Nipah Virus- Outbreaks in India

### Treatment and Medication:

As of 2020, there is no specific treatment [59]. The mainstay of treatment is supportive care.

**Table:7 Treatment of Nipah Virus infection**

S.No	Category	Treatment	Medication
1.	Allopathy	Anti-viral agents [63]	Ribavirin, Acyclovir, Favipiravir and Remdesivir Passive immunization using a human monoclonal antibody.
2.	Ayurvedic	Prophylactic and Immuno modulating therapy [64]	<ol style="list-style-type: none"> <li>1. Amlaki Rasayana 3 gm, twice a day with water.</li> <li>2. Ashwagandadi Avaleha 10 gm twice a day with lukewarm milk.</li> <li>3. Haridra khand 5 gm twice a day with lukewarm milk.</li> <li>4. Samshamani vati 500 mg twice a day.</li> <li>5. Tulasi 3-5 leaves should be consumed a fresh or in tea twice in a day.</li> <li>6. Indukantha kashaya 10 ml with 40 ml of warm water twice a day before food</li> </ol>
3.	Siddha	Metal based medicines [65]	Silver, Gold, Tin, Iron oxide, copper oxide and Zinc oxide nanoparticles.

**Future Prospective:**

- Griffithsin (GRFT), a homodimeric high-mannose oligosaccharide-binding lectin, is currently being evaluated in clinical trials as a topical microbicide against human immunodeficiency virus 1 (HIV-1). In cell culture studies, GRFT, as well as a synthetic trimeric tandem (3mG) and an oxidation-resistant GRFT (Q-GRFT), demonstrated antiviral activity against NiV in the nanomolar range [66]
- ALS-8112 displayed strong antiviral effects against NiV *in vitro* in the low micromolar range, with minimal cytotoxic effects in multiple cell lines except for human peripheral blood mononuclear and lymphoblastoid cells [67]
- Enfuvirtide (Fuzeon™) is an FDA-approved analogous therapeutic for HIV-1 and is also a lipopeptide fusion inhibitor which has the potential to move forward as an effective antiviral. Future development of potent lipopeptide inhibitors for NiV infection is needed [68].

**SARS-CoV 2 (Covid-19):****Introduction:**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a strain of coronavirus that causes COVID-19, the respiratory illness responsible for the COVID-19 pandemic.<sup>[3]</sup> The virus previously had the provisional name 2019 novel coronavirus (2019-nCoV), and has also been called human coronavirus 2019 (HCoV-19 or hCoV-19). First identified in the city of Wuhan, Hubei, China, the World Health Organization designated the outbreak a public health emergency of international concern from January 30, 2020, to May 5, 2023. SARS-CoV-2 is a positive-sense single-stranded RNA virus that is contagious in humans [69].

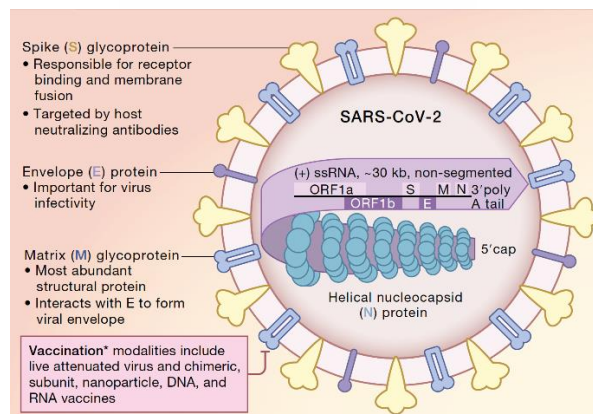
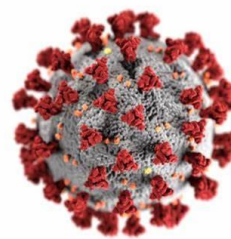
**Novel Coronavirus (COVID-19)**

Figure:13 Structure of Corona Virus

SARS-CoV-2 is a type of coronavirus, which are spherical, enveloped viruses with surface projections that give rise to the corona appearance. Coronaviruses contain a positive-sense RNA genome, which is wrapped up in helical nucleocapsid. The genome size of SARS-CoV-2 is about 30 kb. Among the RNA viruses, coronaviruses have the largest genome size. Coronaviruses are one of the two genera of classification under the family Coronaviridae. Coronaviridae, along with Arteriviridae and Roniviridae, fall under the order Nidoviridae [70].

**Signs and Symptoms:**

Possible symptoms include: Fever or chills, Cough, Shortness of breath or difficulty breathing, Sore throat, Congestion or runny nose, loss of taste or smell, Fatigue, Muscle or body aches, Headache, Nausea or vomiting and Diarrhoea.



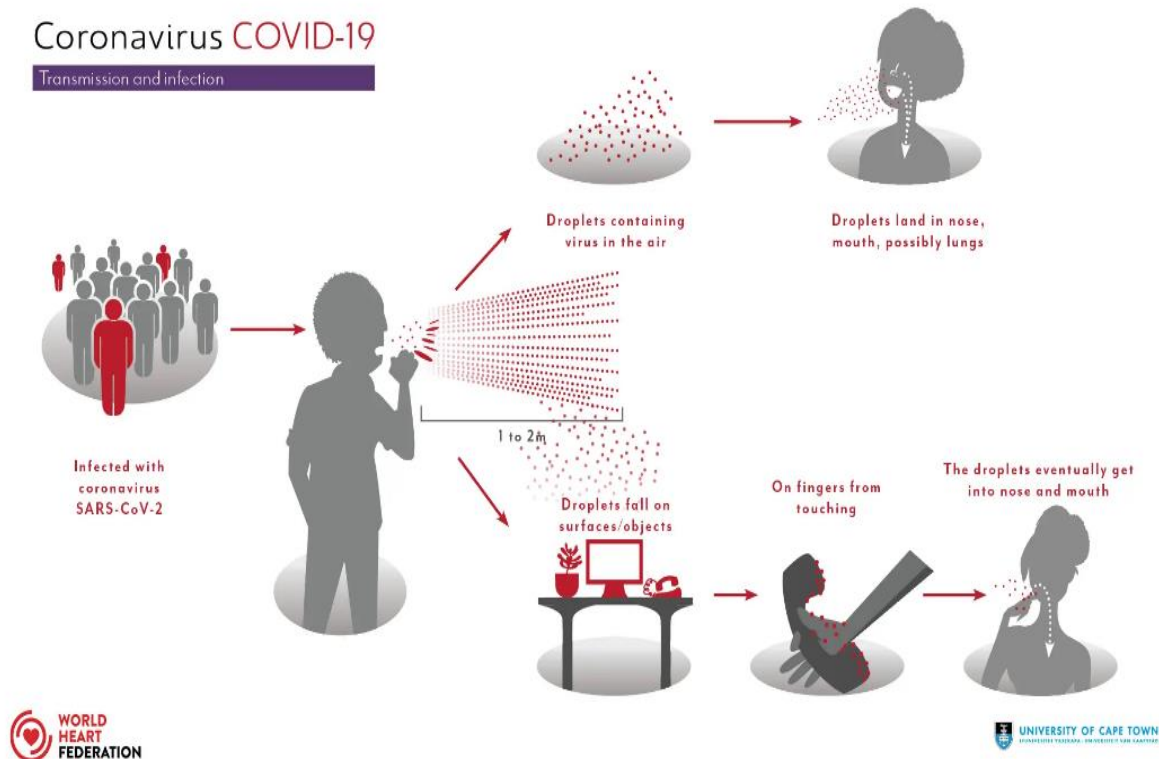
**Transmission:**

Figure:14 Transmission of Corona Virus

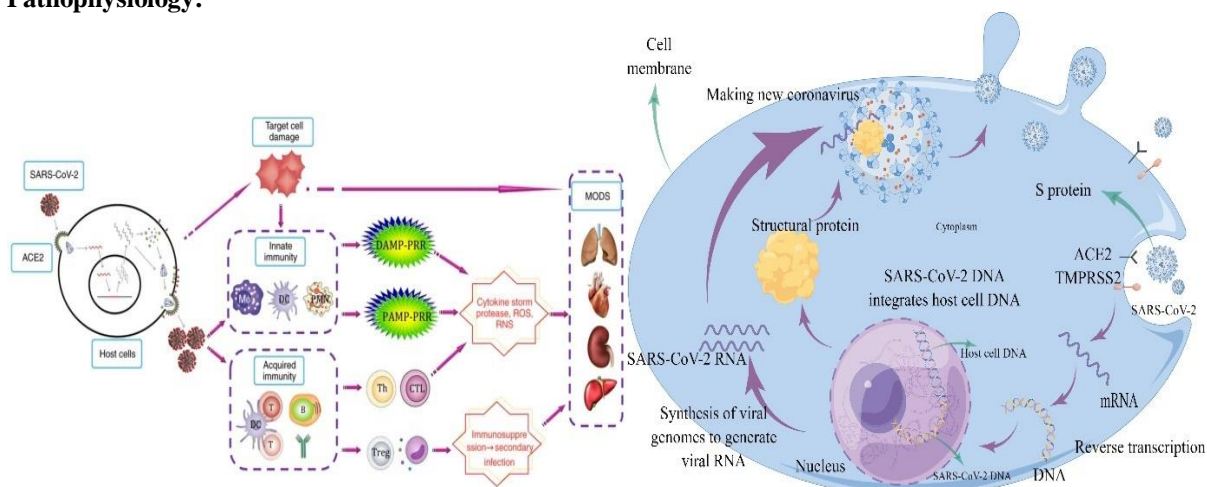
**Pathophysiology:**

Figure:15 Pathology of Corona Virus

**Outbreaks of Corona Virus in India:**

- Globally, the number of new cases by 44% during the past 28-day period of 5 February to 3 March 2024 compared to the previous 28-day period (8 January to 4 February 2024), with over two hundred and ninety-two thousand new cases reported. The

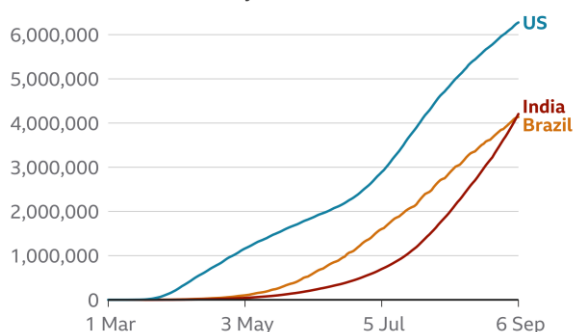
number of new deaths decreased by 51% as compared to the previous 28-day period, with 6200 new fatalities reported. As of 3 March 2024, over 774 million confirmed cases and more than seven million deaths have been reported globally.

- During the period from 5 February to 3 March 2024, COVID-19 new

hospitalizations and admissions to an intensive care unit (ICU) both recorded an overall decrease of 35% and 64% with over 78 000 and 500 admissions, respectively [71].

### India has second-highest number of cases

Total number of officially confirmed cases of coronavirus



Source: Johns Hopkins University, data to 6 September

BBC

Figure:15 Outbreaks of Covid 19 virus

### Treatment and Medication:

1. Antiviral development for SARS-CoV-2 has been disappointing.<sup>[39]</sup> In January 2020, research into potential treatments started,<sup>[40]</sup> and several antiviral drugs were in clinical trials [72].

2.As of February 2021, in the European Union, the use of dexamethasone and remdesivir were

authorized. corticosteroids like dexamethasone showed clinical benefit in treating COVID-19, once randomized controlled trials were performed in 2020 [73].

3.As of February 2021, the monoclonal antibody therapies bamlanivimab/ etesevimab and casirivimab /imdevimab were found to reduce the number of hospitalizations, emergency room visits, and deaths [74].

4.As of July 2021, outpatient drugs budesonide and tocilizumab showed promising results in some patients but remained under investigation [75].

5.The WHO recommendations on which medications should or should not be used to treat Covid-19 are continuously updated. As of July 2022, WHO strongly recommended for non-severe cases nirmatrelvir and ritonavir, and recommended conditionally Molnupiravir, Sotrovimab and Remdesivir [76].

6.For severe cases WHO strongly recommended corticosteroids, IL-6 receptor blockers or Baricitinib and conditionally recommended casirivimab and imdevimab [76].

7.Passive immunization with convalescent plasma or hyperimmune serum has been proposed as a potential treatment for COVID-19 [83].

Table: 8 Treatment of Covid infection

S.No	Category	Treatment	Medication
1.	Siddha [77]	Asymptomatic treatment	Kaba Sura Kudineer (60 ml twice daily, Before food)
		Mild symptomatic treatment	T. Amukkara Chooranam (2 tab. twice daily, After food) T. Athi Mathuram 500 mg (2 tab. twice daily, After food) T. Brahmananda Bairavam (100 mg 2 tab. twice daily, After food) Adathodai Manappagu (10 ml, twice daily, After food) Thippili Rasayanam (5 gm twice daily, After food) Notchi Kudineer (60 ml twice daily, before food)
2.	Ayurveda [78]	Therapeutic medication	Sudarsana Churna - 4 tablets Talisadi Churna - 1tsp with honey (Tid) Dhanwantara Gutika - 2 tablets (Tid) Vidaryadi Ghritam – 15 ml (Bid)

### Future Outcomes:

- As of July 2021, outpatient drugs budesonide and tocilizumab showed promising results in some patients but remained under investigation.

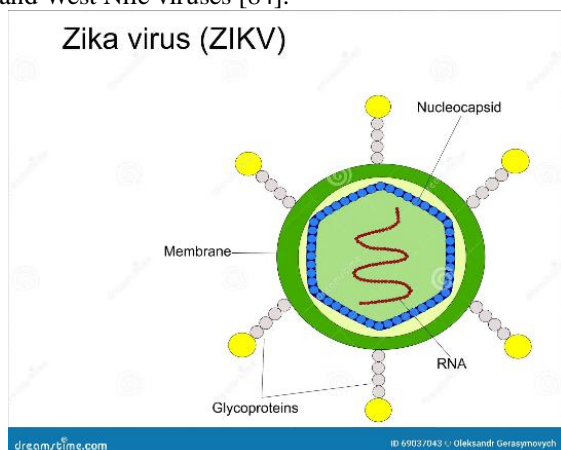
- As of 2021, favipiravir and nafamostat had shown mixed results but were still in clinical trials in some countries.
- As of February 2021, in the United States, only remdesivir had FDA approval for certain COVID-19 patients, and while early

research had suggested a benefit in preventing death and shortening illness duration, this was not borne out by subsequent trials.

- Masitinib was found to inhibit SARS-CoV-2 main protease, showing a greater than 200-fold reduction in viral titers in the lungs and nose of mice, however it is not approved for the treatment of COVID-19 in humans.
- COVID Moonshot is an international collaborative open-science project started in March 2020 with the goal of developing an un-patented oral antiviral drug for treatment of SARS-CoV-2 [79-82].

### ZIKA VIRUS:

Zika virus is a member of the virus family Flaviviridae. It is spread by daytime active Aedes mosquitoes, such as *A. aegypti* and *A. albopictus*. Its name comes from the Ziika Forest of Uganda, where the virus was first isolated in 1947. Zika virus shares a genus with the dengue, yellow fever, Japanese encephalitis, and West Nile viruses [84].



## Zika virus

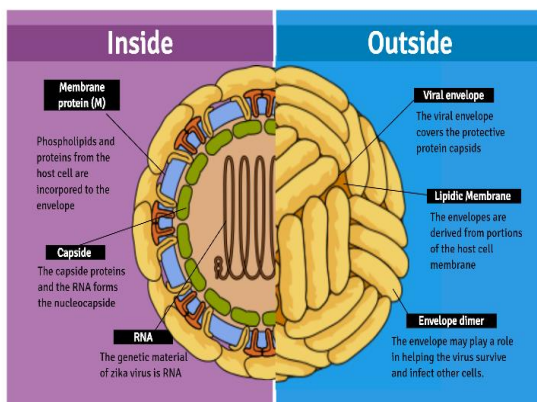


Figure:16 Structure of Zika virus

Zika virus is enveloped and icosahedral and has a non-segmented, single-stranded, 10 kilobase, positive sense RNA genome. It is most closely related to the Spondweni virus and is one of the two known viruses in the Spondweni virus clade. A positive-sense RNA genome can be directly translated into viral proteins. As in other flaviviruses, such as the similarly sized West Nile virus, the RNA genome encodes seven nonstructural proteins and three structural proteins in the form of a single polyprotein (Q32ZE1). One of the structural proteins encapsulates the virus. This protein is the flavivirus envelope glycoprotein, that binds to the endosomal membrane of the host cell to initiate endocytosis. The RNA genome forms a nucleocapsid along with copies of the 12-kDa capsid protein. The nucleocapsid, in turn, is enveloped within a host-derived membrane modified with two viral glycoproteins. Viral genome replication depends on the making of double-stranded RNA from the single-stranded, positive-sense RNA (ss RNA (+)) genome followed by transcription and replication to provide viral mRNAs and new ss RNA (+) genomes [85,86].

### Signs and Symptoms:

Most people infected with Zika virus do not develop symptoms. Among those who do, they typically start 3–14 days after infection, are generally mild including rash, fever, conjunctivitis, muscle and joint pain, malaise and headache, and usually last for 2–7 days. These symptoms are common to other arboviral and non-arboviral diseases; thus, the diagnosis of Zika virus infection requires laboratory confirmation [87].

### Zika Virus Transmission:

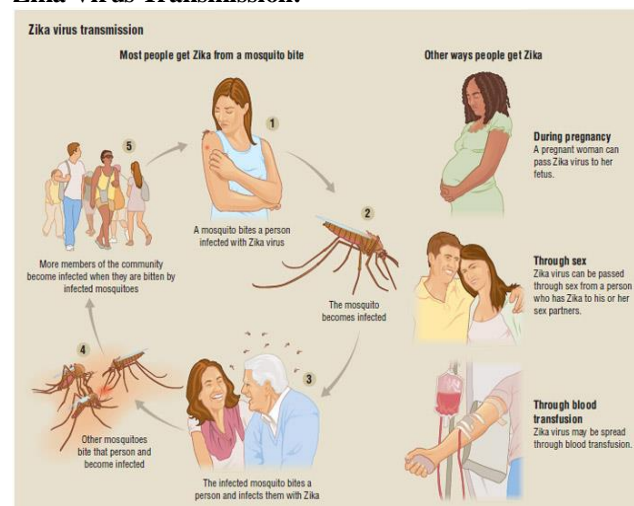


Figure:17 Transmission of Zika virus



### Pathophysiology of Zika Virus:

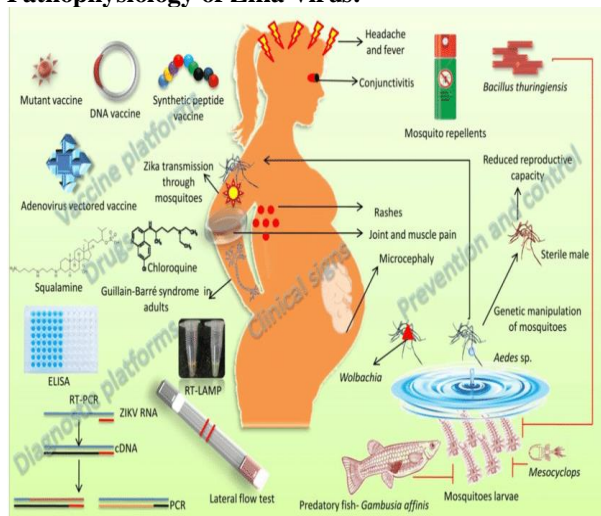


Figure:18 Pathology of Zika Virus

### Outbreaks of Zika Virus in India:

- Since 2013, with the first reported Zika virus (ZIKV) outbreak in the Marquesas Islands<sup>1</sup> and its subsequent spread to Brazil in May 2015.
- On May 15, 2017, the Ministry of Health and Family Welfare, Government of India, reported three laboratory-confirmed cases of

ZIKV disease from Bapunagar area, Ahmedabad, Gujarat, India

- With recent confirmation of one more Zika case from Chennai in India and after screening of a large number of febrile illness samples, yielded only four positive cases.
- In summary, the four cases of ZIKV infection detected in India showed ZIKV local transmission and were not associated with travel history. This also suggested that ZIKV might be present in India since long time.
- Recently, Pune in Maharashtra has witnessed a significant rise in Zika virus cases, with the central government issuing an advisory on Wednesday, July 3. In light of this, a 55-year-old woman has been detected with a Zika virus injection in Pune, bringing the number of cases to seven. Till now (July 2nd, 2024), the city has reported eight cases from Pune (6), Kolhapur (1), and Sangamner (1) [88,89].

### Medication and Treatment:

- It is advised, for an affected person with the zika virus, to drink a lot of water to stay hydrated, to lie down, and to treat the fever and agony with liquid solutions;

Table: 9 Treatment of Zika Virus infection

S.No	Category	Treatment	Medication
1.	Allopathy [90]	Relieve pain and fever  Inhibition of viral entry and replication  Inhibition of viral replication	Acetaminophen or Paracetamol  Chloroquine, Squalamine, Cavinafungin, Nanchangmycin and Duramycin biotin.  Sofosbuvir, Sinefungin, Tetrapeptide Boronic acid
2.	Ayurveda [90]	Act against Zika virus	Berberis vulgaris – Berberine Rheum palmatum – Emodin Silybum marianum – Silymarin Curcuma longa – Curcumin Camellia sinensis - Epigallocatechin gallate Tinospora cardifolia - Cordifolioside B Terminalia arjuna – Tannic acid

### Future Prospectives:

- In June 2016, the FDA granted the first approval for a human clinical trial for a Zika vaccine. In March 2017, a DNA vaccine was approved for phase-2 clinical trials [91].
- As of April 2017, both subunit and inactivated vaccines have entered clinical trials [92].
- Niclosamide, an anti-helminthic approved by the Food Drug Administration (FDA), and the cyclin-dependent kinase inhibitor

demonstrated to significantly inhibit ZIKV infection in vitro [93].

- 30 compounds demonstrated to be effective, decreasing virus infectivity. Eight compounds (ivermectin, daptomycin, mycophenolic acid (MPA), sertraline, pyrimethamine, cyclosporine A, azathioprine, and mefloquine) were selected for tests in human cell lines [93].
- Chloroquine is another compound approved by the FDA to treat malaria that can be administered to pregnant women. The anti-ZIKV properties of chloroquine were tested in Vero cells, human brain microvascular endothelial cells.
- Bromocriptine is a dopamine D2 and D3 receptor agonist, which is used to treat galactorrhea and Parkinson's disease and was also reported to possess anti-viral properties. Bromocriptine was tested for the ability to inhibit viral infection caused by the ZIKV [94].
- Barbosa-Lima et al. synthesized and evaluated the antiviral activity of a number of molecules derived from 2,8-bis (trifluoromethyl) quinoline (N1-(2,8-Bis (trifluoromethyl) quinolin-4-yl) ethane-1,2-diamine 3a, N1-(2,8-Bis (trifluoromethyl) quinolin-4-yl) propane-1,3-diamine 3b, N1-(2,8-bis (trifluoromethyl) quinolin-4-yl) decane-1,10-diamine 3c, N-butyl-2,8-bis (trifluoromethyl) quinolin-4-amine 3d, 2-(2,8-Bis (trifluoromethyl) quinolin-4-yl) amino) ethanol 4, and N-(2-Chloroethyl)-2,8-bis (trifluoromethyl) quinolin-4-amine 5) on ZIKV infection in vitro [95].

## MONKEY POX VIRUS:

### Introduction:

The monkeypox virus (MPV, MPXV, or hMPXV), is a species of double-stranded DNA virus that causes mpox disease in humans and other mammals. The monkeypox virus is a zoonotic virus belonging to the orthopox virus genus, making it closely related to the variola, cowpox, and vaccinia viruses. MPV is oval-shaped with a lipoprotein outer membrane. The genome is approximately 190 kb.

The monkeypox virus, like other poxviruses, is oval shaped, with a lipoprotein outer membrane. The outer membrane protects the enzymes, DNA, and transcription factors of the virus. Typical DNA viruses replicate and express their genome in the nucleus of eukaryotic cells, relying heavily on the host cell's machinery. However, the monkeypox

viruses rely mostly on the protein encoded in their genome that allows them to replicate in the cytoplasm.

The genome of the monkeypox virus comprises 200 kb of double stranded DNA coding for 191 proteins. Similar to other poxviruses, the virions of monkey pox have large oval shaped envelopes. Within each virion there is a core which holds the genome along with the enzymes that assist in dissolving the protein coat and replication.<sup>[14]</sup> The center of the genome codes for genes involved in key functions such as viral transcription and assembly; genes located on the extremities of the viral genome are associated more towards interactions between the virus and the host cell such as spike protein characteristics [96].

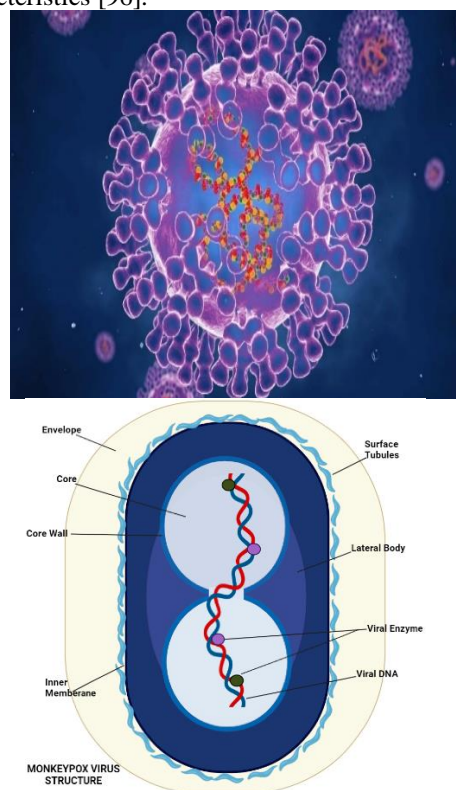


Figure:19 Structure of Monkey Pox Virus

### Signs and Symptoms:

Mpox causes signs and symptoms which usually begin within a week but can start 1–21 days after exposure. Symptoms typically last 2–4 weeks but may last longer in someone with a weakened immune system.

Common symptoms of mpox are: rash, fever, sore throat, headache, muscle aches, back pain, low energy, swollen lymph nodes. Some people may have one or a few skin lesions and others have hundreds or more. These can appear anywhere on the body such

as the: palms of hands and soles of feet, face, mouth

and throat groin and genital areas such as anus.

### Transmission of Monkey Pox Virus:

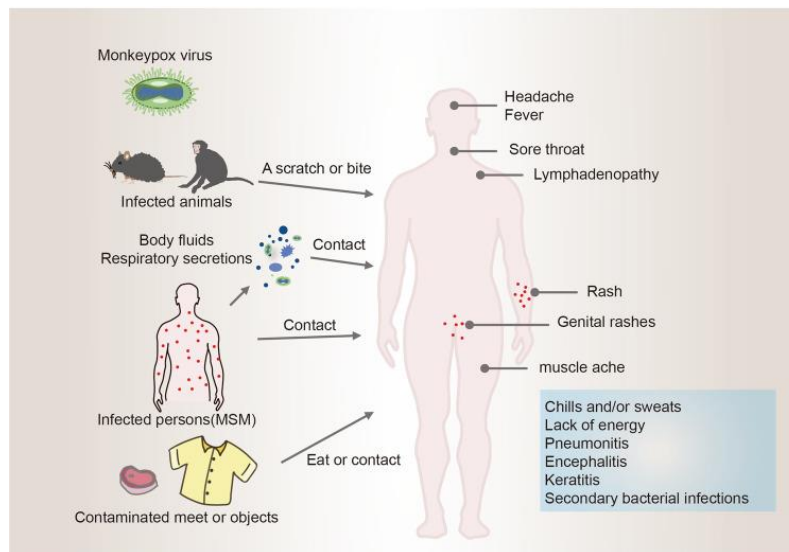


Figure:20 Monkey Pox Virus transmission

### Pathophysiology:

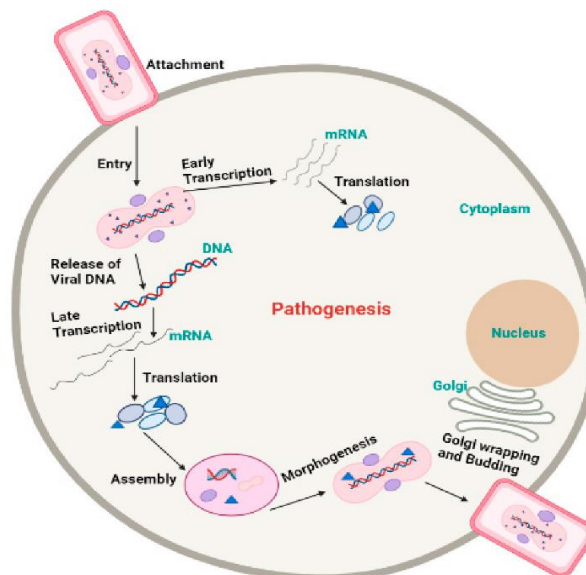


Figure: 21 Pathology of Monkey Pox Virus

### Outbreaks of Monkey Pox Virus in India:

- With the first case in India, there has been progressive rise in the cases in various parts of India. There were 10 cases in India as reported till August 13th 2022 with 30 % cases (3/10) who do not have history of travel or close contact with each other.
- The States of Uttar Pradesh, Bihar, and Telangana also reported numerous suspected cases, however the only states with lab-confirmed monkeypox (MPX) cases are Delhi and Kerala.
- India has confirmed its first death caused by monkeypox in the southern state of Kerala in Aug 2022.
- India was the tenth country to report a mpox case in Asia and the first in South Asia. Currently, India has reported 23 cases of mpox [97-102].

### Medication and Treatment



Table:9 Treatment of Monkey pox Virus Infection

S.No	Category	Treatment	Medication
1.	Allopathy [103]	Anti-viral agents	Tecovirimat (IV and Oral form), Cidofovir, Brincidofovir and Trifluridine.
		Pre-exposure prophylaxis vaccine	Modified vaccinia Ankara (MVA) vaccine and vaccinia immune globulin

**Future Outcomes:**

- Recent research, however, indicates brincidofovir is associated with serious adverse effects in monkeypox patients. Over the past three years, three cases have experienced liver toxicity in the United Kingdom. Further studies are warranted in humans regarding the efficacy of brincidofovir against monkeypox virus [104].
- Second-generation vaccine is ACAM2000, a live attenuated vaccinia vaccine approved in the USA in August 2007 for prevention of smallpox. Its effectiveness has been demonstrated in both animal models and clinical trials [105].
- Several animal model challenge studies of safety and efficacy of LC16m8 have been conducted in mouse, rabbit, and nonhuman primates. Both the intranasal and subcutaneous inoculation models showed no symptoms of monkeypox after immunization with LC16m8 [106].
- Several mRNA-based MPV vaccines have been developed and employed in animal models. These studies have demonstrated robust immunogenicity in mice that received the vaccines and were exposed to the VACV

challenge as well as less severe pathological changes than in control groups [107].

**CHANDIPURA VESICULOVIRUS:****Introduction:**

Chandipura vesiculovirus (CHPV) is a member of the Rhabdoviridae family that is associated with an encephalitic illness, Chandipura encephalitis or Chandipura viral encephalitis, in humans. It was first identified in 1965 after isolation from the blood of two patients from Chandipura village in Maharashtra state, India [108].

Chandipura vesiculovirus is an enveloped RNA virus with an approximate genome length of ~11 kb. Viral genome codes for five polypeptides, namely, nucleocapsid protein N, phosphoprotein P, matrix protein M, glycoprotein G and large protein L in five monocistronic mRNAs. N protein encapsidates genome RNA into a nuclease-resistant form to protect in from cellular RNase function. L and P protein together forms viral RNA dependent RNA polymerase; where catalytic functions for RNA polymerization, capping and poly-A polymerase resides within the L protein and P acts as a transcriptional activator. Matrix protein glues the encapsidated genome RNA, also known as nucleocapsid, with the outer membrane envelope. G protein spikes out of the membrane and acts as a major antigenic determinant [109].

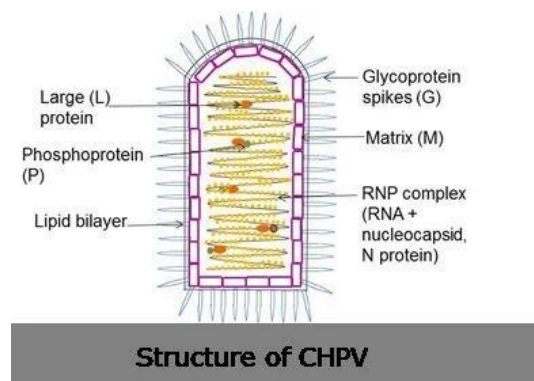
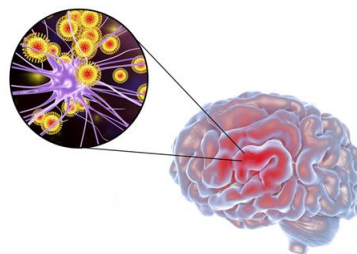
**Chandipura virus encephalitis**

Figure:22 Structure of Chandipura Virus

**Signs and Symptoms:**

Symptoms of Chandipura virus infection typically include fever, headache, convulsions, and unconsciousness, progressing rapidly to coma and death in severe cases. There is no specific treatment or vaccine available for Chandipura virus infection, so management focuses on supportive care and prevention measures such as mosquito control [110].

#### Transmission of Chandipura Virus:

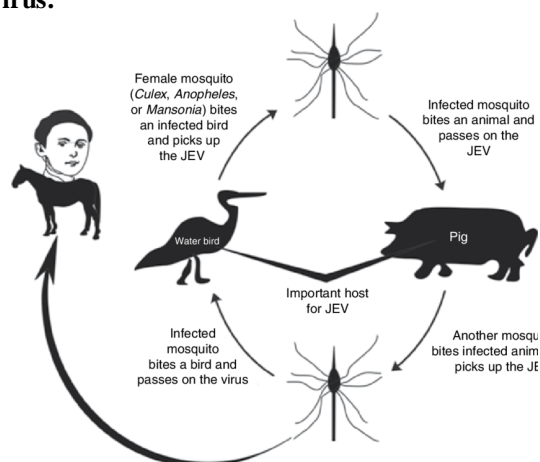


Figure:22 Transmission of Chandipura Virus

#### Pathophysiology:

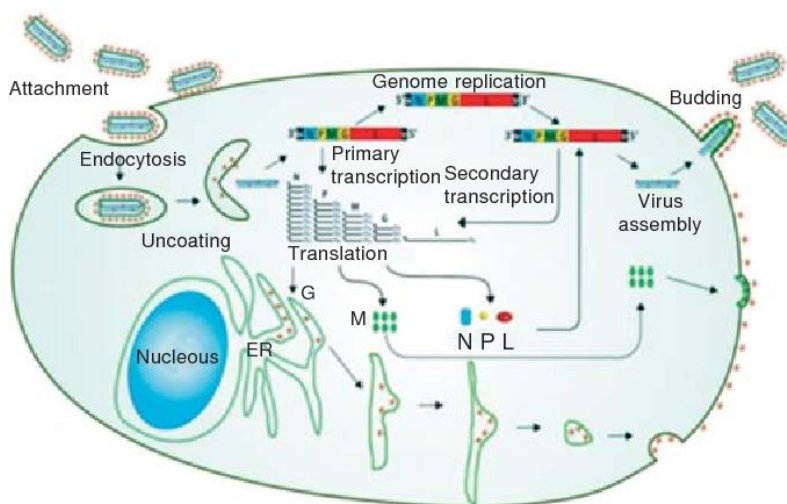


Figure: 23 Pathology of Chandipura Virus

#### Outbreaks of Chandipura Virus in India:

- In 2003, 329 children in Andhra Pradesh and Maharashtra tested positive for the virus, of which 189 succumbed to the virus.
- In 2009, there were 52 positive cases, and 15 fatalities. In 2010, there were 50 positive cases and 16 fatalities. Between 2009 and 2011, there were 110 positive cases, and 3 fatalities.
- An outbreak in Gujarat in Kheda District, Vadodara District, and Panchmahal District killed 17 people in 2010.
- In 2016, a girl from Ahmedabad succumbed to the virus.
- In 2019, a girl from Bhayli, Vadodara succumbed to the virus.

- In July 2024, Sabarkantha district of Gujarat in India experienced an outbreak particularly in children. This outbreak has raised significant public health concerns due to the rapid spread and the severity of symptoms observed in the affected individuals. So far, 38 deaths caused by the virus have been confirmed, and there remains a speculative death toll of 48 [111-117].

#### Treatment and Medication:

- There is no specific treatment or vaccine available for Chandipura virus infection, so management focuses on supportive care and prevention measures such as mosquito control.

- According to a 2014 document by the Gujarat government on 'Epidemiology & Management of Chandipura Encephalitis,' management includes airway, breathing, and circulation support through oxygen therapy and ventilation if necessary.
- It also involves managing fluid and electrolyte balance, hyperpyrexia (extremely high body temperature), raised intracranial pressure, and seizures, as well as preventing secondary bacterial infections [110].

#### Future Prospectives:

- The efficiency of a recombinant vaccine using the complete *G* gene of CHPV isolated from a patient during the 2003 outbreak in AP. The vaccine study was completed in 2008, however, no clinical trials in human has been done so far.
- A beta propio lactone (BPL) (Killed vaccine) inactivated tissue culture based vaccine has also been developed and evaluated for immunogenicity in mice. Though the vaccine candidate has been found to be promising this vaccine awaits clinical trials in humans.
- In the field of antivirals, siRNAs have been found to be promising as inhibition of virus replication was observed both *in vitro* and *in vivo*. The *P* and *M* proteins were targeted due to their importance in virus life cycle. Despite the therapeutic potential, no clinical trials have been carried out for use in humans [118-120].

#### CONCLUSION:

Protection against viral infection by anti-viral agents and serum immunoglobulins is combined with antibody-mediated neutralization of viral infectivity in host cells. Antibodies or drugs affect the viral life cycle at early steps, which may include cross-linking virion particles into non-infectious aggregates, steric hindrance of receptor engagement, and interference with viral disassembly. The pandemics of viral infection are increasing in frequency and infectivity of humans. The care and great caution should be taken against viral infections especially due to transmission of various virus particle. Such pandemics have affected large populations and have caused considerable havoc on healthcare systems, those in developing countries especially in India. The recent Nipah virus and SARS CoV-2 pandemic has brought the whole world to a virtual standstill severely affecting the world. Lessons must be learnt from such pandemics so that adequate strengthening of the healthcare infrastructure and systems can be done in order to prevent the long-term effects of such

pandemics especially in low and middle-income countries, which are as such struggling with poor health infrastructure. Primary healthcare physicians are important vehicles to bring these practices to more and more people, hence educating them is important.

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