

#### PHARMACEUTICAL MICROBIOLOGY

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#### **OBJECTIVES**

- Enveloped RNA Viruses
  - Influenza Virus
  - Measles (Rubeola)
  - Rubella (German Measles, Three-Day Measles)
  - Mumps
  - Human Parainfluenza Virus
  - Respiratory Syncytial Virus
  - Rabies Virus
  - Severe Acute Respiratory Syndrome Coronavirus-2
  - Zika Virus
  - HIV (Human Immunodeficiency Virus)
  - Ebola Virus



#### **OBJECTIVES**

- Non-Enveloped RNA Viruses
  - Poliovirus
  - Rhinovirus
  - Rotavirus

#### VIRAL HEPATITIS

- Hepatitis A Virus
- Hepatitis B Virus
- Hepatitis C Virus
- Hepatitis D Virus
- Hepatitis E Virus



## **ENVELOPED RNA VIRUSES**Influenza Virus

- Influenza A virus is the main cause of epidemics all over the world.
- It is a negative strand RNA virus.
- Its RNA is segmented, so yearly vaccination is required due to antigenic changes.
- There are three types of the virus.

Type A: human and animal strains

Type B: only human strains

Type C: only human strains

#### Influenza Virus

 It has ability to bind to glycoprotein receptors in upper respiratory cells. Infection is limited within respiratory system epithelia.

- It has two major virulence factors.
  - √ Hemagglutinin (HA) glycoprotein
  - ✓ Neuraminidase (NA) glycoprotein

### **ENVELOPED RNA VIRUSES**Influenza Virus

Hemagglutinin (HA) glycoprotein: It binds to sialic acid receptors, which are also found on the surface of erythrocytes. As a result of this, when viruses containing hemagglutinin glycoprotein are exposed to erythrocytes, they cause hemagglutination.

**Sialic acid receptors** of host cells are found on the membranes of upper respiratory track cells. Binding of HA to these receptors, results in the entrance of virus genome into host cell. HA is needed for adsorption. Antibodies produced against HA, prevent the binding of the virus and consequently infection.

### **ENVELOPED RNA VIRUSES**Influenza Virus

**Neuraminidase** (NA) glycoprotein: Neuraminic acid is an important component of mucin. Mucin surrounds mucosal epithelial cells and is a part of the upper respiratory tract defense. Neuraminidase (NA) cleaves neuraminic acid and consequently exposes sialic acid receptors by destroying mucin.

- ✓ NA destroys the mucin barrier
- ✓ HA binds to sialic acid receptors and enables the adsorption of virus to host cells.

#### Influenza Virus

 Viral spread can begin 1 day before the onset of the disease and last for 5-10 days.

Fever with shiver (38 °C), nasal flow, headache, myalgia, fatigue, absence of appetite, nausea, red eyes etc. are all likely symptoms. Sometimes sore throat and coughing accompany.

### **ENVELOPED RNA VIRUSES**Influenza Virus

 Vaccination is the most effective way to prevent infection and severe outcomes caused by Influenza viruses.

#### Types of Influenza Vaccines

- Inactivated Vaccine: These types of vaccines are produced by inactivating the virus with chemicals, heat or radiation. There are three types of inactivated vaccines whole virus, split virus and subunit vaccine. (generally intramuscular injected)
- Live Attenuated Vaccine: These types of vaccines contain weakened strain of virus. (they are given intranasal)

#### Measles (Rubeola)

 The symptoms of measles generally appear about 7 to 14 days after a person is infected.

 Measles typically begins with high fever, cough, runny nose and red, watery eyes (conjunctivitis).

 Two or three days after symptoms begin, tiny white spots (Koplik spots) may appear inside the mouth.

#### Measles (Rubeola)

Three to five days after symptoms begin, a rash breaks out.
 It usually begins as flat red spots that appear on the face at the hairline and spread downward to the neck, trunk, arms, legs, and feet.

 As the skin rash progresses downward, initial rash on the head and neck heals.

# ENVELOPED RNA VIRUSES Measles (Rubeola)

 Being exposed to Measles/Rubeola can cause spontaneous abortion and premature birth during pregnancy.

 Live, attenuated, triple combination vaccine (MMR= Measles, Mumps, Rubella Vaccine) containing measles virus is protective.

 In our country it is administered to all infants at the end of twelve months. Vaccination is repeated in the first year of primary school.

## **ENVELOPED RNA VIRUSES**Rubella (German Measles, Three-Day Measles)

- Rubella is a contagious disease caused by Rubella Virus.
- Most people who get rubella usually have a mild illness, with symptoms that can include a low-grade fever, sore throat, and a rash that starts on the face and spreads to the rest of the body.
- Rash may start around two weeks after exposure and last for three days. It usually starts on the face and spreads to the rest of the body. The rash is sometimes itchy and is not as bright as that of measles.

# ENVELOPED RNA VIRUSES Rubella (German Measles, Three-Day Measles)

- Rubella can cause a miscarriage or serious birth defects in a developing baby if a woman is infected while she is pregnant.
- The best protection against rubella is MMR (measles-mumps-rubella) vaccine. Live, attenuated, triple combination vaccine (MMR) containing measles virus is protective. In our country it is administered to all infants at the end of twelve months. Vaccination is repeated in the first year of primary school.

Mumps is a viral disease caused by the Mumps virus.

- Mumps is best known for the puffy cheeks and swollen jaw that it causes. This is a result of swollen salivary glands.
- The most common symptoms include fever, headache, muscle aches, tiredness, loss of appetite, swollen and tender salivary glands under the ears on one or both sides (parotitis).

- Symptoms typically appear 16-18 days after infection, but this period can range from 12-25 days after infection.
- Some people who get mumps have very mild or no symptoms, and often they do not know they have the disease.
- Most people with mumps recover completely in a few weeks.
- It spreads through saliva or mucus from the mouth, nose, or throat.

#### **Complications include:**

- inflammation of the testicles (orchitis) in males who have reached puberty; rarely does this lead to fertility problems
- inflammation of the brain (encephalitis)
- inflammation of the tissue covering the brain and spinal cord (meningitis)
- inflammation of the ovaries (oophoritis) and/or breast tissue (mastitis)
- deafness

The best protection against Mumps is MMR (measles-mumps-rubella) vaccine. Live, attenuated, triple combination vaccine (MMR) containing mumps virus is protective.

 In our country it is administered to all infants at the end of twelve months.

Vaccination is repeated in the first year of primary school.

# **ENVELOPED RNA VIRUSES**Human Parainfluenza Viruses (HPIVs)

- Human Parainfluenza Viruses (HPIVs) commonly cause respiratory illnesses in infants and young children. But anyone can get HPIV illness.
- Symptoms may include fever, runny nose, and cough.
   Patients usually recover on their own. However, HPIVs can also cause more severe illness, such as croup or pneumonia.
- HPIVs spread from an infected person to other people through the air by coughing and sneezing, close personal contact, such as touching or shaking hands.

## **ENVELOPED RNA VIRUSES Respiratory Syncytial Virus (RSV)**

- Respiratory syncytial virus is a common respiratory virus that usually causes mild, cold-like symptoms.
- Most people recover in a week or two, but RSV can be serious, especially for infants and older adults.
- In fact, RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lung) and pneumonia (infection of the lungs) in children younger than 1 year of age.
- It is also a significant cause of respiratory illness in older adults.

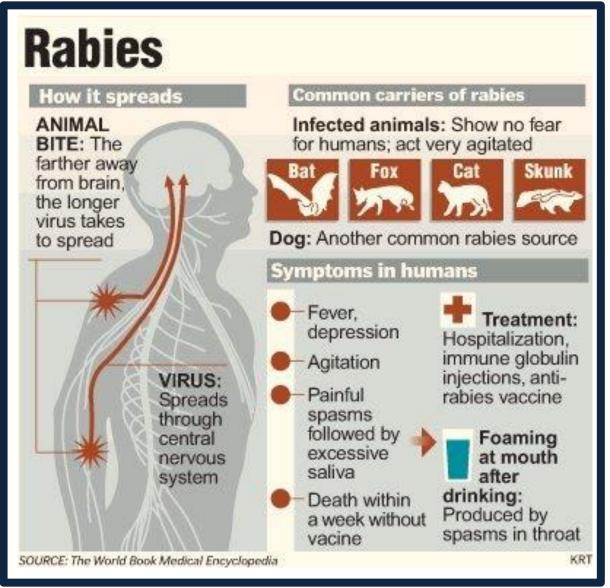
## **ENVELOPED RNA VIRUSES Respiratory Syncytial Virus (RSV)**



https://www.utmb.edu/pedi/categories-tags/2019/11/25/psa-rsv-prevention

#### **Rabies Virus**

- Rabies is a zoonotic disease (a disease that is transmitted to humans from animals) that is caused by a virus.
- The vast majority of rabies cases reported to the Centers for Disease Control and Prevention (CDC) each year occur in wild animals like raccoons, bats, and foxes.
- Rabies infects domestic and wild animals and is spread to people through close contact with infected saliva (via bites or scratches).



https://sites.google.com/site/thedangerousrabies/symptoms-a-diagnosis

#### **Rabies Virus**

 The rabies virus infects the central nervous system, ultimately causing disease in the brain.

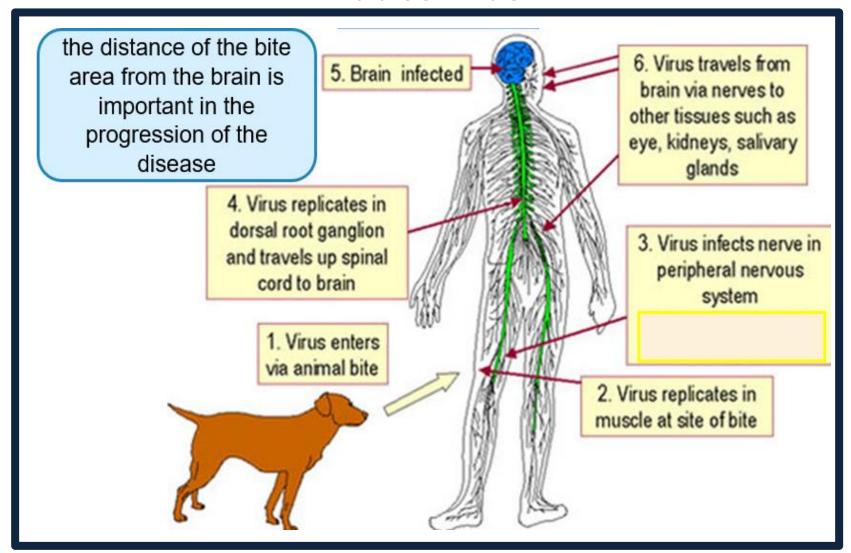
 The early symptoms of rabies in people are similar to that of many other illnesses, including fever, headache, and general weakness or discomfort.

#### **Rabies Virus**

 As the disease progresses, more specific symptoms appear and may include insomnia, anxiety, confusion, slight or partial paralysis, excitation, hallucinations, agitation, hypersalivation (increase in saliva), difficulty swallowing, and hydrophobia (fear of water).

 Death usually occurs within days of the onset of these symptoms.

## ENVELOPED RNA VIRUSES Rabies Virus



https://rabiesiscontagious.weebly.com/the-symptoms-of-rabies-and-the-parts-of-the-body-affected.html

#### **Rabies Virus**

- Negri bodies are a characteristic microscopic finding in the diagnosis of Rabies.
- Rabies is a vaccine-preventable disease.
- Vaccinating dogs is the most cost-effective strategy for preventing rabies in people.
- Human rabies vaccines exist for pre-exposure immunization.
   These are recommended for people in certain high-risk occupations such as laboratory workers handling live rabies and animal disease control staff, wildlife rangers.

#### Coronaviruses

Coronaviruses (CoV) are a large family of viruses that cause illness ranging from the common cold to more severe diseases such as Severe Acute Respiratory Syndrome (SARS-CoV) (2002), Middle East Respiratory Syndrome (MERS-CoV) (2012) and COVID-19 (SARS-CoV-2) (2019).

Coronaviruses are zoonotic, meaning they are transmitted between animals and people.

#### Coronaviruses

Detailed investigations found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans.

The new Coronavirus (**SARS-CoV-2**) first appeared on December 29, 2019, with the lung infection (pneumonia) in people working in a market selling **seafood and live animals** in Wuhan, China.

#### Coronaviruses

Coronavirus is an **enveloped**, **positive-stranded RNA** virus that causes infection in humans and animals.

It is one of the most common viruses that cause upper respiratory infection known as cold.

(positive stranded RNA genome can serve as mRNA and directly translated into protein. It causes infection as soon as it enters the host cell).

## ENVELOPED RNA VIRUSES Coronaviruses

Common signs of infection include respiratory symptoms, fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

Standard recommendations to prevent infection spread include regular hand washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs. Avoid close contact with anyone showing symptoms of respiratory illness such as coughing and sneezing.

SARS-CoV-2 is a newly discovered coronavirus that causes COVID-19 disease.

Most people infected with the COVID-19 virus experience mild to moderate respiratory illness and recover without requiring special treatment.

In older people, and those who have underlying medical problems like cardiovascular disease, diabetes, and chronic respiratory disease are more likely to develop serious illness.

#### **Common symptoms include:**

- fever - tiredness - dry cough

#### Other symptoms include:

- shortness of breath

- aches and pains

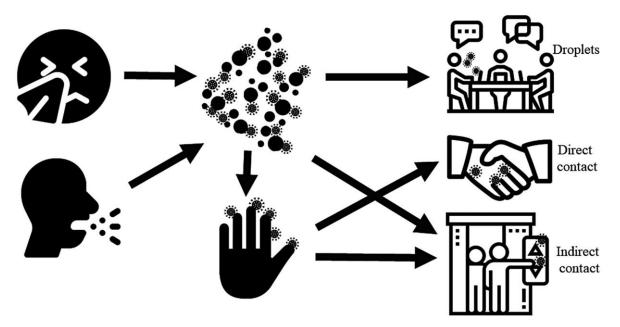
- sore throat

- diarrhea

- nausea

- runny nose.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or Sneezes. COVID-19 transmission routes: droplets, direct contact, and indirect contact



https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cncy.22280

#### To prevent infection and transmission of COVID-19:

- Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub.
- Maintain at least 1 meter distance between you and people coughing or sneezing.
- Avoid touching your face.
- Cover your mouth and nose when coughing or sneezing.

https://www.who.int/health-topics/coronavirus#tab=tab\_2

#### To prevent infection and transmission of COVID-19:

Stay home if you feel unwell.

 Refrain from smoking and other activities that weaken the lungs.

 Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people.

https://www.who.int/health-topics/coronavirus#tab=tab\_2

#### **ENVELOPED RNA VIRUSES**

# Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)

Is there a vaccine, drug or treatment for COVID-19?

- To date, there is no vaccine or treatment option approved against the coronavirus.
- Patients should receive care to relieve symptoms. People with serious illness should be hospitalized.
- Possible vaccines and some specific drug treatments are under investigation. They are being tested through clinical trials.

## **ENVELOPED RNA VIRUSES Zika Virus**

• Zika is spread mostly by the bite of an infected Aedes species mosquito. These mosquitoes bite during the day and night.

• A pregnant woman can pass Zika virus to her fetus during pregnancy. Zika is a cause of microcephaly and other severe fetal brain defects (such as defects of the eye, hearing deficits, and impaired growth).

## **ENVELOPED RNA VIRUSES Zika Virus**

 Zika can be passed through sex from a person who has Zika to his or her partners. Zika can be passed through sex, even if the infected person does not have symptoms at the time.

- Zika can be passed through blood transfusion.
- Many people infected with Zika virus won't have symptoms or will only have mild symptoms. The most common symptoms of Zika are: fever, rash, joint pain, red eyes. Other symptoms include: muscle pain, headache.

### ENVELOPED RNA VIRUSES Zika Virus

- Symptoms can last for several days to a week. People usually don't get sick enough to go to the hospital, and they very rarely die of Zika.
- There is no vaccine to prevent Zika.
- The best way to prevent diseases spread by mosquitoes is to protect yourself and your family from mosquito bites. Prevent sexual transmission of Zika by using condoms. There is no vaccine or medicine for Zika.

### **ENVELOPED RNA VIRUSES HIV (Human Immunodeficiency Virus)**

- HIV causes AIDS (Acquired Immuno Deficiency Syndrome).
- This human virus is a retrovirus belonging to the lentivirus family.
- It has a long incubation period, followed by a slowly progressive fatal outcome.
- The major target of the HIV is immune system. The CD4
  molecule (present on the surface of T lymphocytes and
  macrophages) forms a high affinity receptor for HIV.

# ENVELOPED RNA VIRUSES HIV (Human Immunodeficiency Virus)

 A retrovirus, including HIV, is a simple chemical package containing the viral RNA, along with a few molecules of reverse transcriptase enzyme, which copies the viral RNA into DNA as soon as the virus infects a new cell.

 This DNA then integrates into cellular DNA. It codes for viral proteins, and new copies of the viral genome. Finally, newly formed viral genomes and proteins are assembled into new viruses, which escape from the cell.

#### **ENVELOPED RNA VIRUSES**

### **Symptoms of AIDS**

- Weight loss or abnormally slow growth in children
- Chronic diarrhea for more than a month
- Prolonged fever for more than a month
- Persistent cough for more than a month
- Generalized puritic dermatitis
- An episode of herpes zoster (viral infection)
- Oro-pharyngeal candidiasis (fungal infection in mouth-throat)
- Chronic progressive-disseminated Herpes Simplex infection
- Generalized enlargement of lymph glands (lymphadenopathy)
- Lung diseases and skin tumors (Kaposis' sarcoma)

# ENVELOPED RNA VIRUSES HIV (Human Immunodeficiency Virus)

The common modes of HIV transmission may be as follows:

 Sexual transmission: HIV present in seminal fluid, female genital secretions

 Blood transfusion: If HIV infected blood or blood products are transfused into a healthy man, the recipient develops AIDS.

# ENVELOPED RNA VIRUSES HIV (Human Immunodeficiency Virus)

The common modes of HIV transmission may be as follows:

 Drug abuse: People who inject drugs intravenously can catch AIDS by sharing a needle or syringe with someone who is infected with HIV.

 Mother to baby: HIV can pass from mother to child. An infected woman can pass the virus on to her child during pregnancy, at birth or possibly with her breast milk.

### ENVELOPED RNA VIRUSES Ebola Virus

Ebola Virus Disease (Ebola Hemorrhagic Fever) is a rare and deadly disease most commonly affecting people and nonhuman primates (monkeys, gorillas, and chimpanzees).

It is caused by an infection with one of five known Ebola virus species, four of which can cause disease in people:

- √ Ebola virus (Zaire ebolavirus)
- ✓ Sudan virus (Sudan ebolavirus)
- ✓ Taï Forest virus (Taï Forest ebolavirus)
- ✓ Bundibugyo virus (Bundibugyo ebolavirus)
- ✓ Reston virus (Reston ebolavirus), known to cause disease in nonhuman primates and pigs, but not in people

### ENVELOPED RNA VIRUSES Ebola Virus

- The virus is transmitted to people from wild animals and spreads in the human population through human-to- human transmission.
- It is thought that fruit bats of the Pteropodidae family are natural Ebola virus hosts.
- Ebola is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.

#### **ENVELOPED RNA VIRUSES**

#### **Ebola Virus**

 Ebola then spreads through human-to-human transmission via direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids.

• The incubation period, that is, the time interval from infection with the virus to onset of symptoms is 2 to 21 days.

# **ENVELOPED RNA VIRUSES Ebola Virus**

Humans are not infectious until they develop symptoms.
 First symptoms are the sudden onset of fever fatigue,
 muscle pain, headache and sore throat.

 This is followed by vomiting, diarrhoea, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding (e.g. oozing from the gums, blood in the stools).

### ENVELOPED RNA VIRUSES Ebola Virus

- There are two new treatment options that effects by preventing the replication of the virus. Regeneron (REGN-EB3) and mAb114.
- Ebola vaccine (rVSV-ZEBOV-trade name Ervebo) approved by the FDA on December 19, 2019, is available.
- rVSV-ZEBOV vaccine is administered as a single dose.

https://www.nih.gov/news-events/news-releases/investigational-drugs-reduce-risk-death-ebola-virus-disease

https://www.fda.gov/news-events/press-announcements/first-fda-approved-vaccine-prevention-ebola-virus-disease-marking-critical-milestone-public-health

## NON-ENVELOPED RNA VIRUSES Poliovirus

Poliomyelitis (polio) is a highly infectious viral disease,
 which mainly affects young children.

• The virus is transmitted by person-to-person spread mainly through the fecal-oral route or, less frequently, by a common vehicle (e.g. contaminated water or food) and multiplies in the intestine, from where it can invade the nervous system and can cause paralysis.

### NON-ENVELOPED RNA VIRUSES Poliovirus

- Initial symptoms of polio include fever, fatigue, headache, vomiting, stiffness in the neck, and pain in the limbs. In a small proportion of cases, the disease causes paralysis, which is often permanent.
- There is no cure for polio, it can only be prevented by immunization. Inactivated polio vaccine (IPV) is the only polio vaccine that has been given in the United States since 2000.
  It is given by shot in the arm or leg, depending on the person's age. CDC recommends that children get four doses of polio vaccine.

# NON-ENVELOPED RNA VIRUSES Rhinovirus

It is the predominant cause of the common cold.

 Transmission: via aerosols of respiratory droplets and from fomites (contaminated surfaces), including direct person-toperson contact.

 The primary route of entry for human rhinoviruses is the upper respiratory tract (mouth and nose).

## NON-ENVELOPED RNA VIRUSES Rotavirus (Reoviridae:double-stranded RNA)

- Rotavirus is the most common cause of diarrhoeal disease among infants and young children.
- It is a genus of double-stranded RNA viruses in the family Reoviridae (consists of 11 double-stranded RNA segments, each encoding one viral protein).
- The virus is transmitted by the fecal-oral route. It infects and damages the cells that line the small intestine and causes gastroenteritis

#### **VIRAL HEPATITIS**

 Hepatitis" means inflammation of the liver. Toxins, certain drugs, some diseases, heavy alcohol use, and bacterial and viral infections can all cause hepatitis.

 Viral hepatitis is liver inflammation due to a viral infection. It may present in acute or chronic forms.

 The most common causes of viral hepatitis are the five unrelated hepatotropic viruses Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E.

#### VIRAL HEPATITIS

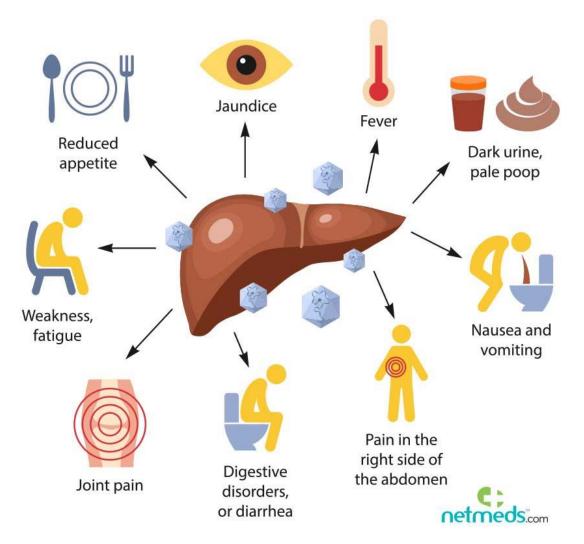
 In addition to the nominal hepatitis viruses, other viruses that can also cause liver inflammation include Cytomegalovirus, Epstein–Barr virus, Yellow fever, Herpes simplex virus.

 Hepatitis A and Hepatitis B can be prevented by vaccination. Effective treatments for Hepatitis C are available but expensive.

### **Hepatitis A Virus**

- Non-enveloped, RNA virus
- Hepatitis A is a liver infection caused by the Hepatitis A virus (HAV). Hepatitis A is highly contagious.
- It is usually transmitted by the fecal-oral route, either through person-to-person contact or consumption of contaminated food or water.
- Unlike Hepatitis B and C, Hepatitis A infection does not cause chronic liver disease and is rarely fatal, but it can cause debilitating symptoms and fulminant hepatitis (acute liver failure), which is often fatal.
- A safe and effective vaccine is available to prevent Hepatitis A.

### Hepatitis A Virus SYMPTOMS OF HEPATITIS A



https://www.netmeds.com/health-library/post/hepatitis-a-causes-symptoms-and-treatment

### **Hepatitis B Virus**

Enveloped, DNA virus

- Chronic Hepatitis B is a serious disease that can result in long-term health problems, including liver damage, liver failure, liver cancer, or even death.
- Hepatitis B is spread when blood, semen, or other body fluid infected with the Hepatitis B virus enters the body of a person who is not infected.

#### **Hepatitis B Virus**

People can become infected with the virus during activities such as:

- Birth (spread from an infected mother to her baby during birth)
- Sex with an infected partner
- Sharing needles, syringes, or other drug-injection equipment
- Sharing items such as razors or toothbrushes with an infected person
- Direct contact with the blood or open sores of an infected person
- Exposure to blood from needle sticks or other sharp instruments

### **Hepatitis C Virus**

- Enveloped, RNA virus
- Chronic infection after several years may cause cirrhosis or liver cancer.
- HCV is spread primarily by blood-to-blood contact associated with intravenous drug use, poorly sterilized medical equipment, needlestick injuries in healthcare, and transfusions. It may also be spread from an infected mother to her baby during birth.
- There is no vaccine against Hepatitis C.

### **Hepatitis E Virus**

- Non-enveloped, RNA virus
- HEV is transmitted by the fecal-oral route. Waterborne and person-to-person spread have been documented.
- Hepatitis caused by HEV is clinically indistinguishable from hepatitis A disease. Symptoms include malaise, anorexia, abdominal pain, arthralgia, and fever.
- The disease is most often seen in young to middle aged adults (15-40 years old).

### **Hepatitis E Virus**

 Pregnant women appear to be exceptionally susceptible to severe disease, and excessive mortality has been reported in this group (%20-25).

There is no licensed hepatitis E vaccine for use in the US.

 Hepatitis E do not lead to chronic hepatitis (except immunocompromised individuals)

	RNA capsid	202	E protein	RNA HBsAg	Man an
Name of Virus	Hepatitis A Virus (HAV)	Hepatitis B Virus (HBV)	Hepatitis C Virus (HCV)	Hepatitis D Virus (HDV)	Hepatitis E Virus (HEV)
Classification	Picornavirus	Hepadnavirus	Flavivirus	Deltavirus	Hepevirus
Viral genome	ssRNA	dsDNA	ssRNA	-ssRNA (-ve)	ssRNA
Transmission	Enteric	Parental	Parental	Parental	Enteric
Incubation period	15-45 days	45-160 days	15-150 days	30-60 days	15-60 days
Chronic Hepatitis	No.	Yes. 10% chance	Yes. >50% chance	Yes. <5% of coinfectious >80% of superinfectious	No.
Cure?	No cure. Treatments usually tackle the symptoms.	No cure. Treatments usually tackle the symptoms.	No cure. Treatments usually tackle the symptoms.	No cure. Treatment: Alpha interferon for 12 months.	No cure. Treatments usually tackle the symptoms

http://www.medical-labs.net/hepatitis-viruses-comparision-table-2704/