Introduction,General properties of viruses, structure, classification of DNA and RNA virus.

TERMS AND DEFINITIONS IN VIROLOGY

Viruses are the smallest infectious agents (ranging from about 20 to 300 nm in diameter) and contain only one kind of nucleic acid (RNA or DNA) as their genome. The nucleic acid is enclosed in a protein shell, which may be surrounded by a lipid-containing membrane. The entire infectious unit is termed a *virion*. Viruses are parasites at the genetic level, replicating only in living cells and are inert in the extracellular environment.

Capsid: The protein shell, or coat, that encloses the nucleic acid genome.

Capsomeres: Morphologic units seen in the electron microscope on the surface of icosahedral virus particles. Capsomeres represent clusters of polypeptides.

Defective virus: A virus particle that is functionally deficient in some aspect of replication.

Envelope: A lipid-containing membrane that surrounds some virus particles. It is acquired during viral maturation by a budding process through a cellular membrane . Virus-encoded glycoproteins are exposed on the surface of the envelope. These projections are called **peplomers**.

Nucleocapsid: The protein–nucleic acid complex representing the packaged form of the viral genome.

Comparison between viruses and Bacteria

Characteristic	Viruses	Bacteria
Cells	No	Yes
Approximate diameter (μm)[1]	0.02–0.2	1–5
Nucleic acid	Either DNA or RNA	Both DNA and RNA
Type of nucleus	None	Prokaryotic
Ribosomes	Absent	70S
Mitochondria	Absent	Absent
Nature of outer surface	Protein capsid and lipoprotein envelope	Rigid wall containing peptidoglycan
Motility	None	Some
Method of replication	Not binary fission	Binary fission

Prions

They are small proteinaceous infectious particles which resist inactivation by procedures that modify nucleic acid. In short infectious agents which lack nucleic acid genome are called prions. they are about 5 nm in diameter, resistant to heat, ultraviolet rays and nuclease. However, they are sensitive to proteases. Some features of prions that cause diseases which are related to central nervous system.

The general properties of viruses are :

1. Do not possess cellular organization.

2. Contain one type of nucleic acid, either RNA or DNA but never both.

3. Lack enzymes necessary for protein and nucleic acid synthesis and so depend upon synthetic machinery of host cells.

4. They multiply by complex process and not by binary fission.

5. They are unaffected by antibiotics.

6 .They are sensitive to interferon.

Evolutionary Origin of Viruses

AThe origin of viruses is not known. There are profound differences among the DNA viruses, the RNA viruses, and viruses that use both DNA and RNA as their genetic material during different stages of their life cycle. It is possible that different types of agents are of different origins.

Two theories of viral origin can be summarized as follows:

1. Viruses may be derived from DNA or RNA nucleic acid components of host cells that became able to replicate autonomously and evolve independently. They resemble genes that have acquired the capacity to exist independently of the cell. Some viral sequences are related to portions of cellular genes encoding protein functional domains. It seems likely that at least some viruses evolved in this fashion.
2. Viruses may be degenerate forms of intracellular parasites. There is no evidence that viruses evolved from bacteria, although other obligately intracellular organisms (eg, rickettsiae and chlamydiae) presumably did so. However, poxviruses are so large and complex that they might represent evolutionary products of some cellular ancestor.

Structure and morphology of viruses

Morphology:

Size: Viruses vary widely in size. The largest among them is pox virus measuring about 300 nm. The smallest viruses is foot and mouth disease virus measuring 20 nm.

The methods of estimating the size of virus particles are:

1. Collodion membrane filter of graded porosity.

2. Ultracentrifugation.

2. Electron microscope.

Shapes:

Some viruses have characteristic shape, e.g. rabies virus has bullet shape, pox viruses are brick-shaped, tobacco mosaic virus is rod-shaped, bacteriophage has head and tail, like sperm, influenza or polio viruses are spheroidal and so on.

Structure and symmetry:

Viruses have central core of nucleic acid which is either RNA or DNA but never both. This central core of nucleic acid is covered by protein coat called capsid. The capsid itself is composed of number of subunits called capsomere (Fig.1).

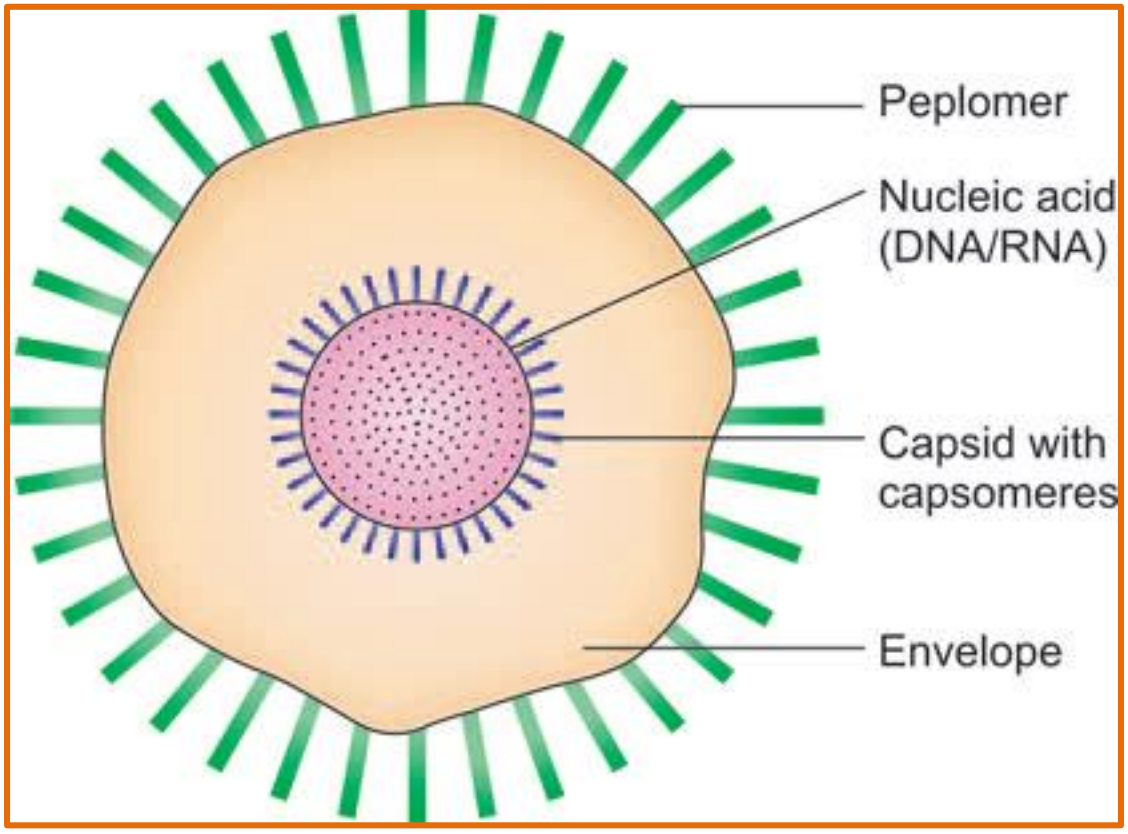

Fig.1: Structure of virus

The capsomere may be arranged as under:

1. Around coiled nucleic acid which is known as helical arrangement.

2. As cubes around spheroidal nucleic acid known as icosahedral arrangement.

3. Some viruses do not fit either helical or icosahedral symmetry due to complexity of these structure, e.g. pox virus, bacteriophage, etc.

Definition of virion

a complete virus particle that consists of an RNA or DNA core with a protein coat sometimes with external envelopes and that is the extracellular infective form of a virus.

Virion may be **enveloped** or **non enveloped.** The envelope is derived from host cell membrane when virus is released by budding. Envelope is lipoprotein in nature.

Protein subunits may be seen as projecting spikes on the surface of the envelope. These are called peplomers. A virus may have more than one type of peplomer, e.g. influenza virus has two peplomers:

1. Triangular spike

2. Mushroom-shaped

CLASSIFICATION OF VIRUSES

The classification of viruses is based on chemical and morphologic criteria. The two major components of the virus used in classification are (1) the nucleic acid (its molecular weight and structure) and (2) the capsid (its size and symmetry and whether it is enveloped). A classification scheme based on these factors is presented in Tables 31–1 and 31–2 for DNA and RNA viruses, respectively. This scheme was simplified from the complete classification to emphasize organisms of medical importance.

TABLE 31–1 Classification of DNA Viruses

Virus family	Envelope present	Capsid symmetry	Virion Size (nm)	DNA mw($x10^6$)	DNA structure	Medical important Viruses
Parovirus	No	Icosahedral	22	2	SS,Liner	B19 virus
Papiloma virus	No	Icosahedral	55	5	DS,circular, supercoild	Human papilloma virus
Hepadna virus	Yes	Icosahedral	42	1.5	D.S incomplete circular	Hepatitis B virus
Herpes Virus	Yes	Icosahedral	100^2	100-150	DS, Linear	Herpes Virus, Cytomegalo Virus
Pox virus	Yes	Complex	250x400	125x185	DS, Linear	Smallpox Virus

SS= single stranded , DS= double stranded

TABLE 31–2 Classification of RNA Viruses

Virus family	Envelope present	Capsid symmetry	Particle Size (nm)	RNA MW $X10^6$	RNA structure	Medically Important Viruses
PicomaVirus	No	Icosahedral	28	25	SS Linear, Positive polarity	Hepatitis A virus
Reovirus	No	Icosahedral	75	15	DS linear,	Rotavirus
Flavivirus	Yes	Icosahedral	45	4	SS linear Positive polarity	Yellow fever virus, Hepatitis c virus
Retrovirus	Yes	Icosahedral	100	7^2	SS linear Positive polarity	HIV, Humen T-cell leukemia virus
Rhabdovirus	Yes	Helical	75x180	4	SS linear, Negative polarity	Rabies virus

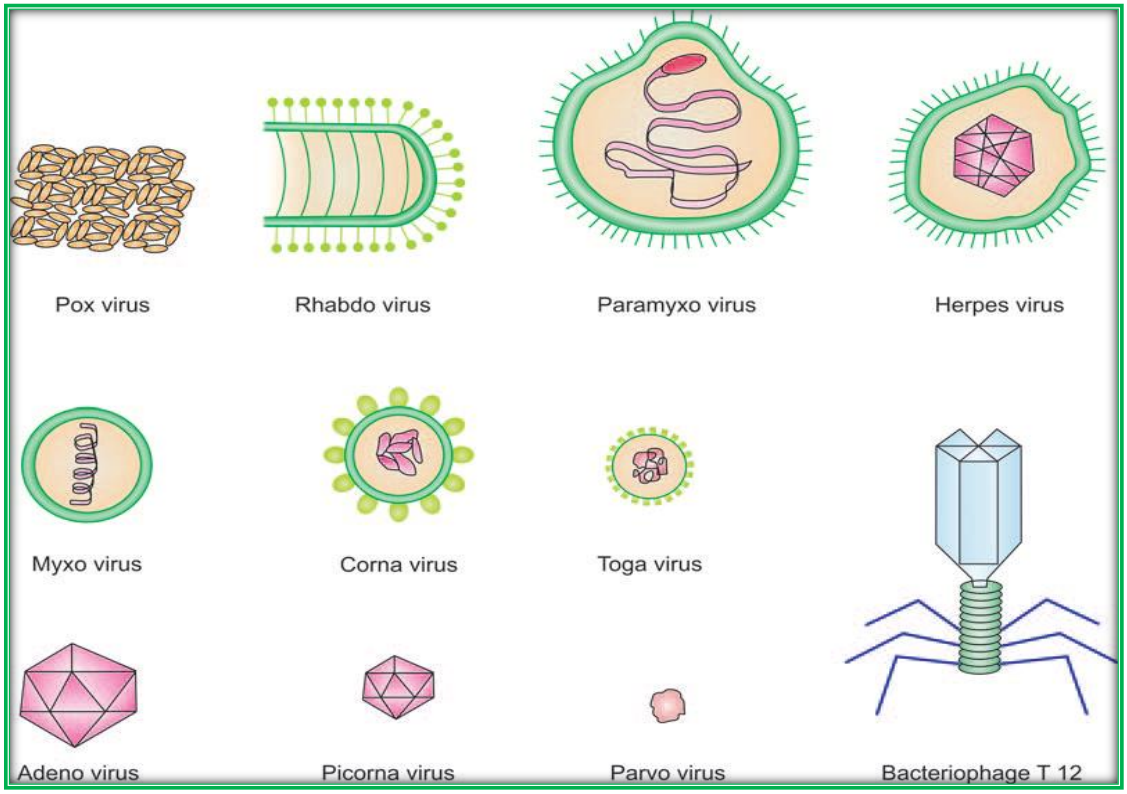

Fig.2 : Different types of viruses الرسم غير مطلوب

ICTV classification

The International Committee on Taxonomy of Viruses (ICTV) developed the current classification system and wrote guidelines that put a greater weight on certain virus properties to maintain family uniformityتوحيد.

The general taxonomic structure is as follows:

Order (-*virales*)

Family (-*viridae*)

Subfamily (-*virinae*)

Genus (-*virus*)

Species (-*virus*)

The orders are the *Caudovirales, Herpesvirales,*

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* Warren Livinson , Review of medical microbiology and Immunology , thirteenth ed. (2014)

* 138. ICTV Virus Taxonomy ICTV Virus Taxonomy Release History (https://talk.ictvonline.org/taxonomy/p/taxonomy releases)

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. *International Committee on Taxonomy of Viruses (ICTV)*. Retrieved 29 September 2017.

* Jawetz Medical Microbiology (Brooks, 27th ed) 2015

Replication of viruses

Viral Multiplication

Virus depends on the **synthetic machinery of host cell** for replication because it lacks **biosynthetic enzymes**.

Steps of viral replication:

A) Adsorption:

The virus is adsorbed at a **particular site** on the host cell which is called **receptor**. In case of poliovirus the receptor is lipoprotein present on the surface of host cell. The host cell receptor for influenza virus are glycoproteins present on the surface of respiratory epithelium. Adsorption or attachment is specific and is mediated by binding of virion surface structure known as legands, to receptors on cell surface. In HIV surface, glycoprotein (gp120) acts as a legand and it binds to the CD4 60 kD glycoprotein on the surface of mature T lymphocyte.

B) Penetration:

Virus particles may be engulfed by animal cell by the mechanism called viropexia. Viropexia is like phagocytosis. In case of enveloped virus, viral envelope may fuse with plasma membrane and release nucleocapsid into the cytoplasm.

C) Uncoating:

This is a process by which the virus lose its outer layer and capsid. In some cases, uncoating is effected by lysozomal enzyme of host cell. For example, in pox virus, uncoating occurs in two steps. Outer coating is removed by lysozyme

present in phagocytic vacuole of host cell. This is the first step. In second step, internal core of virus (nucleic acid and internal protein) is released into cytoplasm and is effected by viral uncoating enzyme. Thus DNA is released.

D) Biosynthesis:

There is synthesis of viral nucleic acid and capsid protein. There is synthesis of regulator protein which shuts down the normal cellular metabolism and direct sequential production of viral component. **DNA viruses synthesize their components in host cell nucleus except pox virus which synthesize their components in cytoplasm**. **Likewise RNA viruses** synthesize their components in cytoplasm of host cell except orthomyxoviruses, para-myxovirus and leukoviruses.

Biosynthesis consists of following steps:

1. Transcription(نسخ) of messenger RNA from viral nucleic acid.

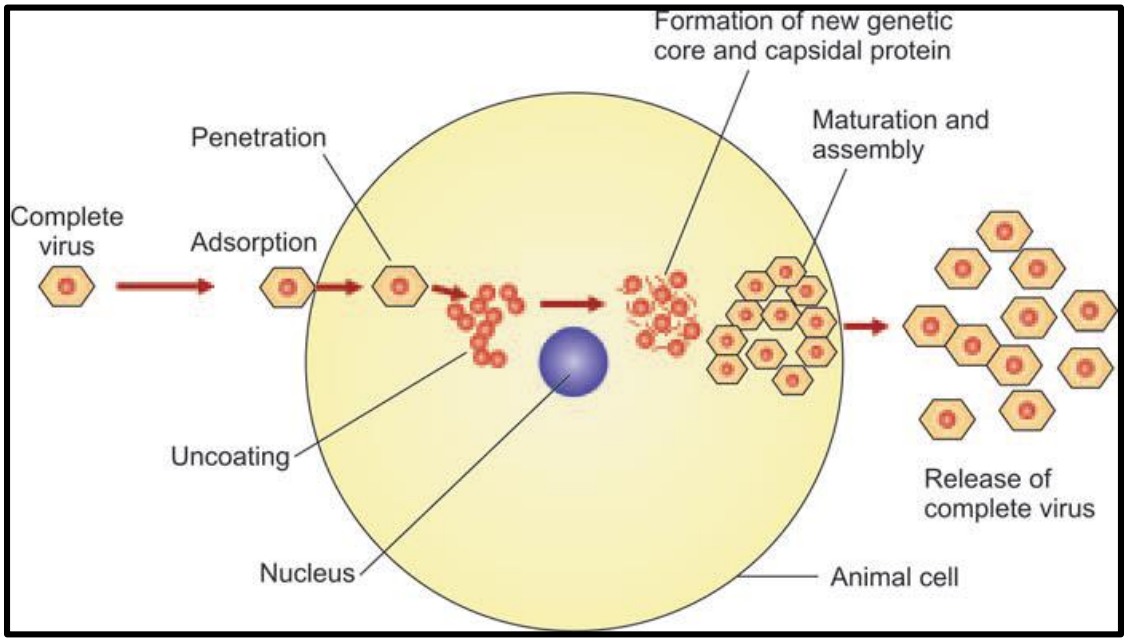
2. Translation(ترجمة) of mRNA into early proteins. They initiate and maintain the synthesis of virus component and shut down the host protein and nucleic acid synthesis.

3. Replication of viral nucleic acid.

4. Synthesis of late proteins, which are the components of daughter وليد virion capsids.

E) Maturation*:* Assembly of daughter virion follows synthesis of viral nucleic acid and proteins. It may take place in nucleus (herpes, adeno) or cytoplasm (picorna, pox). Enveloped virus gets envelope from the cell membrane of the host during a process of budding. Non enveloped viruses are present intracellularly as fully developed virion.

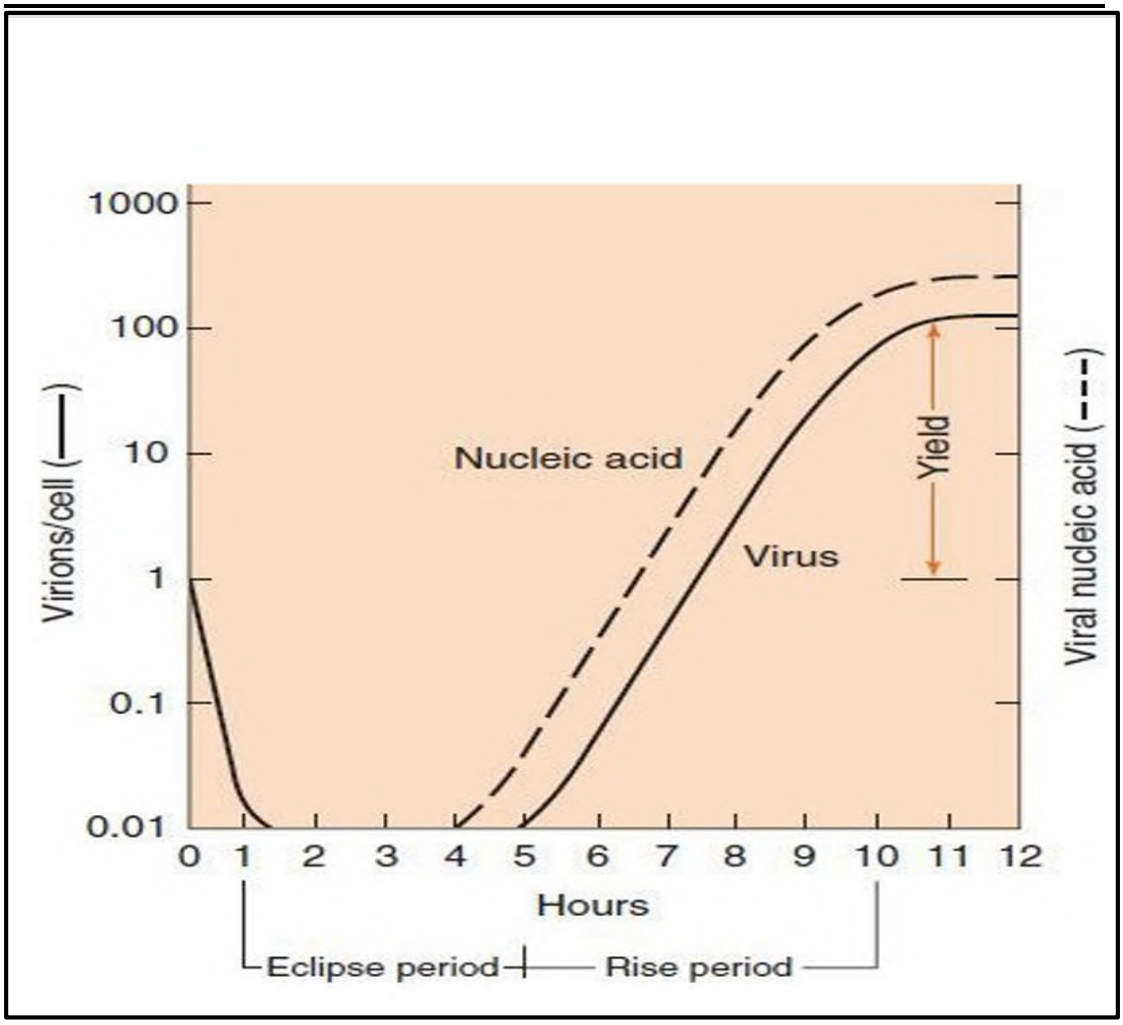
F) Release*:* In bacterial viruses release take place by lysis of infected bacterium. In animal, viruses release occur without lysis (myxo). Some viruses like polio may cause cell lysis during their release.



Viral multiplication

Viral growth curve

The growth curve that when one **virion** (one virus particle) infects a cell, it can replicate in approximately 10 hours to produce hundreds of virions within that cell.



Viral growth curve

Cycle of replication:

a. Fifteen to thirty hours in animal virus

b. Fifteen to thirty minutes in bacterial phage.

Eclipse phase is the time from stage of penetration of virus into host cell till appearance of mature daughter viruses. In this phase, virus cannot be demonstrated in host cell.

REFERENCE

**** Satish Gupte ,The Short Textbook Of Medical Microbiology (Including Parasitology) Tenth Edition(2010).***

***Warren Levinson. Review of medical microbiology and immunology (13 ed)(2014)**

Virus isolation and cultivation

Cultivation Viruses

Since they are obligate intracellular parasites and cannot grow on inanimate culture medium,

Three methods are used for their cultivation:

a. Animals inoculation.

b. Chick embryo.

c. Tissue culture.

a. Animal inoculation:

It is one of the oldest methods for the cultivation of viruses. The poliomyelitis virus after intraspinal or intracerebral inoculation in monkeys causes typical paralytic disease and so isolation of viruses. Suckling mice is susceptible to Cox-sackie viruses with manifestation of severe myositis and paralysis. Smallpox virus may be inoculated in the scarfied skin or cornea of rabbit. Brain tissue of rabied dog when inoculated intra- cerebrally in mice or rabbit develop encephalitis.

Growth of virus in animals may be known by the disease, visible classical lesions or death. Sometimes immunity in experimental animal may interfere with the growth of viruses in that animal. It is not out of place to mention **the other benefit** of animal inoculation , i.e. to **study pathogenesis**, **immune response**, and **epidemiology.**

b. Chick embryo:

They are better than animal inoculation because of following reasons:

i. They are clean and bacteriologically sterile.

ii. They do not have immune mechanism like animals to counteract virus infection.

iii. They do not need feeding and caging.

iv. Chick embryo offers several sites for cultivation of viruses, i.e. chorioallantoic membrane (CAM) for variola or vaccinia and herpes viruses, allantoic cavity provides rich yield of influenza and some paramyxoviruses, amniotic sac may be used for the isolation of influenza virus and yolk sac for the cultivation of chlamydiae, rickettsiae and some viruses (Table 45.2). Allantoic inoculation may be used for growing influenza virus for vaccine purposes. Yellow fever and rabies are other vaccines produced from chick embryo (Fig. 45.3)

Table 45.2: Growth of viruses in chick embryo

Route of inoculation	Virus	Lesion on CAM	Hemagglutination
Chorioallantoic Membrane(CAM)	Poxvirus Herpes simplex Herpes virus B	+ + +	- - -
Amniotic cavity	Influenza virus Mumps virus	- -	+ +
Allantoic cavity	New castle disease Influenza Mumps	- - -	+ + +
Yolk sac	JE virus Nile virus	+ +	- -

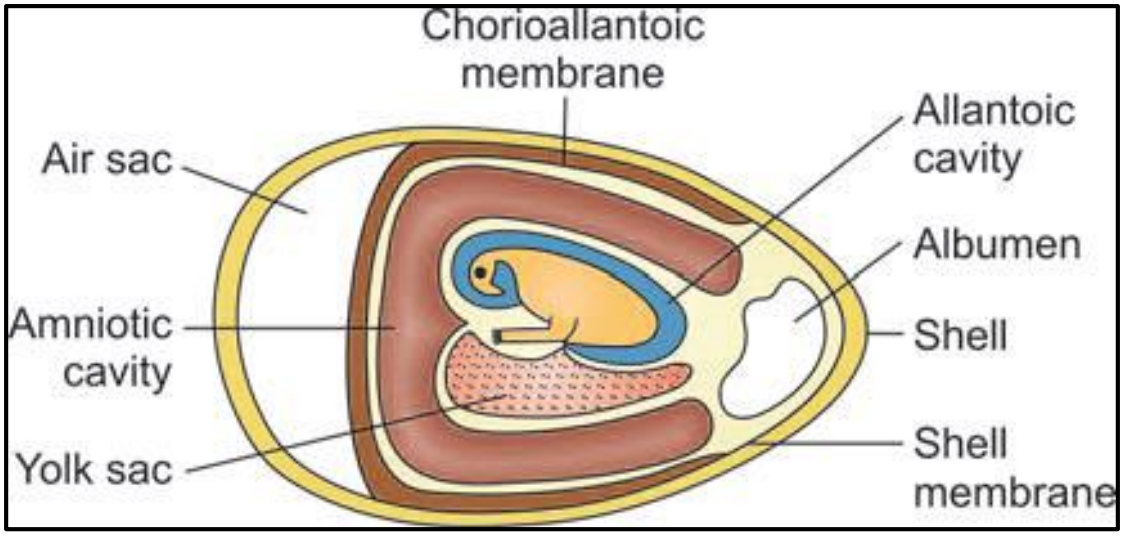


Fig. 45.3: Structure of chick embryo

c. Tissue culture:

Tissue culture of human or animal cells are frequently used for the cultivation of viruses. There are mainly three types of tissue culture:

1. Organ culture, e.g. tracheal ring organ culture is employed for the isolation of coronavirus.

2. Explant culture: Minced tissue may be grown as explant embedded in plasma clots. This is not useful in virology. In the past adenoid(غدي) tissue explant culture were used for adenovirus.

3. Cell culture: This is very popular and useful technique routinely used for cultivation of viruses. From tissue, fragments cells are dispersed by proteolytic enzymes like trypsin and mechanical shake. After washing the cells, they are suspended in growth medium and distributed in petridishes, test tubes or bottles. The cells adhere to glass surface and grow out to form a monolayer sheet and can be seen in situ under low power.

There are three types of cell cultures (Table45.3):

a. **Primary cell cultures:** When normal cells freshly taken from body grown for the first time, they are called primary cell culture. They can be maintained in serial culture. They are useful for isolation and cultivation of viruses for vaccine production, e.g. rhesus monkey kidney cell culture, human amnion cell culture, chick embryo fibro- blast culture, etc.

b. **Diploid cell strains:** They are capable of 100 divisions in culture. They are useful for the isolation of fastidious pathogens and also for the production of viral vaccines. Examples are human embryonic lung cell strain (WI-38) and rhesus embryo cell strain (HL-8).

c. **Continuous cell lines:** They are single type of cells mainly derived from cancer cells. These also can be grown in successive generation by transferring them from one test tube to another without change in character of cells. These are used only for the isolation of virus. Vaccine preparation on these cells is not safe for human use, e.g. HeLa (human carcinoma of cervix cell line).

Table 45.3: Isolation of viruses from cell line

Cell Line	Virus isolation
Primary *African green monkey *Chick embryo fibrolblast	 *HSV, RSV, mumps, rubella *Rabies, pox-virus
Diploid cell *Human fetal lung(WI-38, WRC-5)	Rabies, adeno, CMV
Continuous *Hela *HEp-2 *MDCK *RD *Vero	 *Polio,pox, reo RSV *Adeno, RSV *Influenza *Polio, enterovirus *Polio, rabies, measles

Detection of virus growth on cell cultures:

Viruses multiplying in tissue culture manifest their presence by producing:

1. Changes in the cells called cytopathogenic effects (CPE), e.g. measle virus produces syncytium formation and SV40 produces prominent cytoplasmic vacuolation.

2. When viruses grow in cell culture, cell metabolism is inhibited and there is no acid production. In normal cell culture because of active metabolism there is active acid production. Phenol red (indicator) can detect the presence of acid formation by changing its color into yellow.

3. Hemadsorption: When influenza and para- influenza viruses grow in cell culture their presence may be detected by addition of guinea pig erythrocytes to the culture. If the viruses are multiplying in culture, erythrocytes will adsorb on the surface of cell.

4. Fluorescent antibody straining is also a method of detecting viral multiplication.

5. Hemagglutination test may be performed by using tissue culture fluid, e.g. orthomyxoviruses and paramyxoviruses.

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** Satish Gupte ,The Short Textbook Of Medical Microbiology (Including Parasitology) Tenth Edition(2010).*

Chemotherapy, antviral agent *and* vaccines

Compared with the number of drugs available to treat bacterial infections, the number of antiviral drugs is **very small**.

The major reason for this difference is the:

1. Difficulty in obtaining selective toxicity against viruses

2.Their replication is intimately involved ارتباط وثيق with the normal synthetic processes of the cell**.**

3.Many cycles of viral replication occur during the incubation period when the patient is well . By the time the patient has a recognizable systemic viral disease, the virus has spread throughout the body and it is too late to interdict it.

4.Some viruses (e.g., herpesviruses) become latent within cells, and no current antiviral drug can eradicate them.

5.Another limiting factor is the emergence of drug-resistant viral mutants. For example, when drug-resistant mutants of HIV emerge, it requires that drug regimens be changed. Also, treatment of HIV infection uses multiple drugs, often from different classes, so that if mutants resistant to one drug emerge, another drug will still be effective.

Despite the difficulty, several virus-specific replication steps have been identified that are the site of action of effective antiviral drugs (Table 35–1). Table 35–2 describes the mode of action of antiviral drugs that block early events in viral replication, and Table 35–3 describes the mode of action of antiviral drugs that block viral nucleic acid synthesis.

TABLE 35–1 Stage of Viral Replication Inhibited by Antiviral Drugs

Stage of Viral replication inhibited	Effective Antiviral dugs
Early event s(entry or un coating of the virus)	Amantadine , rimantidin
Nucleic synthesis by herpesvirus	Acyclovir, foscarnet
Nucleic acid synthesis by Human immunodeficiency virus (HIV)	Zidovudine, abacavir
Nucleic acid synthesis hepatitis B virus(HBV)	Adefovir, tenofovir
Nucleic acid synthesis hepatitis C virus(HCV)	Sofodbuvir
Integrase that integrates HIV DNA into cellular DNA	Raltegravir, dolutegravir
Release of influenza virus from infected	Oseltamivir, zanamivir

TABLE 35–2 Antiviral Drugs That Block Early Events

Antiviral Drug	Mode of Action	Virus inhibited
Amantadine, rimantadine	Inhibits uncoating by blocking M2 matrix protin	Influenza virus
Enfuvirtide	Inhibit fusion by binding to gp41 of Human immunodeficiency virus(HIV)	HIV
Maraviroc	Inhibits attachment to cell surface receptor CCR-5	HIV
Palivizumba	Monoclonal antibody that blocks binding of viral fusion protein to receptor on respirotary mucosal cell	Respiratory syncytial virus

TABLE 35–3 Antiviral Drugs That Block Viral Nucleic Acid Synthesis

Mode of action	**Antiviral Drugs**
Inhibition of DNA polymerase of herpesviruses	Nucleoside inhibitors, acyclovir
Inhibition of reverse transcriptase of HIV	Nucleoside inhibitors, tenofovir
Inhibition of reverse transcriptase of hepatitis B viruses	Adefovir, entecavir

Viral Vaccines

Because few drugs are useful against viral infections, prevention of infection by the use of vaccines is very important. Prevention of viral diseases can be achieved by the use of vaccines that induce active immunity or by the administration of preformed antibody that provides passive immunity.

Active Immunity

• Active immunity can be elicited by vaccines containing killed viruses, purified protein subunits, or live, attenuated (weakened) viruses.

• In general, **live viral vaccines are preferable to killed vaccines** for three reasons:

(1) they induce a higher titer of antibody and hence longer-lasting protection.

(2) they induce a broader range of antibody (e.g., both IgA and IgG, not just IgG).

(3) they activate cytotoxic T cells, which kill virus-infected cells.

There are some potential problems with live viral vaccines:

1.the most important of which is reversion to virulence.

2.Transmission of the vaccine virus to others who may be immunocompromised is another concern. Live viral vaccines should not be given to immunocompromised individuals or to pregnant women.

3.Also there may be a second, unwanted virus in the vaccine that was present in the cells used to make the vaccine virus. This second virus may cause adverse effects.

4. Vaccines grown in chick embryos, especially influenza vaccine, should not be given to those who have had an anaphylactic reaction to eggs.

Passive Immunity

• Passive immunity is immunity acquired by an individual by the transfer of preformed antibodies made in either other humans or in animals. These antibody preparations are often called immune globulins. Passive immunity also occurs naturally when IgG is transferred from the mother to the fetus across the placenta and when IgA is transferred from the mother to the newborn in colostrum.

• The main advantage of passive immunity:

1. provides immediate protection.
2. Immune globulin preparations against rabies virus, hepatitis A virus, hepatitis B virus, and varicella-zoster virus are effective.

The main disadvantage : is that it does not provide long-term protection (i.e., it is active only for a few weeks to a few months).

• Passive–active immunity consists of administering both immune globulins and a viral vaccine. This provides both immediate as well as long-term protection. For example, protection against rabies in an unimmunized person who has been bitten by a potentially rabid animal consists of both rabies immune globulins and the rabies vaccine.

*** Warren Livinson , Review of medical microbiology and Immunology , thirteenth ed. (2014)**

ORTHOMYXOVIRUSES

It includes the enveloped RNA viruses capable of adsorbing on to mucoprotein receptor on erythrocytes. This results in hemagglutination. They are 80 to 120 nm in size and spherical in shape. Influenza virus represents this group.

INFLUENZA VIRUSES

General characteristics

1. They are responsible for infectious disease of respiratory tract occurring mostly in epidemic and pandemic forms.
2. The classification of influenza virus into 3 group (A, B and C) is based on the antigenic nature of ribonucleoprotein.
3. Influenza virus is spherical with diameter 80 to 120 nm.
4. The virus has ribonucleoprotein in helical symmetry.
5. Single stranded RNA genome is segmented and nucleocapsid is surrounded by envelope having virus coded protein layer and lipid layer derived from host cell.
6. Attached to lipid layer are hemagglutinin spikes and neuraminidase peplomers (Fig. 50.1).
7. The virus is inactivated at 50°C for 30 minutes, ether, formaldehyde, phenol and salts of heavy metals.

8. Influenza virus is its ability to undergo antigenic variation. Depending on degree antigenic variation may be classified as listed bellow:

Emergence of antigen subtypes of influenza A associated with pandemics or epidemic diseases

1889-90 H2N8 Severe pandemic

1900-03 H3N8 Moderate epidemic

1918-19 H1 N1 Severe pandemic (formerly Hsw N1)

1933-35 H1N1 Mild epidemic (formerly H0N1)

1946-47 H1N1 Mild epidemic

1957-58 H2N2 Severe pandemic

1968-69 H3N2 Moderate pandemic

1977-78 H1N1 Mild pandemic

1988-1989 H1N1/H3N2 Have circulated either in alternating years or at the same time

2009 H1N1(Swine flu) Pandemic April 2009

H5N1 Avian influenza

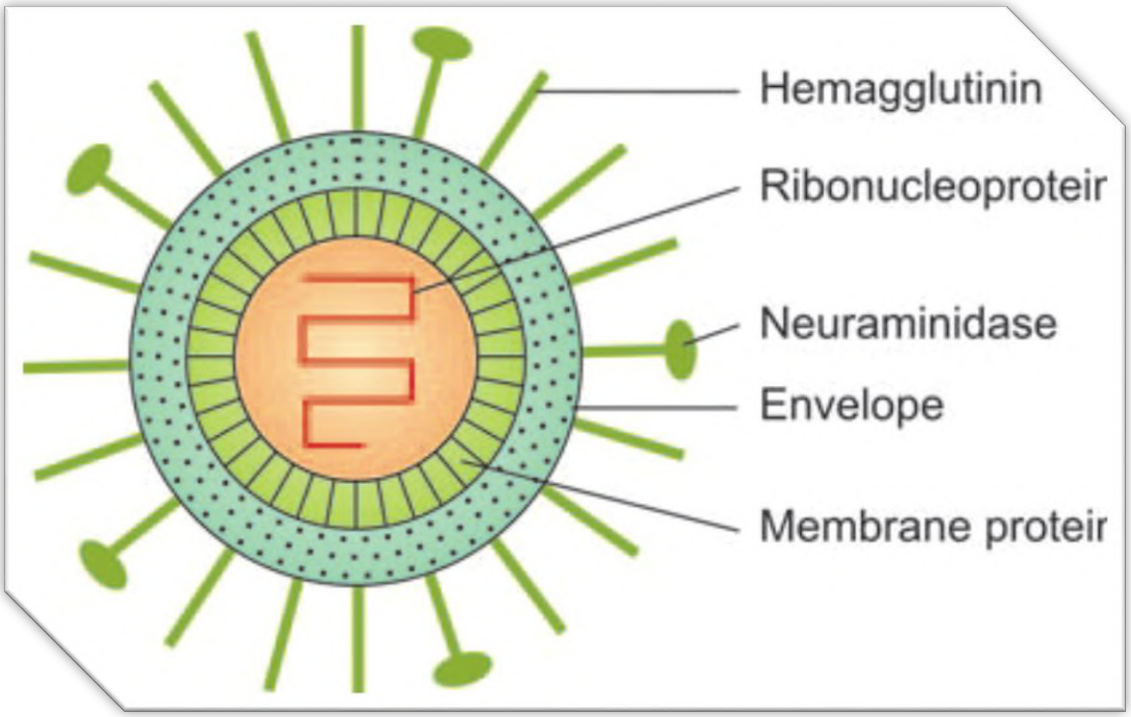

Fig. 50.1: Structure of influenza virus

The virus grows in amniotic cavity and allantoic cavity of chick embryo. It is detected by appearance of hemagglutinin in allantoic and amniotic fluid. They are also grown in monkey kidney cells. Route of entry is respiratory tract. The viral neuraminidase facilitates infection by reducing the viscosity of mucus lining and exposing the cell surface receptor for virus adsorption.

The incubation period is 1 to 3 days. The start is sudden with fever, headache, generalized myalgia (الم عضلي) and prominent respiratory symptoms. If no complication follows the disease resolves in 2 to 7 days. Complications include pneumonia due to bacterial superinfection, congestive heart failure and encep-halitis . Reye's syndrome is associated with influenza B virus.

Diagnosis in the laboratory is established by demonstration of virus antigen (immuno- fluorescence), isolation of virus (chick embryo or monkey kidney cell culture), serology (complement fixation test, hemagglutination inhibition test) and radial immunodiffusion tests in agarose gel .

Vaccinaion

Influenza vaccine is in use. Vaccine may be prepared by growing virus in allantoic cavity and inactivating the virus with formalin. Because of presence of egg protein this vaccine may cause allergic reactions. This difficulty is removed by preparing subunit vaccines (virus treated with ether). The other vaccines in use are: (i) recombinant live vaccines obtained by hybridization between its mutants of established strain, (ii) new antigenic variant, a neura- minidase specific vaccine, and (iii) a live vaccine using temperature sensitive (TS) mutant, etc.

Antiviral drug amantidine hydrochloride which inhibits adsorption of virus to cell is useful in influenza infection.

Combined yearly vaccination of persons at high risk, using the best mix of important antigens and administration of amantidine at time of stress, e.g. surgery or hospitalization, etc. is suggested.

Avian Influenza

Avian Influenza: a disease caused by infection with avian (bird) influenza type A viruses (especially H5N1) , these viruses occur naturally among wild aquatic birds and can infect domestic poultry and other birds

How does avian influenza spread to human:

The avian influenza virus is found in secretions from nares, mouth, and eyes of infected birds , H5N1 can spread from birds to people as a result of direct contact with infected birds .

Epidemic is the rapid spread of **infectious disease** to a large number of people in a given population within a short period of time, usually two weeks or less.

Endemic is that infection is constantly maintained at a baseline level in a geographic area without external inputs. For example, chickenpox is endemic (steady state) in the . UK

Reference

Satish Gupte ,The Short Textbook Of Medical Microbiology) Including Parasitology) Tenth Edition(2010).

REFRENCE:

WWW.WEB.COM

PARAMYXOVIRUSES

They are larger and more pleomorphic than orthomyxoviruses. They possesses hemagglutinins, neuraminidases and hemolysin. They are antigenically stable. This group includes viruses like mumps, parainfluenza, respiratory syncytial and measles.

Mumps

General characteristics :

1. It is responsible for acute infectious disease characterized by parotitis (التهاب الغدد النكفية) .
2. The virus is spherical varying from 100 to 250 nm.
3. The envelope has hemagglutinins, a neuraminidase and hemolysin.
4. The virus can be grown on yolk sac or amniotic fluid of chick embryo, and human or monkey kidney cell culture.
5. They are inactivated at room temperature, ultraviolet light or by chemicals like formaldehyde and ether.
6. Two complement fixing antigens have been identified as soluble (S antigen) and viral (V antigen).
7. Infection may be by inhalation and through conjunctiva.
8. Incubation period is 18 to 21 days.
9. Clinical symptoms start with sudden non-suppurative **enlargement of parotid glands. Skin** over the enlarged parotid glands may be stretched, **red and hot**..

Lab. Diagnosis is confirmed by isolation of virus from saliva, CSF or urine. For this purpose amniotic cavity of chick embryo or monkey or human kidney cell culture may be used. Serological test like complement fixation, hemagglutination inhibition and neutralization tests may be helpful.

Immunization:

Mumps infection confers life long immunity. Normal human gamma globulin prepared from mumps convalescent(نقاهة) serum appears useful for prophylaxis.

For active immunization killed vaccine virus grown in allantoic cavity), live attenuated vaccine is available which can be sprayed into mouth without any side effect.

Respiratory Syncytial Virus

Although these viruses resemble paramyxoviruses structurally but they do not have either **hemagglutinin** or **neuraminidase.** They are responsible for bronchiolitis and pneumonia.

For diagnosis, nasal and pharyngeal secretion are inoculated in human (He La, HEp2) or monkey kidney cell culture. It takes 5 to 14 days' time. Rapid diagnosis may be made by immunofluorescent technique. Serological techniques like complement fixation and neutralization test may be useful. **No vaccine available at present. (why)**

Parainfluenza Viruses

General features

1.They may produce febrile respiratory infections throughout the year.

2.They possess hemagglutinin, neuraminidase and hemolysin.
3.They grow well in human or monkey kidney cell culture.
4.Growth in chick embryo is poor or absent.

5.They are inactivated by heat and by ether.

6. They are classified into four groups: Parainfluenza 1, Parainfluenza 2, Para- influenza 3, Parainfluenza 4.

6.Parainfluenza viruses are responsible for about 10 percent respiratory infection in children.

7.Types 1 and 2 cause croup which is serious clinical disease.
8.Type 3 causes lower respiratory infections and type 4 causes minor respiratory infections.

Measles

is highly acute infectious disease characterized for generalized maculopapular **rash** proceeded by **fever**, cough, nasal and conjunctivitis, etc. (Fig. 50.2)

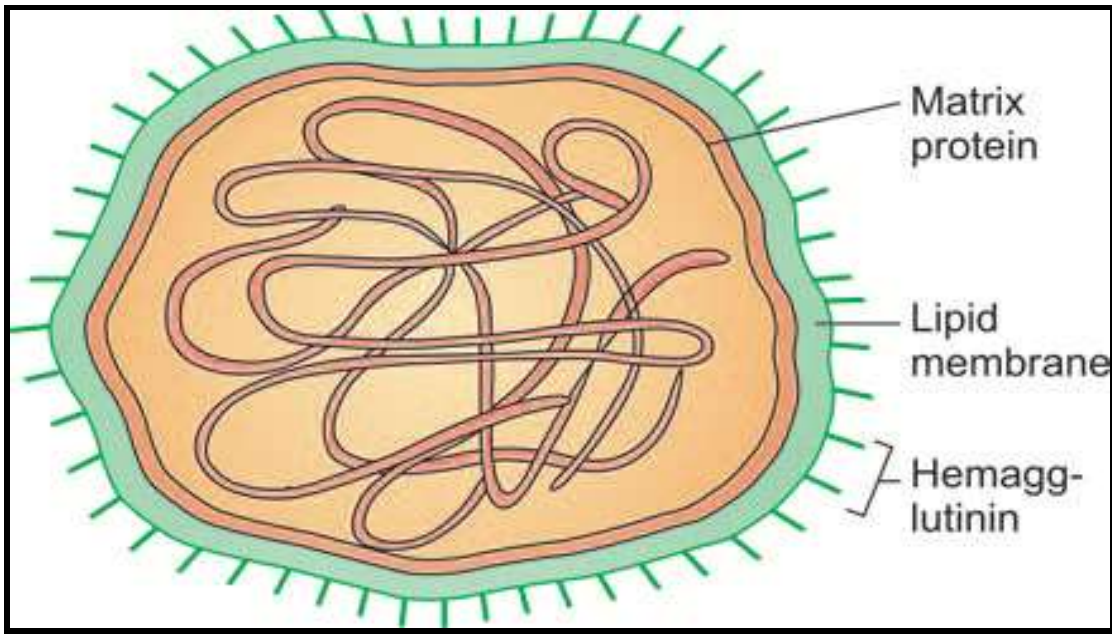

Fig. 50.2: Measles virus

General features of Measles:

1. The viruses possess hemagglutinin and no neuraminidase.
2. They do not grow in eggs but may grow on human embryonic kidney or amnion cell cultures.
3. The virus's core may be inactivated by heat, ultraviolet light, ether and formaldehyde.
4. They are antigenically homogeneous.

5. Incubation period is 10 to 12 days.
6. Infection manifests as fever and respiratory tract involvement, at this stage Koplik spots may be seen on buccal mucosa and 2 to 4 days later rash appears.

Laboratory diagnosis may be established by isolating the virus from nose, throat, conjunctiva, blood and urine. Primary human embryonic kidney and amnion cells are quite useful. Rapid diagnosis of virus growth is possible by immunofluorescence. However, smear can be prepared from nasal, pharyngeal and conjunctival secretion and examined microscopically after staining with Giemsa's method for presence of giant cells and **inclusion bodies (Cowdry type A).** Serological techniques like complement fixation test, neutralization, and hemagglutination inhibition may be useful for establishing diagnosis of measles.

Normal human gamma globulin if given within 6 days of exposure **can prevent disease**. Live attenuated vaccine is developed. **This vaccine can be given in combination with mumps and rubella vaccines (MMR).**

Rubella Virus

It is an enveloped RNA virus causing rash and lymphadenopathy in children**. In adults**, there is involvement of joint and purpura. **Infection in early pregnancy** may lead to developmental **defects in fetus**.

General features of Rubella virus:

1. The virus is pleomorphic, spherical, 50 to 70 nm in diameter and enveloped.
2. It has one type of antigen (hemagglutinin).
3. It is heat labile and inactivated by ether and chloroform.
4. Rubella virus can be grown in primary African green monkey kidney tissue cell lines (VERO, RK 13), human amnion and thyroid tissue culture.
5. It enters the body by **inhalation and replicaion of virus occurs in cervical lymph nodes**.
6. After incubation period (2 to 8 weeks) viremia occurs which lasts till rash, fever and lymph- adenopathy appears.
7. Arthritis is common complication especially in females.
8. If rubella occurs in early pregnancy the fetus may die otherwise congenital malformation (تشوه) is common in first trimester.

Diagnosis can be established by virus isolation from blood (early stage) and throat swabs. Growth on rabbit kidney or vero cell culture is detected. However, serological diagnosis is made by hemagglutination inhibition, neutralization, complement fixation, In congenital rubella diagnosis is made by **demonstrating lgM.**

The vaccines (live attenuated) are available , They are administered subcutaneously.

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Picornaviruses(Enteric viruses, Rhinovirus group)

Picornaviruses are the smallest (28 nm in diameter) RNA viruses, non-enveloped and resistant to ether. Picornavirus group of medical importance includes:

A. Enteroviruses **B. Rhinoviruses**

Enteroviruses

General features:

1. Enteroviruses are transient inhabitants of the human alimentary tract.
2. Enteroviruses may be isolated from the throat or lower intestine.
3. The medical important viruses of this group are polio, Echo and coxsackie viruses.
4. Enteroviruses are stable, and resistant to bile and ether.
5. They remain intact in water and sewage for quite a long time.

The examples of Enteroviruses:

a. Poliovirus: They are 30 nm diameter with capsomere arranged in icosahedral symmetry and are spherical. They are resistant to ether, chloroform and bile. They survive in low pH and low temperature. They are killed by formaldehyde, cholinination and lyophilization. By neutralization poliovirus strains are classified into types I, II and III. Type I is the commonest and is responsible for epidemic. Natural infection occurs only in man.

Pathogenicity of poliovirus

The virus enters body by ingestion or inhalation. The virus multiplies in lymphatic tissue of alimentary canal, entering regional lymph nodes and then viruses are carried to blood stream. From here viruses are taken to spinal cord and brain. They destroy neurons with degeneration of Nissl body. Lesions are mostly in anterior horn of spinal cord. Sometimes we may find extensive lesions like encephalitis. The incubation period is about 10 days with range from 4 days to 4 weeks.

Laboratory diagnosis is made by isolation of viruses from throat (early stage) and feces (throughout the course of disease). After processing specimen is inoculated into tissue culture and virus growth is indicated by cytopathic effects in 2 to 3 days. Sero diagnosis is not of much use, still complement fixation and neutralization test may be used.

Immunization is achieved by using vaccine. Salk killed polio vaccine (inactivated poliovaccine) is formalin inactivated consisting of 3 types of polioviruses, It gives 80 to 90 percent protection against paralytic poliomyelitis, Killed vaccination is given by injection. On the other hand, live polio vaccine is also available and is prepared by growing the attenuated strain in monkey kidney cells. Live vaccine is easy to administer as it is given orally, much more economical, single dose gives lifelong immunity and gives local immunity in the intestine.

b. Coxsackieviruses*:*

They are called coxsac- kievirus as first of all they were isolated from patients coming from the village of coxsackie in New York. They are classified into group A and B. By neutralization method group A viruses are divided into 24 types.

Characteristically the viruses have the ability to infect suckling mice and not the adult mice. All group B viruses grow on monkey kidney tissue culture and some group A viruses grow in HeLa cells.

They may cause vesicular pharyngitis (group A), aseptic meningitis (groups A and B), minor respiratory infections.

The laboratory diagnosis may be made by isolating the viruses from lesion or feces by inoculation in suckling mice. Since there are several antigenic types so sero diagnosis is not feasible.

c. Echoviruses:

Their description designation is **enteric cytopathogenic human orphan viruses (ECHO viruses).** They are classified into 33 serotypes. They infect man naturally. They are not pathogenic to laboratory animals.

Laboratory diagnosis is by inoculating feces, throat swab or CSF on monkey kidney tissue culture and virus growth is detected by cytopathogenic changes.

Rhinoviruses

Rhinoviruses are the common cold viruses. They are the most commonly recovered agents from people with mild upper respiratory illnesses.They are usually isolated from nasopha- ryngeal secretions but may also be found in throat and oral secretions. Rhinoviruses are also responsible for about half of asthma infections. Human rhinoviruses can be divided into major and minor receptor groups. Viruses of the **major group** use **intercellular adhesion molecule-1 (ICAM-1) as receptor**, and those of the **minor group** bind members of the **low-density lipoprotein receptor (LDLR) family**.

They differ from enteroviruses in being more acid **labil**e, Depending upon **growth in tissue culture**, rhinoviruses are classified as **H strains (grow only on human cells) and M strains (grow equally well on human as well as monkey cells**).

Because of too many **serotypes (over 100) it is impossible to make ideal vaccine.** However, antiviral chemo- therapy may be helpful in bringing specific control.

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