وزارة التعليم العالي والبحث العلمي
الجامعة التقنية الجنوبية
المعهد التقني العمارة
قسم تقنيات المختبرات الطبية

# الحقيبة التدريسية لمادة الفايروسات

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## الصف الثاني

تدريسي المادة
م.م لينا محمد زكي

الفصل الدراسي الاول

# جدول مفردات مادة الفايروسات

| Details | Week |
|---|---|
| Introduction , General properties of virus , structure, classification of DNA & RNA viruses. | 1 |
| Replication of DNA and RNA virus | 2 |
| Virus isolation & cultivation. | 3 |
| Chemotherapy , antiviral agent & vaccines. | 4 |
| Influenza viruses | 5 |
| Paramyxo & Robella viruses. | 6 |
| Enteric viruses, Rhinovirus group. | 7 |
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| Herpes viruses | 9 |
| Oncogenic viruses | 10 |
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| Rubies & other neurotropic viruses **Details** | 12 **Week** |
| Arbo viruses & viral haemorrhagic viruses | 13 |
| Virus identification in genera **Virus identification in genera** | 14 **1** |
| Retro & Adeno **Equipments needed for virology lab.** | 15 **2** |
| **Viral culture & isolation.** | **3** |
| **Elisa tests for viral identification** | **4** |
| **PCR** | **6& 5** |
| **Electron microscope for virus identification** | **7** |
| **Viral DNA extraction** | **9& 8** |
| **Viral RNA extraction** | **10** |
| **Detection by Neutralization test (Nt)** | **11** |
| **Detection by haemagglutination inhibition (HI)** | **12** |
| **Serological diagnosis and Immunological detection of** | **14& 13** |

**الهدف من دراسة مادة الفايروسات (الهدف العام):**

تهدف دراسة مادة **الفايروسات** للصف الثاني الى:

Article goals: acquaint students about virus and diseases caused by how to diagnose and Treat.

## الفئة المستهدفة:

طلبة الصف الثاني / قسم تقنيات المختبرات الطبية

التقنيات التربوية المستخدمة:

1. سبورة واقلام
2. الشاشة الذكية
3. عارض البيانات Data Show
4. جهاز حاسوب محمول Laptop

**Week 1**

**Introduction and General Properties of Viruses**

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**Topics**:

Definition and history of viruses

General properties of viruses

Virus structure: capsid, envelope, nucleic acid

Classification of viruses: DNA vs RNA viruses

**Objective**: To understand the basic structure and classification of viruses as a foundation for studying viral mechanisms and diseases

.


**Virus:**

is infectious particle containing one type of nucleic acid and surrounded by protein coat. The viral particle has ability to replicate only in living host cell, and cause disease.

- The term virus, which come from the Latin word for poison.
- Because the viruses pass through bacterial filters, therefore the viruses were known as (filterable viruses). But some bacteria may be smaller than largest virus, filterability is no longer regarded as unique feature of viruses.

**General properties of viruses:**

Viruses are unlike any other forms of organisms. They are different from other infectious organisms in the following specific properties:

1. Viruses possession of only one type of nucleic acid , either DNA or RNA , but never both.
2. Viruses are not considered as cell because they do not have a cellular composition and inert metabolically. They lack cellular organelles such as: nucleus, cytoplasm, mitochondria, ribosome, Golgi apparatus, and endoplasmic reticulum.
3. Viruses are not capable of independent replication ,but they replicate only within living host cell, therefore they are known as obligate intracellular parasites. Viruses inside living host cell are active, whereas outside living cells are inactive. Therefore viruses fall at linked between living and nonliving things.

- Viruses can not grow on inanimate culture media(non-living), but grow in tissue culture(living cells).

4. Viruses can not replicate by binary fission or mitosis ,but they replicate by

complex process .

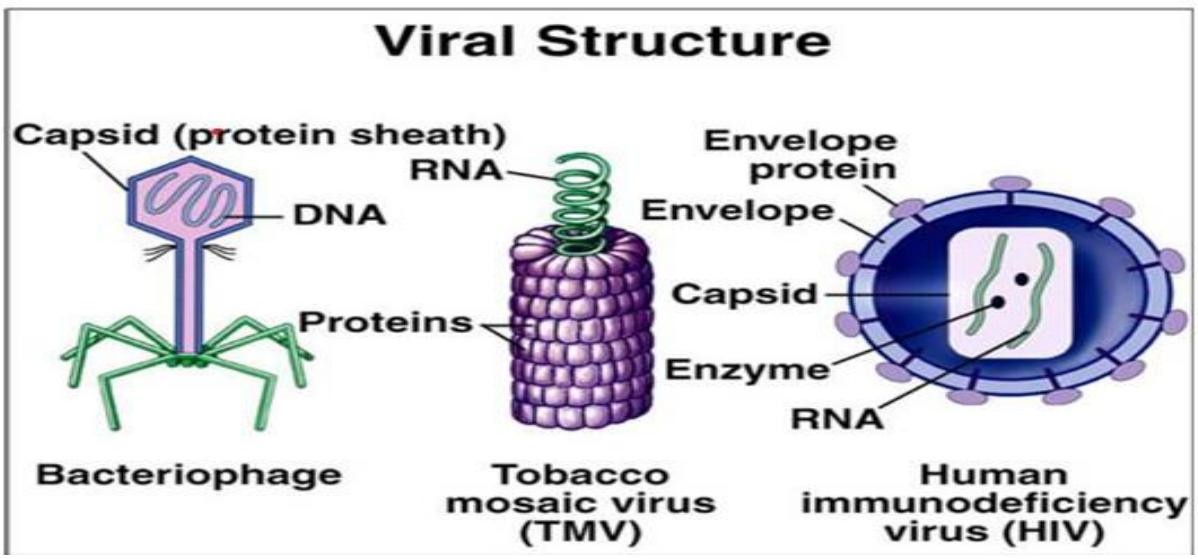
· The viruses produce many copies of their nucleic acid and proteins, and then reassemble into multiple progeny viruses.

· One virus can replicate to produce hundreds of progeny viruses , whereas other organisms , one cell divides to produce only two daughter cells.

5. All viruses are pathogenic, and the viruses infect all types of organisms in nature( such as anim

als, plants, fungi, bacteria).

6. Viruses can not seen by light microscope( therefore the viruses termed as submicroscopic agents), but they can seen by electronic microscope.




7. Viruses are unaffected by antibiotic agents but sensitive to antiviral chemotherapy agents and interferon .

**Table:** Comparison of medical important organisms.

| Characteristic | viruses | bacteria | fungi | protozoa |
|---|---|---|---|---|
| Cells | no | yes | yes | yes |
| Diameter (µm) | 0.02-0.3 | 1-5 | 3-10(yeasts) | 15-25 (trophozoites) |
| Nucleic acid | either DNA or RNA | both | both | both |
| Type of nucleus | none | prokaryotic | eukaryotic | eukaryotic |

| | | | | |
|---|---|---|---|---|
| Mitochondria | absent | absent | present | present |
| Ribosome | absent | 70s | 80s | 80s |
| Nature of outer surface | capsid and lipoprotein | rigid wall contain envelope | rigid wall peptidoglycan | flexible with chitin membrane proteins |
| Motility | none | some | none | most |
| Method replication | not binary fission | binary fission | budding or mitosis | mitosis of |

**Shape and size of viruses :**

The shapes of viruses may be sphere, rods , bullets, or brick . The shapes are determined by the arrangement of subunits of protein coat . Viruses are very small and have vary widely range in size , ranged from 20-300nm in diameter. The smallest virus is polio virus has a diameter about 20nm. The largest are poxvirus (300nm). The smallest bacteria, *Mycoplasma* spp. has diameter 0.2µm(200nm).

Most cells (animals, plants, microorganisms)are measured in micrometer (µm), whereas cellular parts and viruses are measured in nanometer (nm).

**Structure of viruses :**

All Viruses consist from at least two main components: nucleic acid in center and covered by protein .

**Nucleic acid (viral genome)** : The viruses have central core of nucleic acid , which is either DNA or RNA but not both . The nucleic acid is important part of virus structure because it represent infective particle. Viral nucleic acid can be either single stranded (ss) or double stranded (ds) , linear or circular , segmented or non-segmented genome.All DNA viruses have dsDNA (except parvoviruses have ssDNA). Most RNA viruses possess ssRNA (except reoviruses are dsRNA). Nucleic acid of most DNA viruses and most RNA viruses is linear, but in some DNA viruses and RNA viruses is circular . DNA genome always a single molecule(non-segmented), whereas RNA genome can

exist either single or multiple molecules (segmented).

All viruses contain single copy of genome (haploid),except retroviruses have two copies of RNA (diploid).

**Capsid(Protein coat)** : The central core is surrounded by protein coat which called capsid . The capsid made up number of subunits called capsomeres The capsid serve several important functions:

- The capsid gives shape of virus.
- Protect viral genetic materials from external harmful effects ( such as nuclease enzymes) .
- Mediated attachment of viruses to specific receptor on surface of host cells and facilitate transfer of viral nucleic acid from one host to another.
- Act as antigen that induce neutralizing antibodies and activate cytotoxic T-cell to kill virus-infected cells.

The unit composed of together; nucleic acid and capsid protein is called **nucleocapsid** (or nucleoprotein, NP).

Certain DNA viruses and most RNA viruses have an **envelope** (membrane-like envelope) . The other viruses are non-enveloped(naked). The envelope is consist from lipoproteins which derived from cytoplasmic membrane of host cell when virus released by budding (except herpes viruses envelope which derived from nuclear membrane). The envelope may be covered with projecting **spikes** (glycoprotien). The projections may act as viral antigens or may have role in attachment of virus to cellular receptors.

The most viral proteins are structural, whereas, some proteins are functional proteins such as **viral enzymes** eg: polymerase and neurominidase enzymes .

The complete structural unit of entire virus particle is called **virion** . In some viruses, the virion may be consists of only nucleocapsid, whereas in other viruses the virion is more complex , this includes nucleocapsid plus surrounding envelope and spikes.

The virion is mature infective viral particle , by which the virus invade other cells.

## Symmetry types of virus particles:

The symmetry depending up on the ways in which the capsomeres are arrangement.

**Icosahedral symmetry:** cubic multiple faces(polyhedron) , in which the capsomeres are arranged in pattern consisting of 20 triangular faces. Most DNA viruses are icosahedral .

**Helical symmetry**: In which the capsomeres are arranged in spiral form around nucleic acid that appears rod-shape (tubular shape). Most RNA viruses are helical.

**Complex symmetry:** Some viruses don't exhibit icosahedral or helical symmetry but are more complicated in structure, eg ; Bacteriophage (viruses infect bacteria) have complex shape consist from head (in icosahedral shape) contain nucleic acid, and tail (in helical shape) has set of fibers which helping in attachment of virus to host cell bacterium.

## Classification and nomenclature of viruses:

The following properties have been used as a basis for classification of viruses:

1. viral genome properties:
    a. Type of nucleic acid (may be DNA or RNA).
    b. Molecular weight of nucleic acid.
    c. Number of strands (whether single strand or double strand)of nucleic acid.
    d. Nucleic acid form(may be linear or circular ).
    e. Number and size of nucleic acid segments.
    f. Manner of replication.
2. Capsid properties including :
    a. Shape and size of viral particle.
    b. Number of capsomeres in capsid.
    c. Type of symmetry of nucleoprotein.
    d. Presence or absence of envelope.
    e. Presence or absence of spikes.
3. Biological properties including:

a. Susceptibility to physical and chemical agents , especially ether and detergents , and stability to pH and temperature.
b. Host specificity (natural host range).
c. Mode of viral transmission.
d. Organ specificity(tissue tropism) and pathogenicity .

The nomenclature of viruses is not as in other organisms (not classified into genus and species), but the viruses are classified into groupings which called families, the family names have the suffix-viridae . Each family , subdivided into genera. The genus names carry the suffix-virus. Names of viruses are derived from:

1. The name of disease caused by virus(eg:Influenza virus, Hepatitis virus).
2. The locality where the virus was first isolated (such as ; West Nile virus).
3. The name of scientists responsible for isolating virus(such as; Epstein-Barr virus).
4. Unique epidemiological characteristics of virus (such as; Arboviruses, these are arthropod-borne viruses).

**Viruses families: Families of**
**DNA viruses:**

ssDNA viruses: Parvoviridae , such as ; parvovirus B19 .
dsDNA viruses: Adenoviridae such as adenovirus.
Herpesviridae ; such as herpes simplex,cytomegalovirus.
Hepadnaviridae ;such as hepatitis–B virus.
Papovaviridae ; such as papillomavirus , polyomavirus. Poxviridae ; such as poxvirus, vaccinia virus.

**Families of RNA viruses:**

ssRNA(+) viruses:Caliciviridae ; such as hepatitis-E virus
Coronaviridse; such as coronavirus.
Flaviviridae; such as yellow fever, hepatitis-C virus. Picornaviridae; such as poliovirus, hepatitis-A virus.
Togaviridae; such as rubella virus.
ssRNA(-) viruses: Arenaviriae; such as Lassa virus.
Bornaviridae; such as Borna virus.

Bunyaviridae; such as California encephalitis virus. Filoviridae; such as Ebola virus and Marburg virus. Orthomyxoviridae; Influenza virus Paramyxoviridae; such as Measles, Mumps virus. Rhabdoviridae; such as Rabies virus.

ssRNR(RT) viruses: Retroviridae; such as HIV. dsRNA viruses: Reoviridae; such as Rotavirus.

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## Week 2: Replication of DNA and RNA Viruses

**Topics**:

Viral life cycle overview

DNA virus replication mechanisms

RNA virus replication strategies

Differences in replication based on genome type

**Objective**: To explain the mechanisms of viral genome replication and the differences between DNA and RNA virus replication

## Replication of Viruses (Life cycle of virus)

Stages of viral replication:

1-Attachment

2-Penetration

3-Uncoating

4- Gene expression and biosynthesis

5-Assembly

6-Release

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## 1-Attachement to host cell:

The first stage in viral infection is attachment of virus to specific receptor on the surface of host cell:

A- Receptor molecules **differ for different viruses**. For example, HIV attaches to CD4 receptor on helper T-cell and Rabies virus binds to acetylcholine receptor.

B- The attachment of virus **determines the organ specificity** such as hepatitis virus infect liver, influenza virus infect respiratory tract, and so on.

C- The specificity of attachment **determines the host rang** of viruses. Some viruses have the narrow range, whereas have abroad ranged.

## 2-Penetrat

Following attachment, virions can enter cells by one of the following ways:

**A- Endocytosis:** in which the virus is accumulated inside cell. (naked and enveloped viruses)

**B- Fusion** with Plasma Membrane (just enveloped)

The virus fuses directly with the plasma membrane of the cell, and enter into host cell.

## 3-Uncoating

Uncoating occurs at the same time with or shortly after penetration, **Uncoating is removing the capsid proteins**. Uncoating may be occurring **in cytoplasm** or **in nucleus**. A low pH and within presence of cellular enzymes which lead to dissolve the proteins of capsid , then result in uncoating and release of viral nucleic acid into infected host cell. The viral nucleic acid may remain in cytoplasm or

migrate to nucleus.

## 4-Gene expression and biosynthesis:

Virus cannot replicate by binary fission or mitosis, but they replicate by complex process. When the viral genome released inside living host cell, the virus is control on host cell biosynthesis, inhibition of macromolecules synthesis and use the energy of host cell in synthesis of viral macromolecules.

### The gene expression involves:

**A- Replication of viral genome** (synthesis of viral nucleic acids).

The **DNA viruses** replicate **in nucleus** (except **pox viruses** in **cytoplasm)**, whereas the **RNA viruses** are replicate in the **cytoplasm** (except **retro viruses** and **influenza virus** in **nucleus**).

**B- Transcription of viral mRNA**: synthesis of mRNA in viruses in various pathways,

Transfer of genetic information from parental genome to mRNA is called transcription.

**C- Translation of mRNA (synthesis of viral proteins):** Once the mRNA of either DNA viruses or RNA viruses is synthesized, and it translated by ribosome of host cell into viral protein.

## Replication of nucleic acid

**A- Double strand DNA .V**

It like cellular DNA requires (DNA polymerase) to create new copies of DNA with assist of host cell enzymes.

And virus use( ddrp) DNA dependent RNA polymerase or transcriptase enzyme to make mRNA then translated to proteins

B- RNA viruses

Its must provide its own polymerase

1. Double stranded RNA .v one strand is first transcribed by viral (Rdrp) RNA dependent RNA polymerase
2. In ssRNA .V there are 3 routes for mRNA formation.
   A. The (+ sense strand act directly as mRNA
   B. The (- sense strand ) must be first transcribed by viral (Rdrp)

RNA dependent RNA polymerase into (+sense ) then to mRNA.

3. Retroviruses which contain (ss RNA) by action of reverse transcription will produce complementary ssDNA which is converted to ds DNA then it enter the nucleus and is either integrated in host cell genom causing transformation or is transcribed by host cell polymerase into m RNA.

2

## 5-Assembly of Viruses

The virus produces many copies of their nucleic acid and proteins. The newly viral genome and structural proteins are assembling to form many progeny( strain, offspring) viruses.

assembly of viral nucleic acid into capsid is accruing either in cytoplasm or in nucleus of infected cell.

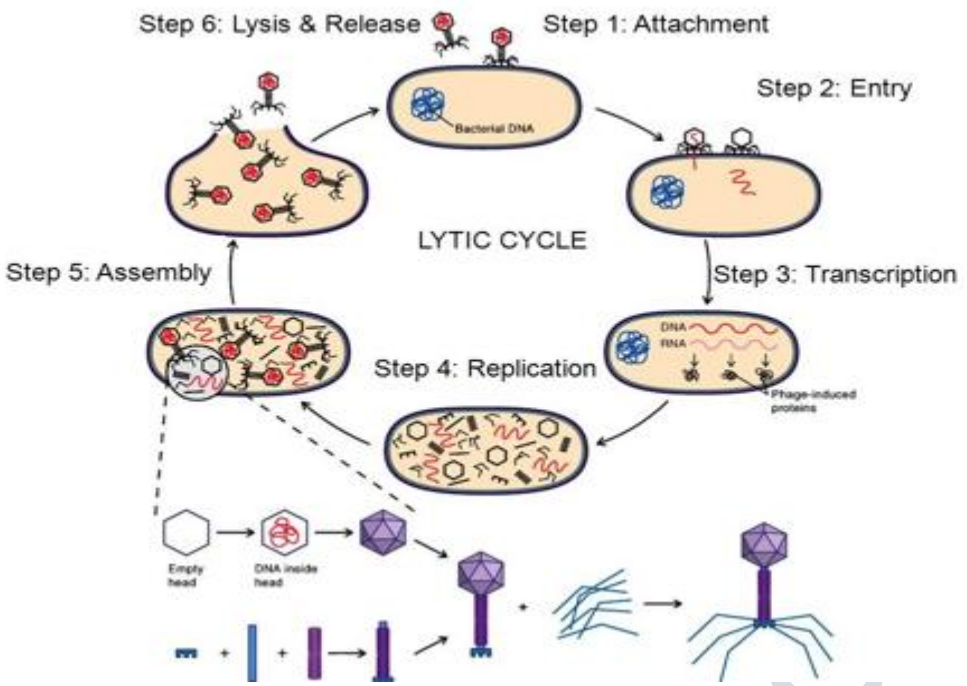
## 6- Release of virus

The virus mature particles are released from the infected cell by one of two processes:

**A- Lysis of infected cell.**

B- **Budding (without lysis)** through the outer cell membrane.

Some viruses are enveloped; they acquired their envelopes from cell membrane during releasing, while other enveloped viruses acquire their envelope from nuclear membrane of infected cell.




## Week 3: Virus Isolation and Cultivation

**Topics:**

Techniques for virus isolation

Cultivation methods: embryonated eggs, cell cultures, lab animals

Cytopathic effects

Detection and quantification of viral growth

**Objective**: To learn how viruses are isolated and cultivated for study, diagnosis, and vaccine production.

## Cultivation and isolation of

## viruses 1- Cultivation of viruses

Because viruses are **obligate intracellular parasites** their growth requires susceptible host cells capable of replicating them and they **cannot be** grown on any inanimate culture media.

**The primary purposes of viral cultivation are:**

1- **To isolate and identify** viruses in clinical specimens.

2- **To prepare** viruses for vaccines.

3- **To do detailed research** on viral structure, multiplication cycles, genetics and effects on host cells.

**Three methods are employed for the cultivation of viruses:**

1- animal inoculation (living animals). 2- embyronated eggs (chicken embryos). 3- cell culture.

**Animal inoculation**

uses of animal inoculation

1- primary isolation of certain viruses

2- for the study of pathogenesis, immune response and epidemiology of viral diseases.

3- for the study of oncogenesis.

**Animals**

1- monkeys: monkeys find only **limited application** in virology.

2- mice: infant mice (suckling) may be inoculation by **several routes** intracerebral, subcutaneous, intraperitoneal or intranasal. growth of the virus in inoculated animals may be indicated by death, disease or visible lesions.

## Embyronated eggs

The embryonated hen's egg was first used for the cultivation of viruses by **Goodpasture (1931)** and the method was further developed by **Burnet**, the embyryonated eggs (**8-11 days old**) are inoculation by several routes for the cultivation of viruses such as chorioallantoic membrane (CAM), allantoic cavity, amniotic cavity and yolk sac, after inoculation eggs are incubated for **2-9 days.**

## Chorioallantoic membrane (CAM)

Inoculation on the chorioallantoic membrane (CAM) produce visible lesions (pocks), each infectious virus practical can form one pock, different viruses have different pock morphology.

## Allantoic cavity

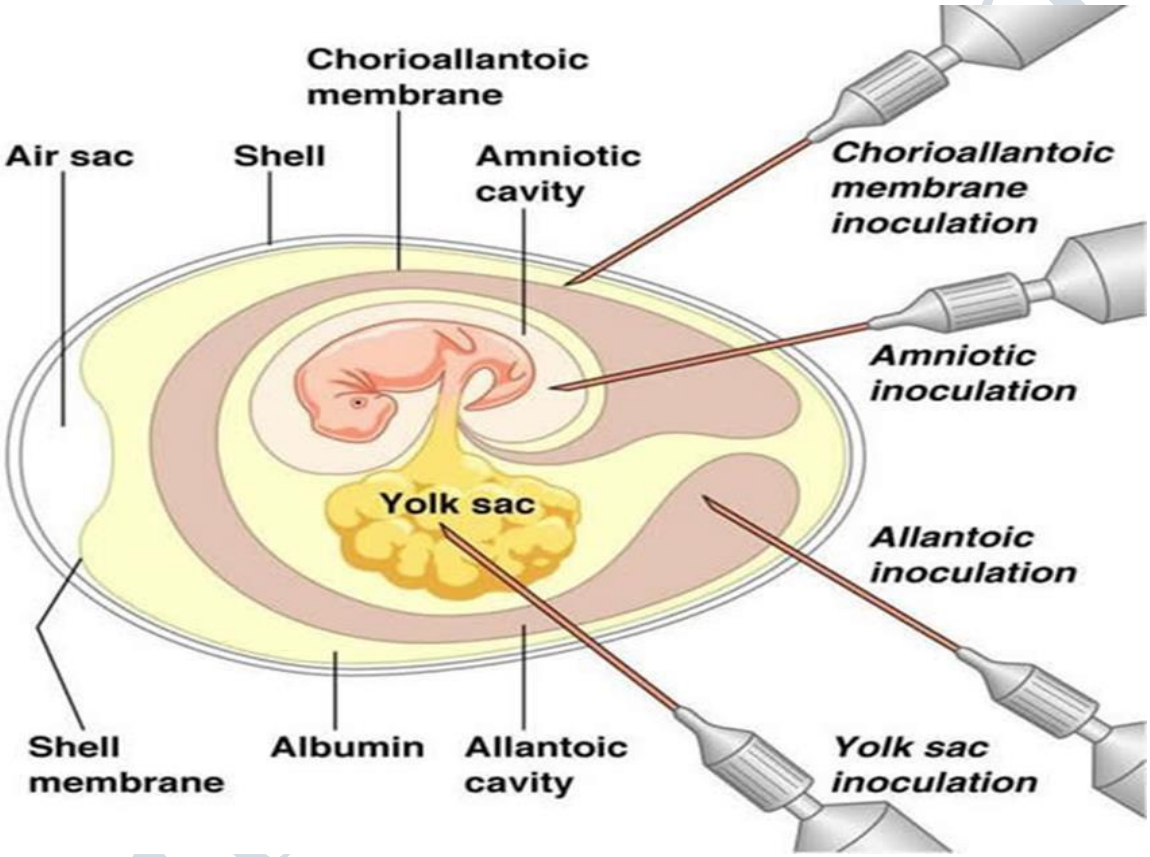
Inoculation into the allantoic cavity provides a rich yield of Influenza and some Paramyxoviruses for **vaccine production**.

## Amniotic s

Inoculation into the amniotic sac is employed for the primary isolation of the Influenza virus

**Yolk sac**

yolk sac inoculation is used for **the cultivation of some viruses**.




**Parts of Embryonated Egg**

## Tissue culture

**Three types** of tissue cultures are available :

**1- Organ culture:** organ cultures are useful for the **isolation of some viruses which appear to be highly specialized parasites of certin organs**

for example the tracheal ring organ culture for the isolation of coronavirus, small bits of organs can be maintained in vitro preserving their orginal architecture and function.

**2- Explant culture:** this method is **now seldom employed in virology.**

**3- Cell cultures:** this is the type of culture is routinely empoloyed for growing viruses.

## Classification of cell cultures

1- primary cell culture. 2- diploid cell strains. 3- continuous cell lines.

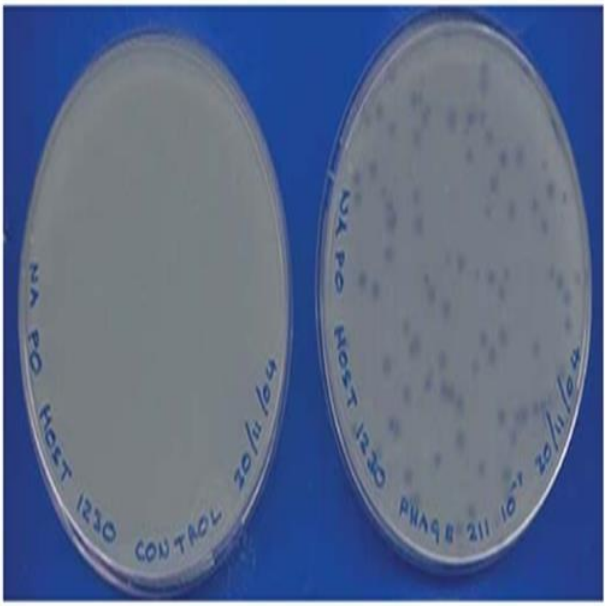
### Growth medium

The essential constituents of the growth medium are **physiologic amounts of essential** amino acids, vitamins, salts, glucose and a buffering system generally consisting of bicarbonate in equilibrium with atmosphere containing about **5%** Carbone dioxide, this is supplemented with upto **5%** calf or fetal calf serum, **antibiotics** are added to prevent bacterial contaminants and **phenol red** as indicator.

### 2- Isolation of viruses

Virus isolation it is imperative that the specimen be collected properly and transported with least dealy to the laboratory, **the reasons** are that many viruses are labile and that the samples are susceptiple to bacterial and fungal overgrowth, viruses are best transported and stored on ice and in special media. many viruses can be isolated as a result of their ability to **form** discrete visible zones and plaques (areas where cells are killed or altered by

the virus infection) in the host cells, to isolate viruses, we use the **three methods** used to cultivation viruses.



**Plaques formed by West Nile virus in a cell monolayer**

Both flasks were inoculated with virus. Plaque formation in the flask on the right has been inhibited by West Nile virus-specific antibody.

**Plaques formed by a phage in a bacterial culture**

## Isolating viral constituents

viruses must be broken down into their component parts by adding special detergents e.g. sodium dodecyl sulfate to isolate the virus, these molecules include the proteins that surround and line the outer membrane and viral nucleic acid, to separate these molecules from each other (**proteins, enzymes** and **nucleic acids**) we use the electrophoresis device, as the electric field pulls the molecules through the gel so that the separation is according to their **weights.**

## Objectives

The objective of the lecture is how to isolate and diagnose the virus, identify the three isolation methods and show some key details

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## Week 4: Chemotherapy, Antiviral Agents, and Vaccines

**Topics**:

Principles of antiviral therapy

Types and mechanisms of antiviral drugs

Challenges of antiviral treatment

Types of vaccines and immunization strategies

**Objective**: To understand the available therapeutic and preventive measures against viral infections.

## Antiviral Agents

- A medication or another agent that kills viruses or inhibits their capability to

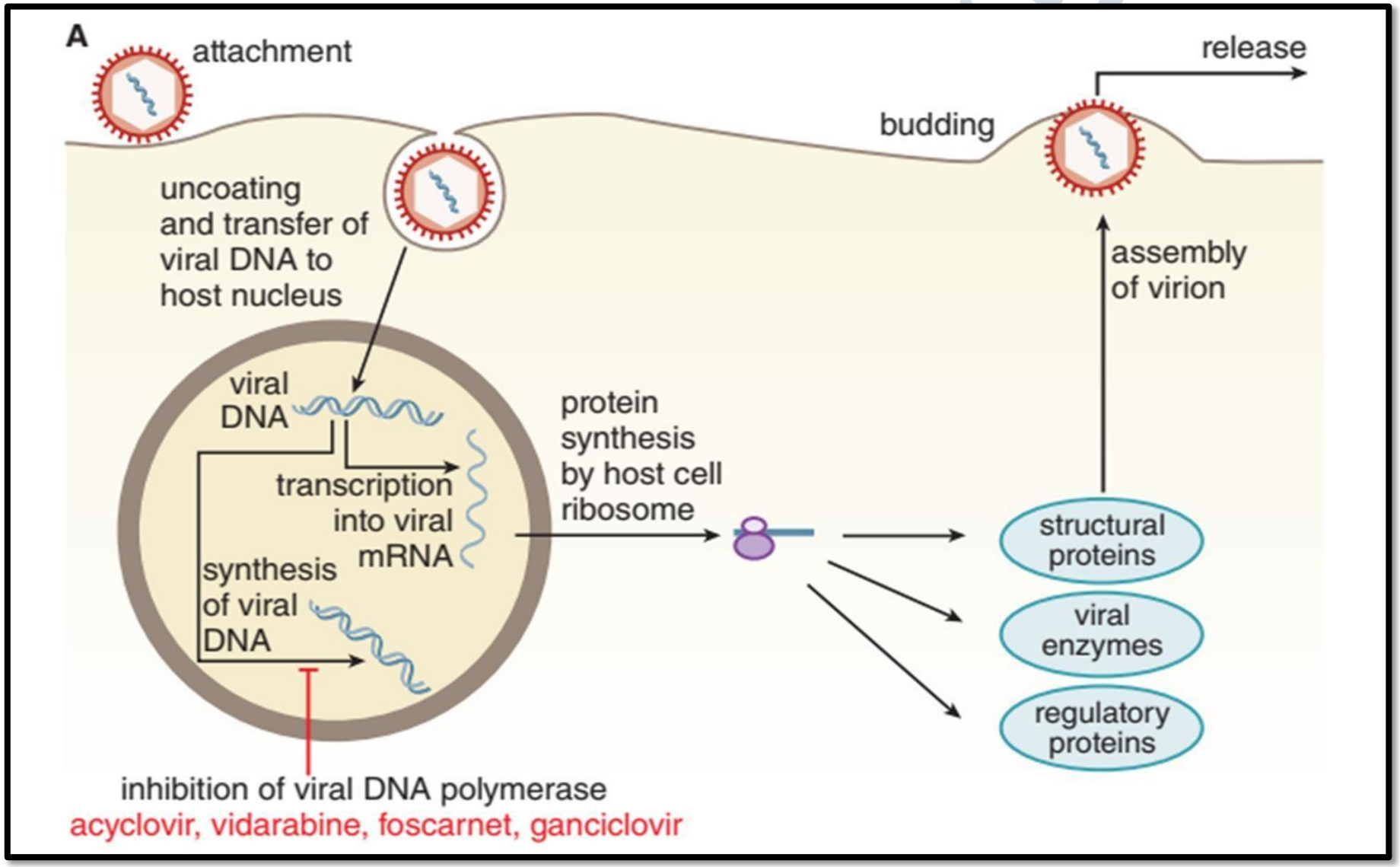
replication.

- Viruses are obligate intracellular microorganisms, drugs that target viral processes must penetrate host cells.
- Therefore, drugs that negatively impact on a virus are also likely to negatively impact normal pathways of the host.

How they act?

- 1. Attachment of the virus to receptors on the host cell surface;
- 2. Entry of the virus through the host cell membrane;
- 3. Uncoating of viral nucleic acid;
- 4. Synthesis of early regulatory proteins, eg, nucleic acid polymerases;
- 5. Synthesis of new viral RNA or DNA;
- 6. Synthesis of late, structural proteins;
- 7. Assembly (maturation) of viral particles; and
- 8. Release from the cell. Antiviral agents potentially target any of these steps

**Replication of virus**



## Antiviral Agents

- (1) Anti-herpes agents
- (2) Anti HIV agents
- (3) Drugs used for hepatitus B & C
- (4) Anti influenza agents

## (1) Anti-herpes agents

- **Drugs:** • Acyclovir• Famciclovir
- **Mechanism of action:**
- Inhibits herpres virus DNA Polymerase.
- Gets combined in viral DNA and stops lengthening of DNA strands.
- **Adverse effects**
- nausea, diarrhoea may occur
- renal toxicity &
- neurologic effects

## □ (2) Anti HIV agents

- Classes of Anti-retroviral drugs nowadays
- 1. **NRTI** (nucleoside/nucleotide Reverse transcriptase inhibitors)
- 2. **NNRTI** (non-nucleoside Reverse transcriptase inhibitors)
- 3. **PI** (Protease inhibitors)
- 4. **FI** (Fusion inhibitors)
- 5. HIV integrase inhibitors

# 1. NRTI (nucleoside/nucleotide Reverse transcriptase inhibitors)

- **Drugs:** •Tenofovir •Didanosine (ddI)

- **Mechanism of action:**

- NRTIs act by competitive inhibition of HIV-1 reverse transcriptase – Incorporation into growing viral DNA chain causes premature chain termination due to inhibition of binding with the incoming nucleotide.

- **Adverse effects:**

- •neurotoxic •neuropathy Pancreatitis

## 2.NNRTI (non-nucleoside reverse transcriptase inhibitors)

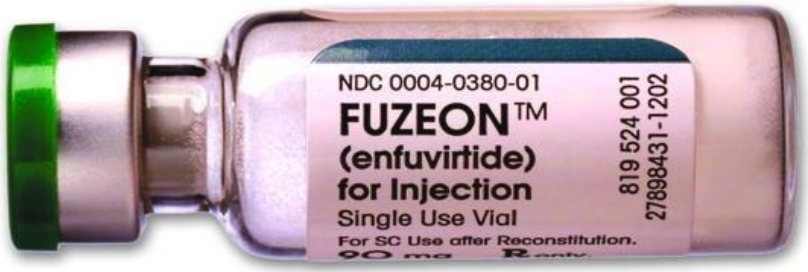
- **Drugs:** •Delavirdine •Etravirine
- **Mechanism of action:**
- Bind directly to HIV-1 reverse transcriptase, resulting in inhibition of RNA and DNA dependent polymerase activity.
- It do not require phosphorylation to be active.
- **Adverse effects:**
- •Skin rash •GI intolernce

# 3. PI Protease inhibitors

- **Drugs:** •Indinavir •Ritonavir
- **Mechanism of action:**
- PIs prevent the processing of viral proteins into functional conformations, resulting immature, noninfectious viral particles.
- **Adverse effects:**
- •Redistribution of accumulation of body fat

# 4. FI (Fusion inhibitors)

- **Drugs:**
  - Enfuvirtide
- **Mechanism of action:**
  - Fusion inhibitor that blocks HIV entry into cell ,binds to subunit of the viral envelope glycoprotein.
- **Adverse effect:**
  - local injection site reactions.



# 5. HIV integrase inhibitors

- **Drugs:** •Dolutegravir
- **Mechanism of action:**
- Integrase strand transfer inhibitors prevent integration of the viral DNA into the host DNA by inhibiting the viral enzyme integrase
- bind integrase, a viral enzyme essential to the replication of HIV.

## (3) Drugs used for hepatitus B & C

- The goals of chronic HBV therapy
- • To assist suppression of HBV replication, resulting in slowing of progression of hepatic disease
- • To prevent complications (ie, cirrhosis, hepatic failure), and
- • To reduce the need for liver transplantation.

# (4) Anti influenza agents

- **Drugs:** Zanamivir & Rimantidine
- **Mechanism of action:**
- Interfere with release of progeny influenza virus from infected host cells.
- Inhibit the uncoating of viral RNA within infected host cells plus preventing its replication.
- **Adverse effects:**
- Pneumonia, Asthma

# Interferons

- Interferons are host cytokines that use complex antiviral, immunomodulatory actions.
- Interferons appear to functions by Induce intracellular signals for resulting inhibition of viral penetration, translation, transcription, protein processing, maturation and release.

# Interferon Inducers

- Agents that stimulate the production and release of interferons.
- **Adverse effects:**
- Neurotoxicities

**There are two types of viral vaccines**

**1- Killed virus vaccines**

Inactivated (killed virus) vaccines are made by purifying viral preparation to a certain extent and then inactivating viral infectivity in a way that does minimal damage to the viral structural proteins, mild **formalin treatment** is frequently used, killed virus vaccines prepared from whole virions generally stimulate the development of circulating antibody against the coat proteins of the virus conferring some degree of resistance to that virus strain.

**Advantages** of inactivated vaccines are that there is no reversion to virulence by the vaccine virus and that vaccines can be made when no acceptable attenuated virus is available.

**Disadvantages** of killed virus vaccines include relatively brief immunity requiring boosting shots to maintain effectiveness, poor cell mediated response, occasional hypersensitivity to subsequent infection and extreme care is required in their manufacture to make certain that no residual live virulent virus is present in the vaccine.

### 2- Attenuated live virus vaccines

Live virus vaccines utilize virus mutants that antigenically overlap with wild type virus but are restricted in some step in the pathogenesis of disease, attenuated live virus vaccines have **Advantage** of acting more like the natural infection with regard to their effect on immunity, they multiply in the host, tend to stimulate longer lasting antibody production, induce a good cell mediated response and induce antibody production and resistance at the portal of entry.

**Disadvantages** of attenuated live virus vaccines include a risk of reversion to greater virulence, severe infection in immunocompromised hosts and limited storage and shelf life in some cases.

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## Week 5: Influenza Viruses

**Topics**:

Types of influenza viruses (A, B, C)

Antigenic shift and drift

Epidemiology and pandemics

Vaccine development

**Objective**: To explore the biology, transmission, and control of influenza viruse

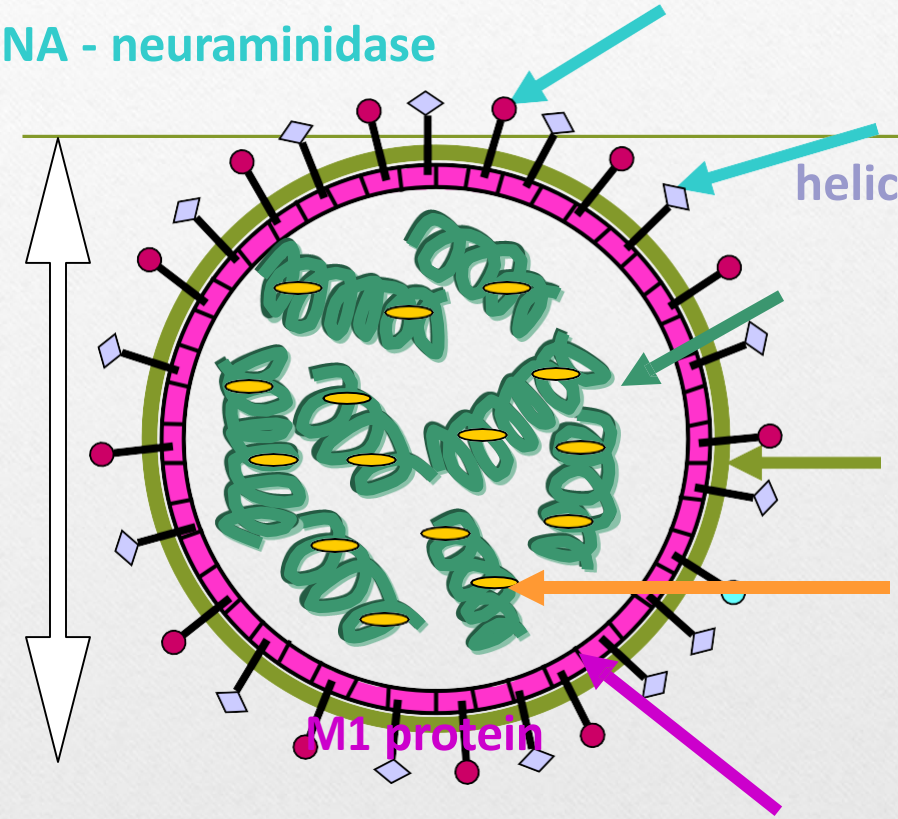
# Influenza virus

## Introduction

Orthomyxoviridae is a family of RNA viruses. It includes seven genera: Influenzavirus A, Influenzavirus B, Influenzavirus C, .

These genera contain viruses that cause influenza in vertebrates, including birds, humans, and other mammals.

## STRUCTURE OF VIRION

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# General classification

- Orthomyxoviruses are large, enveloped virus
- helical nucleocapsids
- Negative sense, 8 segmented **RNA genome.**
- Pleomorphic: laboratory strains are often spherical, whereas clinical strains are often filamentous.

Replicate of genom in the **nucleus**.

- Upon budding, the host cell is killed.
- contain two viral surface proteins called the **hemagglutinin (H)** and the **neuraminidase (N)**

# Classification according capsid

Family : Orthomyxoviridae comprises : Influenzavirus A: infect humans,

birds, pigs and other cusses epidemic

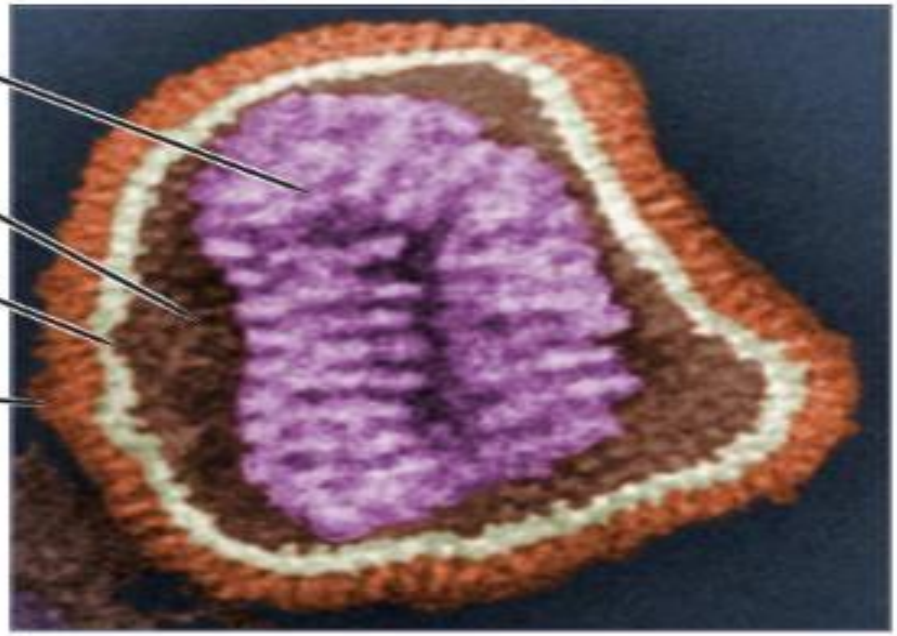
Influenzavirus B: infect humans only

Influenzavirus C: infect humans and pigs

# antigenic variations

Type A viruses are divided into types based on differences in two viral surface proteins called the

- **hemagglutinin(H)** (for attachment with host cell receptors, antibody response ( about 16 types in A V)
- **neuraminidase (N)**. Important foe release and degraded mucous layer of host tissue as respiratory tract (more than 9 types in A V)




## Envelope glycoproteins

- ✓ *Hemagglutinin (HA) —*
  - Viral attachment protein: Binds sialic acid on epithelial cells.
  - Fusion protein (envelope to cell membrane)
  - Elicits neutralizing antibody response.
- HA types determine species/tissue infected.
- ✓ *Neuraminidase (NA) —*
  - Facilitates virion release: Cleaves sialic acid

Nucleoprotein antigens determine A, B, C, etc.

HA & NA types determine Influenza A subtype. Ex: H1N1

# Antigenic changes:

- – **Genetic drift** Minor changes include **mutations**, which can lead to epidemics; both influenza A and B undergo these kinds of changes. –**Genetic shift** Major changes include **re-assortment**, which can lead to and pandemics; influenza A virus is associated with pandemics. – Reassortment occurs when viruses with segmented genomes create a hybrid strain. – An example of this is the H1N1 pandemic strain that arose in 2009; this strain contained genetic

information from avian, human, and swine influenza viruses.

# M1& M2 proteins

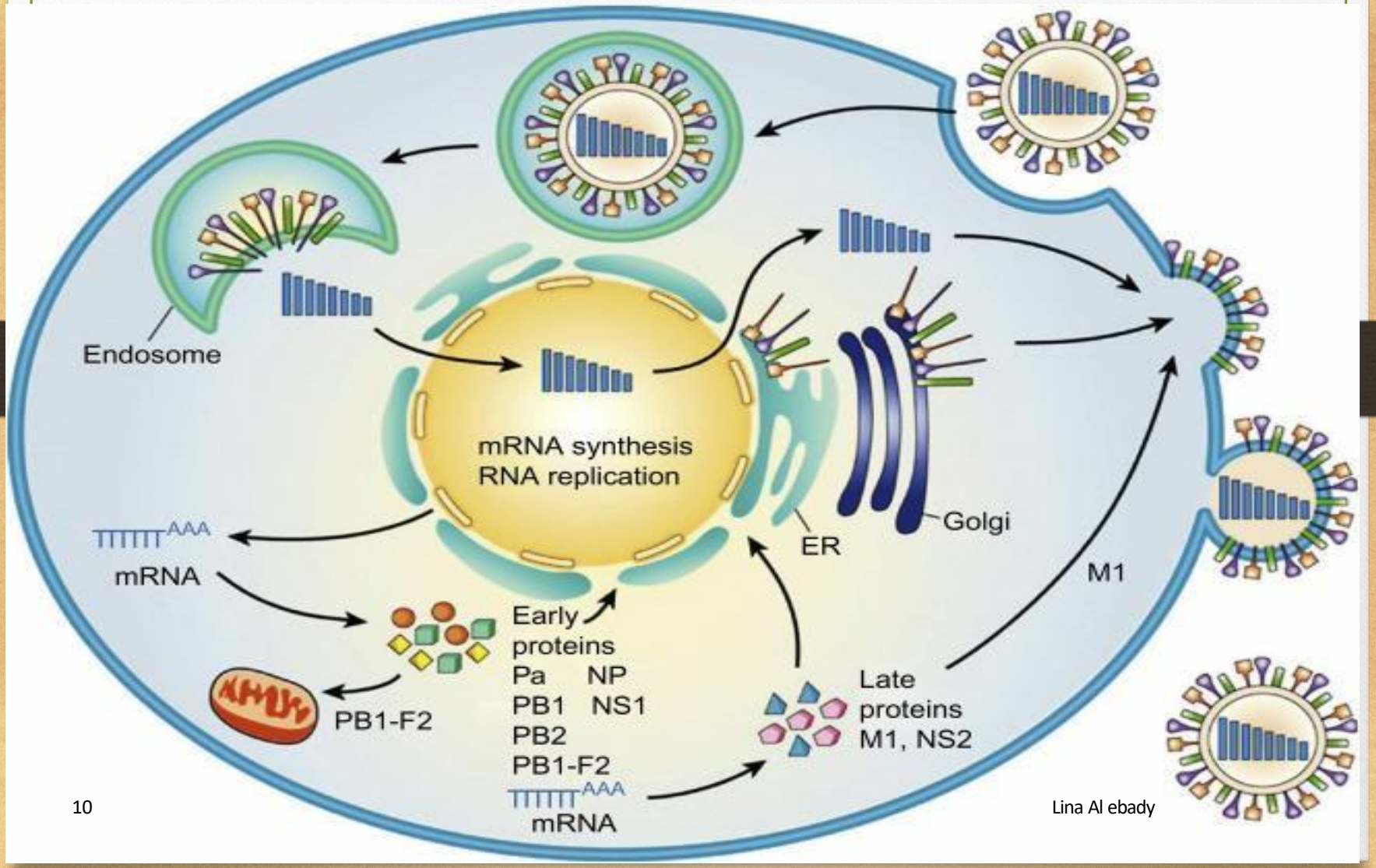
– Matrix protein (*M1*) promotes virion assembly.

Envelope

– Membrane protein (*M2*) facilitates viral uncoating and release from the host cell;

it does so by formation of proton channels that allow for acidification, which is necessary for membrane fusion. – **Amantadine and rimantadine** target M2 of Influenza A, thus blocking viral releasing

Viral Replication:



## Steps of influenza pathogenesis:

- The virus reaches the **mucosal epithelia** via respiratory droplets.
  - –the virus uses **sialic acid receptors** on host epithelial cells to gain access to host cells for replication.

# Steps of influenza pathogenesis:

- Replication primarily occurs in the **tracheobronchial** tree
- Infection triggers release as cytokines, type 1 interferons, and pro-inflammatory cells.
- In turn, the adaptive immune system is triggered, and T-cells are activated and antibodies are produced. – These agents provide future protection against re-infection by the same influenza strain.

## Symptoms of influenza

- **Symptoms of influenza** include fever, headache, cough, chills, muscle pain, sore throat, sinus inflammation and others; recently indicate that these symptoms are primarily caused by the host immune response.

# Complications:

- In some individuals, complications from the flu can be life-threatening.
- **Pneumonia** can result from viral infection or from secondary bacterial infections.
- **Organ inflammation or failure** can occur.
- **Sepsis.**
  Indicate that individuals at higher-risk for these complications include
- Very young children (under the age of 5)
- Pregnant women
- Adults over the age of 65

# Influenza

## Potential complications

### Pneumonia

Viral or 2° bacterial infection.

### Organ inflammation/Failure

### Sepsis

### High-risk populations

Immunocompromised:

- ✓ Very young children (< 5)
- ✓ Pregnant woman & < 2 weeks postpartum
- ✓ Adults > 65 years

## Prevention & treatment

- Seasonal Vaccine
  3 or 4 component vaccines.
  Prevent flu/reduce severity.
- Antiviral drugs
  Reduce severity/complications.

# Diagnosis

- Based on the symptoms
- ElISA (presence antigen)
- Cellline culture (isolation virus)
- PCR (RNA identification)
- Heamagglutination

**Week 6: Paramyxoviruses and Rubella Virus**

**Topics**:

Characteristics of paramyxoviruses (measles, mumps, RSV)

Rubella virus structure and disease

Pathogenesis and immunity

Vaccination (MMR)

**Objective**: To understand the clinical and epidemiological aspects of paramyxoviruses and rubella.

# Paramyxoviruses and rubella virus

## Paramyxoviridae

- **a. Measles – rubeola**
- **b. Mumps**

- **c. Parainfluenza**
- **d. RSV – respiratory syncytial virus**

## Paramyxoviruses

- All members of the **Paramyxoviridae** family initiate infection via the respiratory tract. Replication of the respiratory pathogens is limited to the respiratory epithelia, whereas measles and mumps become distributed throughout the body and produce generalized disease.

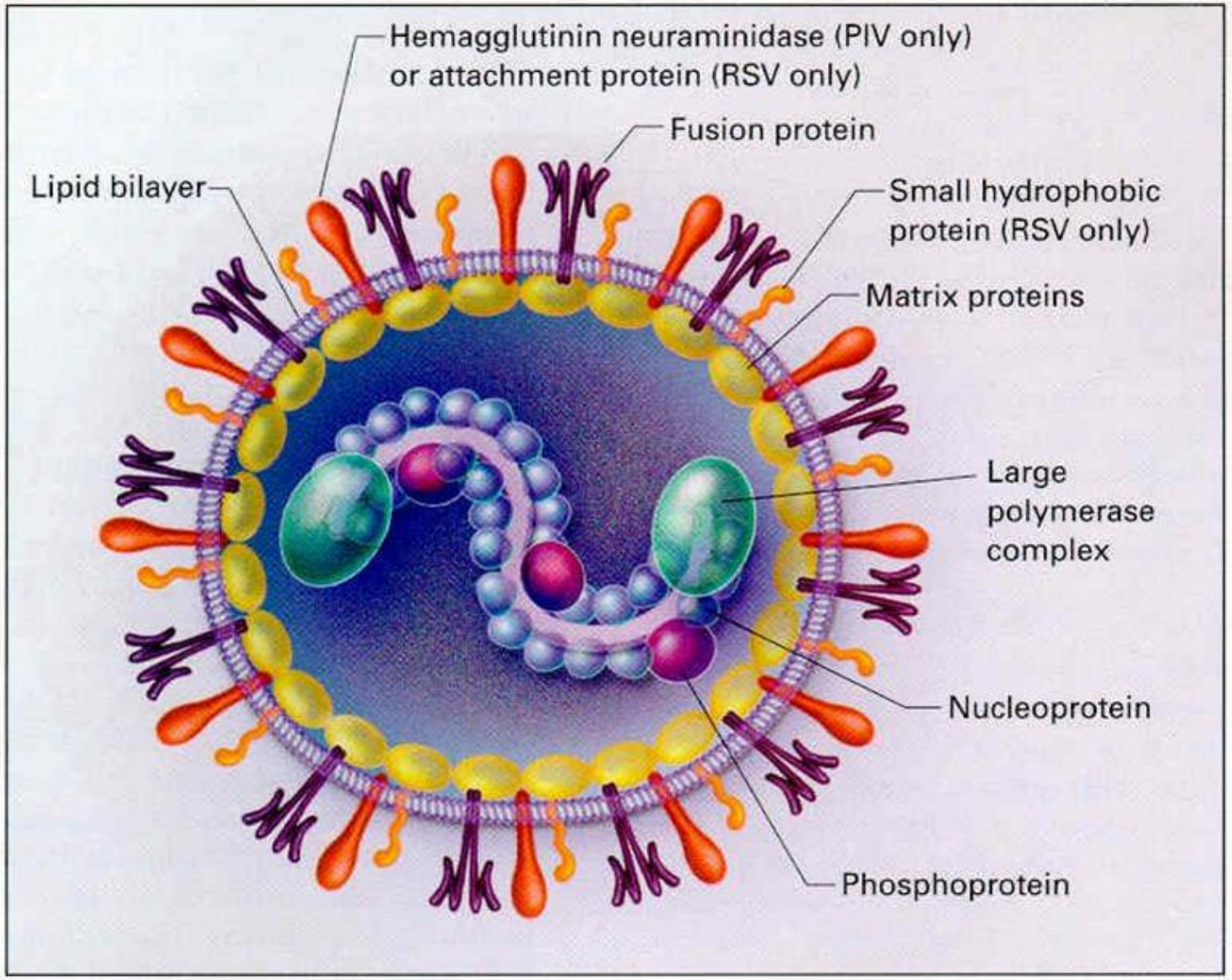
## Properties of Paramyxoviruses

- **Virion:** Spherical, pleomorphic, 150 nm or more in diameter (helical nucleocapsid)
- **Composition:** RNA (1%), protein (73%), lipid (20%),

carbohydrate (6%)

- **Genome:** Single-stranded negative RNA, linear, nonsegmented
- **Envelope:** Contains viral glycoprotein (G, H, or HN) (which sometimes carries hemagglutinin or neuraminidase activity) and fusion (F) glycoprotein
- **Replication:** Cytoplasm; particles bud from plasma membrane
- **Outstanding characteristics:** Antigenically stable

Particles are labile yet highly infectious



## Transcription, Translation, & RNA Replication

- Messenger RNA transcripts are made in the cell cytoplasm by the viral RNA polymerase, and viral proteins are synthesized in the cytoplasm.

**Maturation**

- The virus matures by budding from the cell surface. Progeny nucleocapsids form in the cytoplasm and migrate to the cell surface.


- MeaslesMeasles (Rubeola) Virus Infections

- Measles is an acute, highly infectious disease characterized by fever, respiratory

symptoms, and a maculopapular rash. Complications are common and may be quite serious.

## Pathogenesis & Pathology

- Humans are the only natural hosts for measles virus.
- The virus enter to the human body via the respiratory tract, where it multiplies locally; the infection then spreads to the lymphoid tissue, where further multiplication occurs. Primary viremia distributes the virus.

## Pathogenesis & Pathology

- Finally, a secondary viremia seeds the epithelial surfaces of the body, including the skin, respiratory tract, and conjunctiva, where main replication occurs that after multiplication of virus in lymphocytes

## *Pathogenesis & Pathology*

- The described events occur during the incubation period, which typically lasts 8–12 days but may last up to 3 weeks in adults.
- Involvement of the central nervous system is common in measles.

## *Clinical Findings*

After an incubation period of 8–12 days, measles is typically a 7-11days illnes.

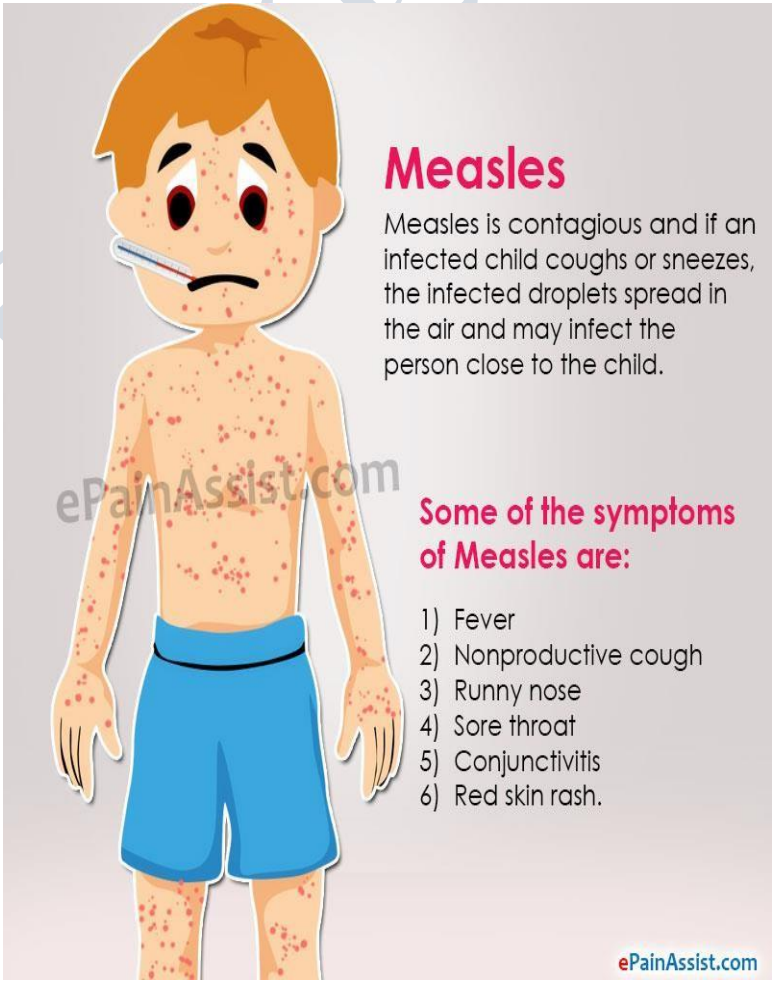
- The prodromal phase is characterized by fever, sneezing, coughing, running nose, redness of the eyes, Koplik spots, and lymphopenia. The conjunctivitis is commonly associated with photophobia.

## Clinical Findings

- Koplik These spots contain giant cells and viral antigens and appear about

  2 days before the

  rash.



## Clinical Findings

- The most common complication of measles is
- 1. otitis media (5–9% of cases)
- 2. Pneumonia is the most common life- threatening complication of measles, caused by secondary bacterial infections.

## Laboratory Diagnosis

- 1. Antigen & Nucleic Acid Detection Measles antigens can be detected directly in epithelial cells from

  respiratory secreation

- 2. Detection of viral RNA by RT-PCR

## Laboratory Diagnosis

- 3. Isolation & Identification of Virus Nasopharyngeal and conjunctival swabs, blood samples, respiratory secretions,

  and urine collected from a patient.

- 4. Serology

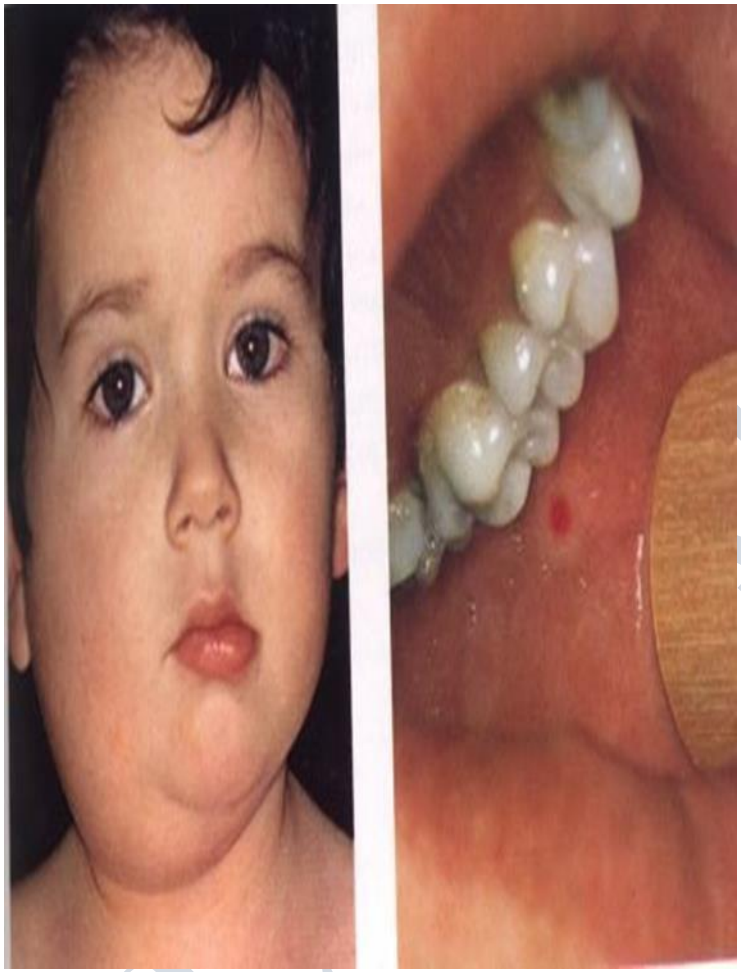
  Serologic confirmation of measles infection depends on a fourfold rise in antibody titer

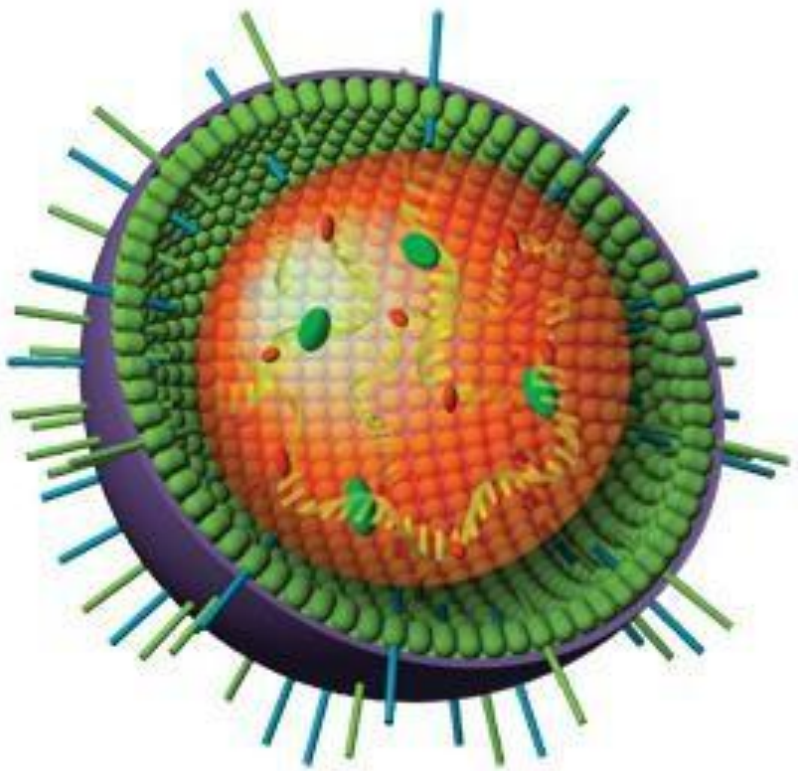
## Treatment, Prevention, & Control

vaccine

- The use of killed measles virus vaccine was discontinued by 1970, as certain vaccinees.

# Mumps





# Mumps Virus Infections

- Mumps is an acute infectious disease characterized by nonsuppurative enlargement of one or both salivary glands. Mumps virus mostly causes a mild childhood disease, but in adults complications including meningitis and orchitis are common. More than one-third of all mumps infections are asymptomatic.

## Pathogenesis & Pathology

1. Primary replication occurs in nasal or upper respiratory tract epithelial cells.
2. Viremia then distributes the virus to the salivary glands and other major organ systems as kidney and CNS.

- The incubation period may range from 2 to 4 weeks but is typically about 14–18 days.

## Laboratory Diagnosis

- 1. Isolation & Identification of Virus

The most suitable clinical samples for viral isolation are saliva, cerebrospinal fluid, and urine.

- 2. Nucleic Acid Detection

RT-PCR is a very sensitive method .

- 3. ELISA can be designed to detect either mumps-specific IgM antibody or mumps- specific IgG antibody.

## Treatment, Prevention, & Control

- Two doses of MMR vaccine are recommended for school entry.

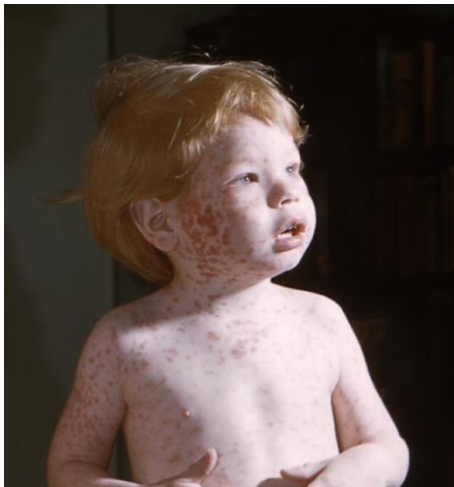
# Envelope Spikes of Paramyxoviruses

| Virus | Hemagglutinin | Neuraminidase | Fusion protein[1] |
|---|---|---|---|
| Measles virus | + | - | + |
| Mumps virus[2] | + | + | + |
| Respiratory syncytial virus | - | - | + |
| Parainfluenza virus[2] | + | + | + |

# RUBELLA

***(German Measles)***

- Acute infectious, viral disease of older children and young adults, characterized by mild prodromal symptoms, typical rash and painful lymphadenopathy

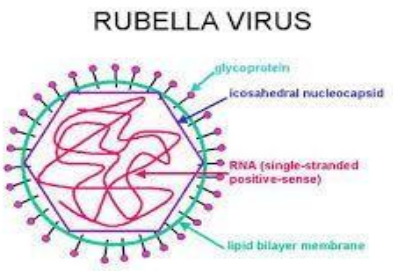


## Epidemiological Determinants

### *Agent Factors*

❑ Agent

- Rubella virus, RNA virus (Toga virus family)
- One antigenic type




- Rapidly inactivated by chemical agents, low Ph ,and UV light

- Age –> 3-10 yrs ( developing countries

Immunity – Life long after first attack

### Environmental Factors

- Occurs in seasonal pattern, during winter and spring season

### Transmission

- Droplet infection, droplet nuclei, inhalation by respiratory system

### Incubation Period

- 2 to 3 weeks ( average 18 days)

### Clinical Findings

- Fine maculopapular rash Minute, pinkish Starts on face

within 24 hours of the onset of the prodermal symptoms, spreads to trunk on 2nd day and extremities on 3rd dayClears more rapidly, disappears in 3 days So it is also called as 3-day measles Rash absent (25% cases) in subclinical cases, Conjunctivitis may occur

## Complication

- Arthritis common among women
- Thrombocytopenic
- Encephalitis is very rare
- Common dreadful complication is congenital malformations of the fetus in a pregnant mother

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Lina Alebady

## Week 7: Enteric Viruses and Rhinoviruses

**Topics**:

Common enteric viruses (rotavirus, norovirus)

Transmission and pathogenesis

Rhinovirus and common cold

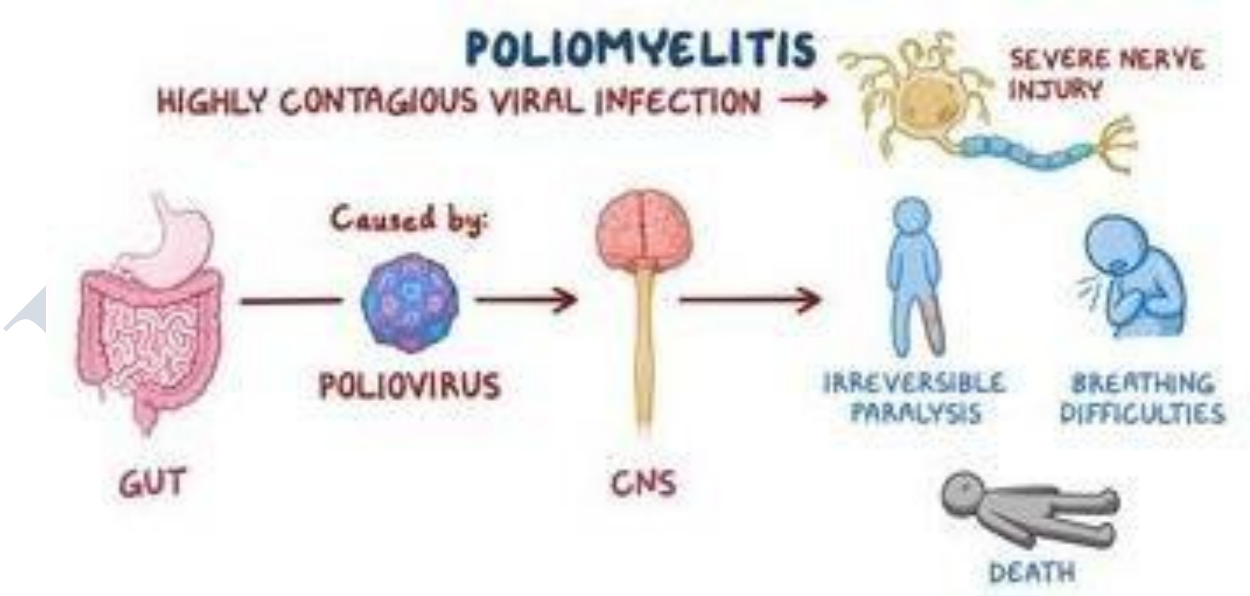
Diagnosis and control

**Objective**: To describe the major enteric and respiratory viruses and their impact on public health.

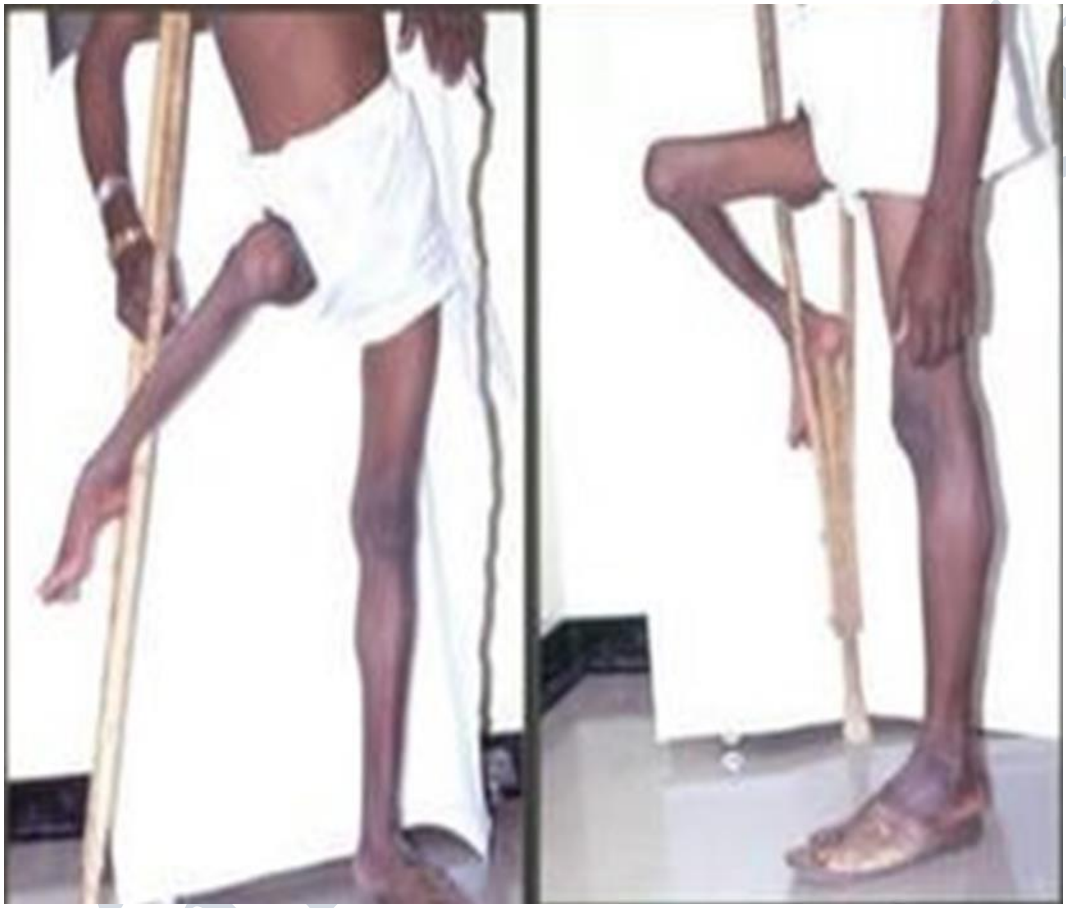
## Picornaviruses (Enterovirus and Rhinovirus groups)

Picornaviridae represent a **very large** virus family with respect to the number of members but one of the smallest in terms of virion size and genetic complexity, they include **two major groups** of human pathogens : enteroviruses and rhinoviruses.

Many picornaviruses cause diseases in humans ranging from severe paralysis to meningitis, myocarditis, respiratory illnesses, undifferentiated febrile illness and conjunctivitis. etiology is difficult to establish because different viruses may produce the same syndrome, same picornavirus may cause more than a single syndrome and some clinical symptoms cannot be distinguished from those caused by other types of viruses, the most serious disease caused by any enterovirus is **poliomyelitis.**



**Enteroviruses** are transient inhabitants of the human alimentary tract and may be isolated from the throat or lower intestine, Rhinoviruses are associated with the respiratory tract and isolated chiefly from the nose and throat, less common picornaviruses associated with human illness include hepatitis A virus, parechovirus, cardiovirus and Aichi virus.



## Polioviruses

poliomyelitis is an acute infectious disease that in its serious form affects the central nervous system (**CNS**), the destruction of motor neurons in the spinal cord results in flaccid paralysis. **most** Poliovirus infections are subclinical and does not multiply in muscle. Poliovirus particles are enteroviruses they

are inactivated when heated at 55°C for 30 minutes and Polioviruses are **not affected** by ether or sodium deoxycholate.

# What is Poliomyelitis

- Poliomyelitis (polio) is a highly infectious viral disease, which mainly affects young children. The virus is transmitted through contaminated food and water, and multiplies in the intestine, from where it can invade the nervous system.

**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 nasopharyngeal secretions but may also be found in throat and oral secretions. these viruses as well as Adenoviruses, Enteroviruses and Influenza viruses cause **upper respiratory tract** infections including the common cold syndrome, Rhinoviruses are also responsible for about half of asthma exacerbations.

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## Week 8: Viral Pathogenesis and Genetics

**Topics**:

Mechanisms of viral pathogenesis

Host-virus interactions

Genetic variations in viruses

Mutation, recombination, reassortment

**Objective**: To analyze how viruses cause disease and how their genetic variability affects virulence and transmission.

## Viral Pathogenesis

Viral pathogenesis is the process by which a viral infection leads to disease.

the common of viral infections are subclinical. It is not in the interest of the virus to severely harm or kill the host.

The significances of viral infections depend on the interplay between a numbers of viral and host factors.

## Outcome of Viral Infection

☒ **Acute Infection**

- Recovery with no excess effects
- Recovery with excess effects e.g. acute viral encephalitis leading to neurological sequelae.
- Death
- Continue to chronic infection

☒ **Chronic Infection**

1- Silent subclinical infection for life e.g.(cytomegalo .v) CMV, (Epstein–Barr virus) EBV.

2- A long silent period before disease e.g. HIV, SSPE , PML

3- Reactivation to cause acute disease e.g. herpes.

4- Chronic disease with declines and aggregations e.g. HBV, (hepatitis )HCV.

5- Cancers e.g. (Human herpes-8)HHV-8

## Factors included in Viral Pathogenesis

For pathogenic virus, there are a number of critical stages in replication which

determines the nature of disease they produce which included;

1-Entry into the Host

2-Course of Infection (Primary Replication, Systemic Spread, Secondary Replication)

3-Cell/Tissue Tropism

4-Cell/Tissue Damage

5-Host Immune Response

6-Virus Clearance or Persistence

## 1- Entry into the host

The first stage in any virus infection. In the case of pathogenic infections, the site of entry can influence the disease symptoms produced. Infection can occur via:

**A- Skin,** cannot support virus replication. Most viruses which infect Through the skin need a opening to enter this effective barrier, e.g. cuts or scratches.

**B- Respiratory tract-** the respiratory tract and all other mucosal surfaces possess immune defense mechanisms, as well as non-specific inhibitory mechanisms (ciliated epithelium, mucus secretion, lower temperature) which virus must overcome.

**C- Gastrointestinal tract-** a hostile environment; gastric acid, bile salts, etc. Viruses that spread by GI tract must be adapted to this hostile environment.

**D- urogenital tract-** comparatively less hostile than the others.

**E-Conjunctiva and other mucous membranes** - rather exposed site and relatively unprotected

## 2-Course of Viral Infection

### Primary Replication

After entry to potential host, the virus must initiate an infection by entering a ready cell. This often determines whether the infection will remain localized at the site of entry or spread to become systemic infection.

**Localized infections**

| Virus | primary replication |
|---|---|

| | |
|---|---|
| Rhinoviruses | upper respiratory tract |
| Rotaviruses | Intestinal epithelium |
| Papillomaviruses | Epidermis |

**Systemic Infections**

| Virus | primary replication | secondary replication |
|---|---|---|
| Enteroviruses | Intestinal epithelium | Lymphoid tissues, C.N.S |
| Herpesviruses | Oropharynx or G.U. tract | Lymphoid cells, C.N.S |

**Secondary replication**

Occurs in systemic infections when a virus reaches other tissues in which it is capable of replication, e.g. poliovirus (gut epithelium- nervous in brain &spinal cord). If the virus can be prevented from reaching tissues where secondary replication can occur, generally no disease results.

**Spread throughout the host**

Apart from direct cell-cell contact, there are 2 main mechanisms for spread throughout the host:

**Via the bloodstream**

**Via nervous system**

Virus may get into the blood stream by direct vaccination- e.g. Arthropod vectors, blood transfusion or I.V drug .

The virus may travel free in the plasma (Togaviruses, Enteroviruses) or in association with red cells (Orbiviruses) platelets (Herpes simplex virus). As above, spread to nervous

system is preceded by primary viaremia.

### 3- Cell/ Tissue tropism

In virology, Tissue tropism is the cells and tissues of a host that support growth of a particular virus or bacteria. Some viruses have a broad tissue tropism and can infect many types of cells and tissues. Other viruses may infect primarily a single tissue

### 4- Host immune response

Has a major impact on the outcome of an infection. In the most cases the virus is cleared completely from the body and results in complete recovery. In other infections, the immune response is unable to clear the virus completely and the virus persists. In general, cellular immunity plays the major role in clearing virus infection whereas humeral immunity protects against reinfection.

### 5- Cell /Tissue damage

Virus may replicate widely throughout the body without any disease symptoms, if they do not cause significant cell damage or death. Retroviruses do not generally cause cell death, being released from the cell by budding rather than by cell lysis and cause persistent infections, even being passed vertically to offspring if they infect the germ line.

Equally, Picornaviruses cause lysis and death of the cells in which they replicate, leading to fever and increased mucus secretion in the case of Rhinoviruses, paralysis or death (usually due to respiratory failure) for Poliovirus.

### 6- Viral Clearance or Persistence

The majority of viral infections are cleared but certain viruses may cause persistent infections. There are 2 types of chronic persistence infections.

1- True Latency -the virus remains completely latent following primary infection e.g. Herpes simplex virus.

2- Persistence e- the virus replicates continuously in the body at a very low level e.g. (HIV).

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## Week 9: Herpesviruses

**Topics**:

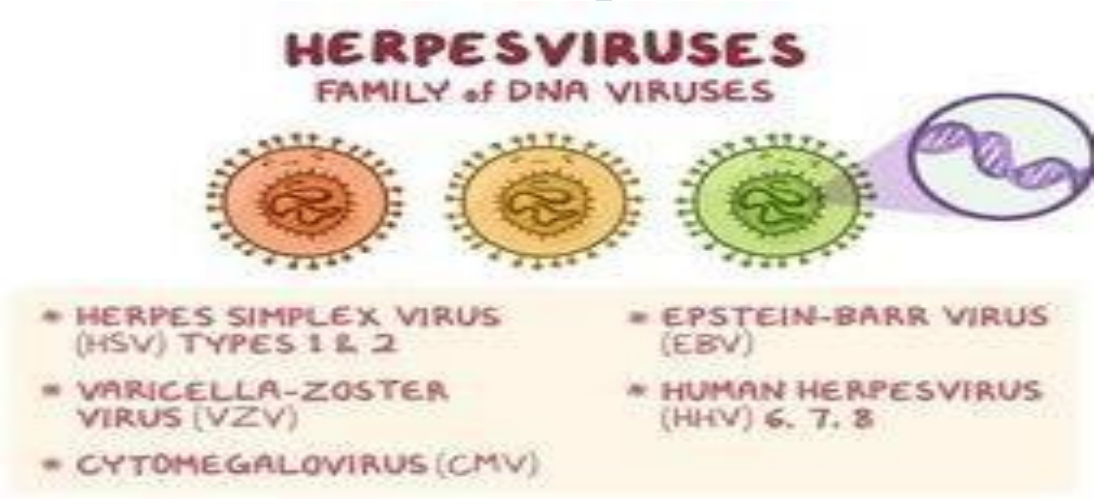
Overview of herpesvirus family

Latency and reactivation

Types (HSV-1, HSV-2, VZV, CMV, EBV)

Diseases and complications

**Objective**: To examine the biology and clinical significance of herpesviruses, including latency and immune evasion.




Herpesvirus family contains several important human viral pathogens. Clinically, herpesviruses exhibit a **wide spectrum** of diseases, some have an

**extensive** host cell range and others have a **narrow** host cell range. the outstanding property of herpesviruses is their ability to establish lifelong **persistent infections** in their hosts and to undergo **periodic reactivation**, their frequent reactivation in elderly and immunosuppressed patients causes serious health complications, curiously, the reactivated infection may be clinically quite different from the disease caused by the primary infection.

## Important Properties of Herpesviruses

**Virion**: Spherical, 150–200 nm in diameter and cubic.

**Genome**: Double stranded DNA, linear and 125–240 kbp.

**Proteins**: More than 35 proteins in virion.

**Envelope**: Contains viral glycoproteins, Fc receptors.

**Replication**: Nucleus, bud from nuclear membrane.

## Outstanding characteristics:

Establish latent infections

Persist indefinitely in infected hosts

Frequently reactivated in immunosuppressed hosts

Some cause cancer

## Overview of Herpesvirus Diseases (some)

- HSV-1 is transmitted primarily in saliva, whereas HSV-2 is transmitted by sexual contact.
- HSV-1 infections occur mainly on the face, whereas HSV-2 lesions occur in

the genital area.

- Although transmission occurs most often when active lesions are present, asymptomatic of both HSV-1 and HSV-2 does occur and plays an important role in transmission.
- 1) The virus replicates in the skin or mucous membrane at the initial site of infection.
- 2) Migrates up the neuron and becomes latent in the sensory ganglion cells.
- 3)HSV-1 becomes latent in the trigeminal ganglia, whereas HSV-2 becomes latent in the lumbar and sacral ganglia.

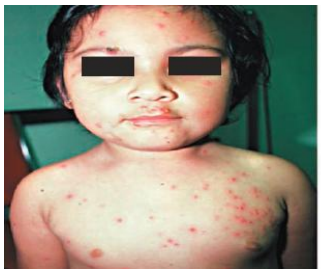
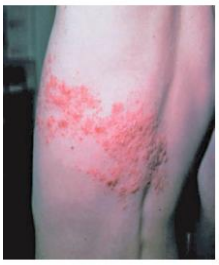
4)The virus can be reactivated from the latent state by a variety of inducers (e.g., sunlight, hormonal changes, trauma, stress, and fever)

**Varicella-Zoster**

- ✓ Varicella (chickenpox) and herpes zoster (shingles) are caused by a single virus
- ✓ Chickenpox follows primary infection in a non-immune individual, whereas herpes zoster is a reactivation of the latent virus
- ✓ VZV is similar to the HSV in its morphology
- ✓ Only one antigenic type of VZV is known

**CMV** replicates in epithelial cells of the respiratory tract, salivary glands and kidneys and persists in lymphocytes, CMV is an important cause of congenital defects, neonatal hearing loss and

mental retardation.

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- **Week 10: Oncogenic Viruses**

**Topics**:

Viruses associated with cancer (HPV, EBV, HBV, HCV, HTLV)

Mechanisms of oncogenesis

Viral oncogenes and host factors

Prevention and screening

**Objective**: To explore the relationship between viral infections and cancer development.

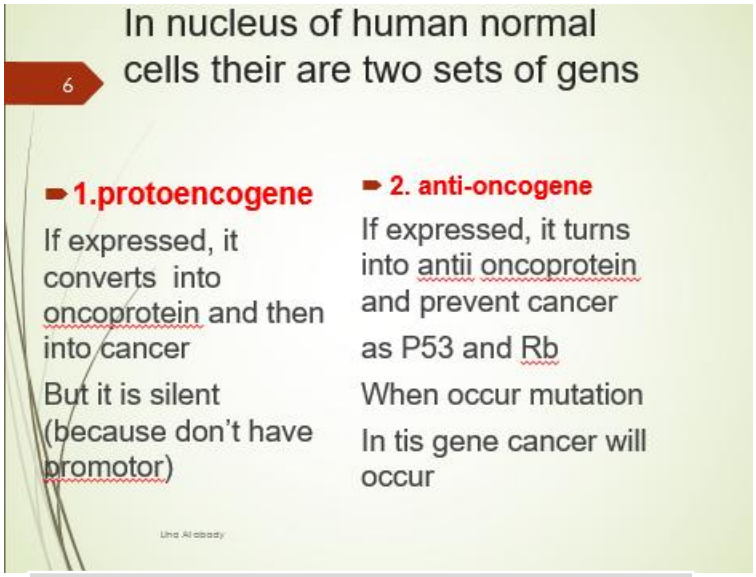
**Introduction**

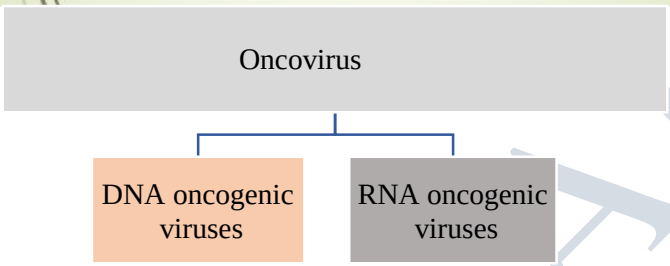
- An **oncovirus** is a virus that induced cancer.
- Globally, almost 20% of cancers are related to infection agents.

11..9% causes by viruses.

- This term originated from studies of highly transforming retroviruses in the 1950–60s, often called oncornaviruses to mean their RNA virus origin.

- Now oncogenic virus refers to any virus with a DNA or RNA genome causing cancer and is the same "tumor virus" or "cancer virus".
- The huge majority of human and animal viruses do not cause cancer,




- **DNA oncogenic viruses**

**Human papilloma** virus (HPV), a DNA virus, causes transformation in cells through interfering with tumor suppressor proteins such as p53.

- **Kaposi's sarcoma-associated herpesvirus (KSHV or HHV-8)** is associated with Kaposi's sarcoma, a type of skin cancer.
- **Epstein-Barr virus (EBV or HHV-4)** is associated with four types of cancers.
- **Merkel cell polyoma virus** – a polyoma virus – is associated with the development of Merkel cell carcinoma.
- **Human cytomegalovirus** (CMV or HHV-5) is associated with mucoepidermoid carcinoma and possibly other malignancies.

- **RNA oncogenic viruses**

- Some RNA viruses have also been associated such as the **hepatitis C virus**
- as well as certain retroviruses, e.g.,
- **human T-lymphotropic virus (HTLV-1)**
- **Rous sarcoma virus (RSV)**

| Virus | Associated cancer types |
|---|---|
| Hepatitis viruses, including hepatitis B (HBV) and hepatitis C (HCV) | Hepatocellular carcinoma (liver cancer). |
| Human T-lymphotropic virus (HTLV) | Adult T-cell leukemia |
| Human papillomaviruses (HPV) | Cancers of cervix, anus, penis, vulva/vagina, and oropharyngeal cancer. |
| Kaposi's sarcoma-associated herpesvirus (HHV-8) | Kaposi's sarcoma, multicentric Castleman's disease and primary effusion lymphoma |
| Merkel cell polyomavirus | Merkel cell carcinoma |
| Epstein–Barr virus (EBV) | Burkitt's lymphoma, Hodgkin's lymphoma, Post-transplant lymphoproliferative disease and Nasopharyngeal carcinoma. |

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## Week 11: Hepatitis Viruses

**Topics:**

Types of hepatitis viruses (A, B, C, D, E)

Transmission and epidemiology

Acute vs chronic infection

Vaccines and treatment options

**Objective**: To compare different hepatitis viruses and their impact on liver health and public health.

### Hepatitis Viruses

Viral hepatitis is a **systemic disease** primarily involving the liver most cases of acute viral hepatitis in children and adults are caused by one of the following **five agents**: Hepatitis A virus (HAV) the etiologic agent of viral hepatitis type A (infectious hepatitis), Hepatitis B virus (HBV) which is associated with viral hepatitis B (serum hepatitis), Hepatitis C virus (HCV) the agent of hepatitis C (common cause of posttransfusion hepatitis), Hepatitis D (HDV) a **defective virus** dependent on coinfection with HBV and Hepatitis E virus (HEV) the agent of enterically transmitted hepatitis.

**Symptoms of a viral liver can include:**

Hepatitis viruses produce acute inflammation of the liver resulting in a clinical illness characterized Jaundice (a change in the color of the skin and the whites of the eyes to a yellow color), feeling sick, abdominal pain, lack of appetite, nausea,

vomiting, diarrhea, slight rise in temperature and headache. regardless of the virus type, identical histopathologic lesions are observed in the liver during acute disease.

## Pathology

Hepatitis is a general term meaning inflammation of the liver microscopically, there is spotty parenchymal cells degeneration with necrosis of hepatocytes and a diffuse lobular inflammatory and disruption of liver cell cords and accompanied by reticuloendothelial (Kupffer) cell hyperplasia, the damaged hepatic tissue is usually restored in 8–12 weeks.

## Different of Hepatitis virus

| Virus | Hepatitis A | Hepatitis B | Hepatitis C | Hepatitis D | Hepatitis E |
|---|---|---|---|---|---|
| **1- Family** | Picornaviridae | Hepadnaviridae | Flaviviridae | Unclassified | Hepeviridae |
| **2- Genus** | *Hepatovirus* | *Orthohepadnavirus* | *Hepacivirus* | *Deltavirus* | *Hepevirus* |
| **3- Virion** | 27 nm, cubic | 42 nm, Spherical | 60 nm, spherical | 35 nm, spherical | 30–32 nm, cubic |
| **4- Envelope** | No | Yes | Yes | Yes | No |
| **5- Genome** | ssRNA | dsDNA | ssRNA | ssRNA | ssRNA |
| **6- Genome size (kb)** | 7.5 | 3.2 | 9.4 | 1.7 | 7.2 |
| **7- Stability** | Heat and acid Stable | Acid sensitive | Ether sensitive, acid sensitive | Acid sensitive | Heat stable |
| **8- Chronic disease** | Never | Often | Often | Often | Never |
| **9- Oncogenic** | No | Yes | Yes | Unknown | No |
| **10-Incubation period** | 15-45 day | 45-160 day | 15-150 day | 30-60 day | 16-60 day |

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## Week 12: Rabies and Neurotropic Viruses

Topics:

Rabies virus structure and pathogenesis

Other neurotropic viruses (e.g., poliovirus, arboviruses affecting CNS)

Transmission routes

Vaccination and post-exposure treatment

**Objective**: To understand viruses that target the nervous system and their prevention.

### Rabies viruses and other neurotropic viruses Rabies viruses

Many different viruses can invade the central nervous system and cause disease, Rabies is an acute infection of the central nervous system that is almost always **fatal** and the virus is usually transmitted to humans from the **bite** of a rabid animal, although the number of human cases is small rabies is a major public health problem because it is widespread among animal reservoirs.

### Structure

Rabies virus is a rhabdovirus with morphologic and biochemical properties in common

with vesicular stomatitis virus of cattle and several animal, plant, and insect viruses. Rhabdoviruses are rod or bullet shaped particles measuring 75 × 180 nm, the particles are surrounded by a membranous envelope with protruding spikes 10 nm long, peplomers are composed of trimers of the viral glycoprotein. inside the envelope is a ribonucleocapsid, genome is single stranded, negative sense RNA, 12 kb and molecular weight 4.6 × 106 million.

## Classification

The viruses are classified in the family **Rhabdoviridae**, Rabies viruses belong to the genus ***lyssavirus***.

**Infection** rhabdoviruses are very widely distributed in nature, infecting vertebrates, invertebrates, and plants. many of the animal rhabdoviruses infect insects but rabies virus does not.

### Reactions to physical and chemical agents

Rabies virus survives storage at 4°C for weeks and at −70°C for years and it is inactivated by CO2, so on dry ice it must be stored in glass sealed vials.

Rabies virus is **killed rapidly** by exposure to ultraviolet radiation or sunlight, by heat (1 hour at 50°C) by lipid solvents (ether, 0.1% sodium deoxycholate) by trypsin by detergents and by extremes of pH.

### Clinical Findings

Rabies is primarily a disease of lower animals and is spread to humans by **bites of rabid animals** or by **contact with saliva from rabid animals**, the disease is an acute, fulminant, fatal encephalitis and the incubation period in humans is typically **1–3 months** but may be as short as 1 week or more than a year and it is usually shorter in children than in adults

## Important Properties of Rhabdoviruses

**Virion:** Bullet shaped, 75 nm in diameter × 180 nm in length.

**Composition:** RNA (4%), protein (67%), lipid (26%) and carbohydrate (3%).

**Genome:** Single stranded RNA, linear, nonsegmented, negative sense, molecular weight 4.6 million, and size 12 kb.

**Proteins:** Five major proteins.

**Envelope:** Present.
**Replication:** Cytoplasm, virions bud from plasma membrane.

**Neurotropic viruses**: that cause infection include Japanese Encephalitis, polio, mumps, measles and rabies as well as diseases caused by members of the family Herpesviridae such as herpes simplex, varicella zoster, Epstein Barr and cytomegalovirus.

### Terminology

A neurotropic virus is said to be **neuroinvasive e.g. Herpes Simplex Virus** if it is capable of accessing or entering the nervous system and **neurovirulent** e.g. **Rabies virus** if it is capable of causing disease within the nervous system. Both terms are often applied to central nervous system infections.

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## Week 13: Arboviruses and Viral Hemorrhagic Fevers

### Topics:

Overview of arboviruses (Dengue, Zika, Chikungunya)

Transmission via arthropods

Viral hemorrhagic fevers (Ebola, Marburg)

Outbreak control strategies

**Objective**: To identify vector-borne and hemorrhagic viruses and assess the risks and control measures.

## Arboviruses and viral haemorrhagic virus

### Arboviruses

The arthropod borne viruses (arboviruses) represent ecologic groupings of viruses with complex transmission cycles involving arthropods, these viruses have diverse physical and chemical properties and are classified in several virus families, the major arbovirus diseases worldwide are yellow fever, dengue and Japanese B encephalitis.

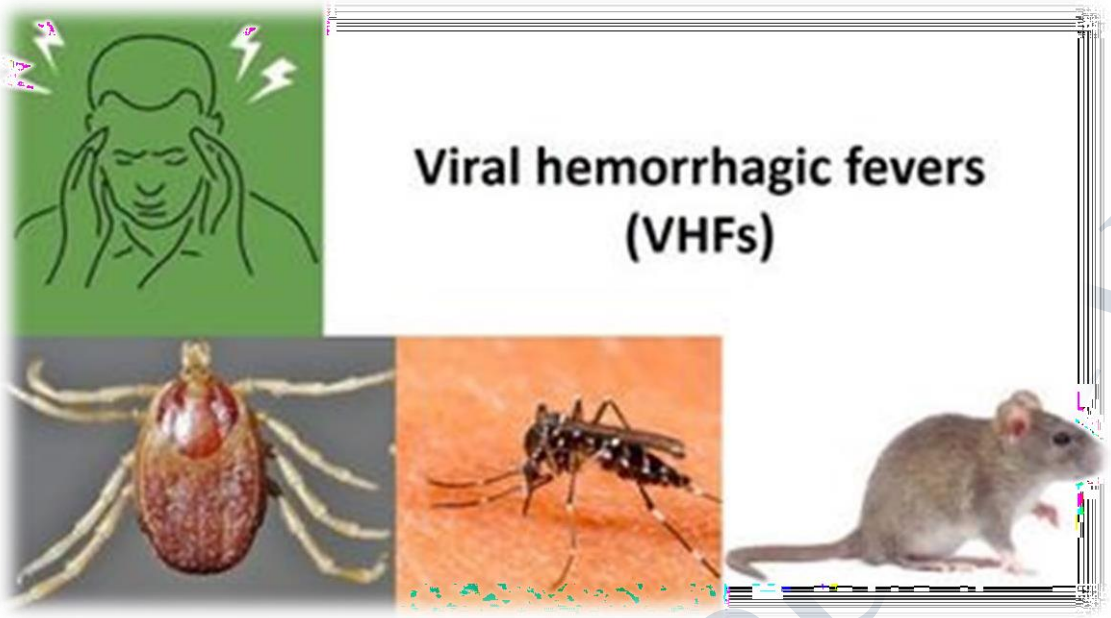
### Classification

Arboviruses are classified among Bunyaviridae, Flaviviridae, Reoviridae and Togaviridae families.

**Transmission** of arboviruses by bloodsucking arthropods from one vertebrate host to another.

### Human arboviruses infection

Diseases produced by arboviruses may be divided into **three clinical syndromes :** (1) fevers of an undifferentiated type with or without a maculopapular rash and usually benign, (2) encephalitis (inflammation of the brain), often with a high case-fatality rate and (3) hemorrhagic fevers also frequently severe and fatal and some arboviruses may be associated with more than one syndrome e.g. dengue.




## viral haemorrhagic viruses

Viral hemorrhagic fevers (VHFs) are a group of diseases that are caused by several distinct families of viruses, the term **"viral hemorrhagic fever"** refers to a condition that affects many organ systems of the body and damages the overall cardiovascular system and reduces the body's ability tofunction on its own. symptoms of this type of condition can vary but often include bleeding or hemorrhaging, some VHFs cause relatively mild illness while others can cause severe life threatening disease and most VHFs have no known cure or vaccine.

**common characteristics:**

1- They are RNA viruses meaning viruses that have ribonucleic acid (RNA) as their genetic material.

2- They are covered or enveloped in a lipoprotein outer layer making it easier to destroy these viruses with physical (heat, sunlight and gamma rays) and chemical (bleach, detergents and solvents) methods.

3- They naturally exist in animal or insect populations referred to as host populations.

4- They spread to people when a person encounters an infected animal or insect host and after the initial spread into the human population and some VHF viruses can continue to spread from person to person.

5- Outbreaks of VHFs in people can be difficult to prevent since they cannot be easily predicted.

**Transmition**

Person to person transmission of some VHFs can occur, VHF viruses can spread to people when they come in contact with infected animals or insects. for many VHFs person to person transmission can then continue often

## Week 14: Adenoviruses, Poxviruses, and Parvoviruses

**Topics:**

Structure and replication of adenoviruses

Poxviruses (smallpox, monkeypox)

Parvoviruses (B19)

Clinical relevance and vaccines

**Objective**: To describe the characteristics and diseases associated with these diverse DNA viruses.

**Adeno , pox and parvo viruses**

**Adenoviruses**

Adenoviruses can replicate and produce disease in the respiratory, gastrointestinal, urinary tracts and in eye, many adenovirus infections are subclinical and virus may persist in the host for months and about one third of the 57 known human serotypes are responsible for most cases of human adenovirus disease, a few types serve as models for cancer induction in animals.

**Important Properties of Adenoviruses Virion:** cubic,

70–90 nm in diameter.

**Composition:** DNA (13%) and protein (87%). **Genome:** Double stranded DNA, linear and 26–45 kbp. **Proteins:** Important antigens.

**Envelope:** None. **Replication:** Nucleus. **Poxviruses**

Poxviruses are the largest and most complex of viruses infecting humans and the family encompasses a large group of agents that are similar morphologically and share a common nucleoprotein antigen, Infections with most poxviruses are characterized by a rash.

## Parvoviruses

Parvoviruses are the smallest DNA animal viruses, Parvovirus B19 is pathogenic for humans and has a tropism for erythroid progenitor cells.

## Classification

There are **two subfamilies** of Parvoviridae: the Parvovirinae, which infect vertebrates and Densovirinae which infect insects.

**Compere between poxviruses and parvoviruses**

| **Poxviruses.** | Charectrastc | Parvoviruses |
|---|---|---|
| Complex. | **1- Virion symmetry** | Cubic. |
| 300–400 nm in length × 230 nm. | **2- Virion diameter** | 18–26 nm. |
| 9••130–375 kbp. | **4- Size of genome** | 5.6 kb. |

| | | |
|---|---|---|
| DNA (20%), protein (80%). | **5- Composition** | DNA (3%), protein (90%), lipid (5%). |
| Double stranded DNA. | **6- Genome** | Single stranded DNA |
| contain more than 100 polypeptides. | **7- Proteins** | One major (VP2) and one minor (VP1). |
| Present. | **8- Envelop** | None. |
| Cytoplasm. | **9- Replication** | Nucleus. |
| Large and complex. | **10- Size** | Very simple. |
| smallpox virus. | **11- Example** | B19. |

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## Week 15: Retroviruses and AIDS

**Topics**:

Retrovirus replication (HIV as a model)

Reverse transcription

HIV structure, transmission, and lifecycle

Pathogenesis and AIDS progression

Antiretroviral therapy

**Objective**: To understand the unique replication strategy of retroviruses and the global impact of HIV/AIDS

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## Retroviruses and ADIS

## Retroviruses

There are RNA viruses that belong to family Retroviridae (Re = Revers, tr = transcriptase) members of this family possess the characteristic biochemical feature is the presence of RNA dependent DNA polymerase (revers transcriptase) within the virus. Retroviruses are spherical, enveloped viruses, 80–110 nm in diameter, whose genome contains two copies of linear, positive sense and single stranded RNA.

Each monomer RNA is 7–11 kb in size and particles contain a helical nucleocapsid within an cubic capsid and replication is unique, the virion contains a reverse transcriptase enzyme that produces a DNA copy of the RNA genome this DNA becomes circularized and integrated into host chromosomal DNA and the virus is then replicated from the integrated "provirus" DNA copy and virion assembly occurs by budding on plasma membranes. Hosts remain chronically infected.

## AIDS

Human Immunodeficiency Virus (HIV) types derived from primate lentiviruses are the etiologic agents of Acquired Immune Deficiency Syndrome (AIDS), illness was first described in **1981** and HIV-1 was isolated by the end of **1983** since then AIDS has become a worldwide epidemic.

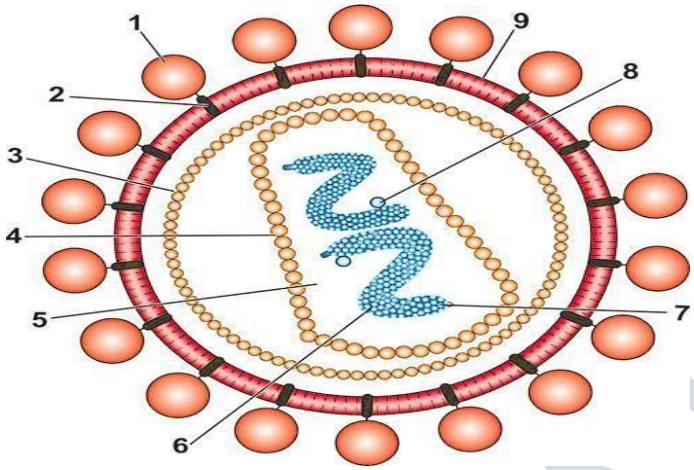
Millions are now infected worldwide once infected individuals remain infected for life. within a decade if left untreated the vast majority of HIV infected individuals develop fatal opportunistic infections as a result of HIV induced deficiencies in the immune system. AIDS is one of the most important public health problems worldwide at the start of the 21st century.

### Routes of transmission

Virus is present in the blood, semen, cervical and vaginal secretions and these sources are important in transmission, HIV is spread only by three modes

1- sexual contact with infected persons (heterosexual or homosexual) efficiency anal intercourse 1% and vaginal intercourse 0.1%.

2- by blood and blood products, efficiency >90%.



## Clinical Findings

Symptoms of acute HIV infection are **nonspecific** and include fatigue, rash, headache, nausea, and night sweats, AIDS is characterized by pronounced suppression of the immune system and development of a wide variety of severe opportunistic infections or unusual neoplasms. the more serious symptoms in adults are often preceded by a prodrome that can include fatigue, malaise, weight loss, fever, shortness of breath, chronic diarrhea, white patches on the tongue and lymphadenopathy. the interval between primary infection with HIV and the first appearance of clinical disease is usually long in adults averaging about **8–10 year.**

**مدة المحاضرة:** 1 ساعة نظري 2 ساعة عملي

**الأنشطة المستخدمة:**

1. أنشطة تفاعلية صفية
2. أسئلة عصف ذهني
3. أنشطة جماعية (إذا تطلب الامر)
4. واجب بيتي
5. واجب الكتروني

**أساليب التقويم:**

1. التغذية الراجعة الفورية من قبل التدريسي (التقويم البنائي).
2. اشراك الطلبة بالتقويم الذاتي (تصحيح اخطائهم بأنفسهم).
3. التغذية الراجعة النهائية (التقويم الختامي)،