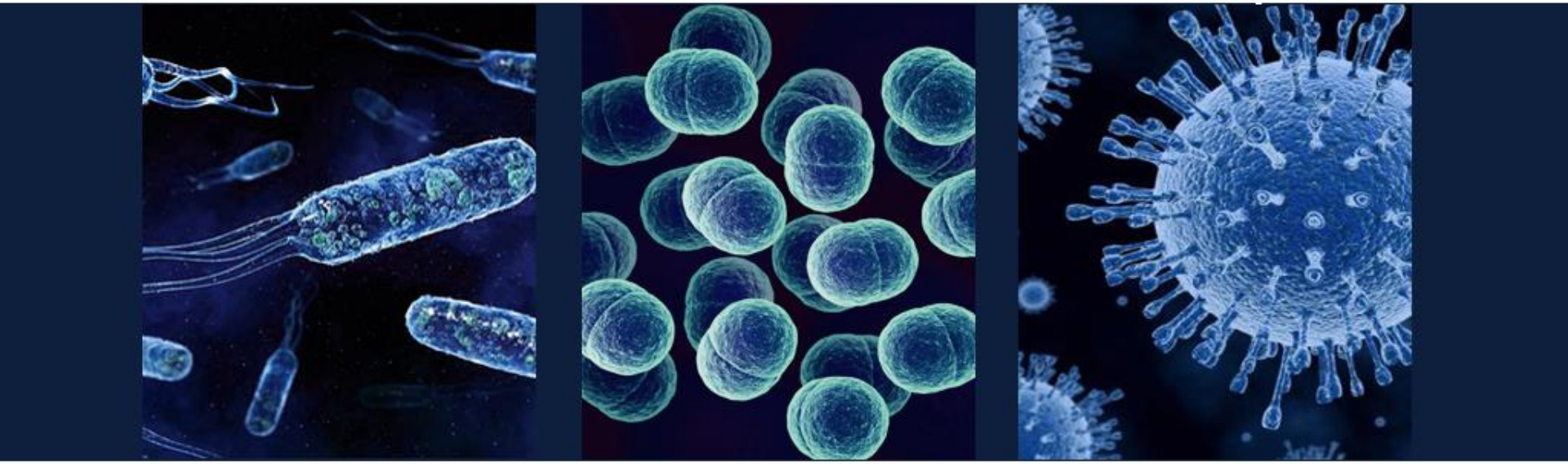
جامعة الملك سعود
King Saud University

MICROBIOLOGY TEAM 435

هذا العمل لا يغني عن المرجع الأساسي للمذاكرة



Lecture 8

Viral Pathogenesis

Objectives:

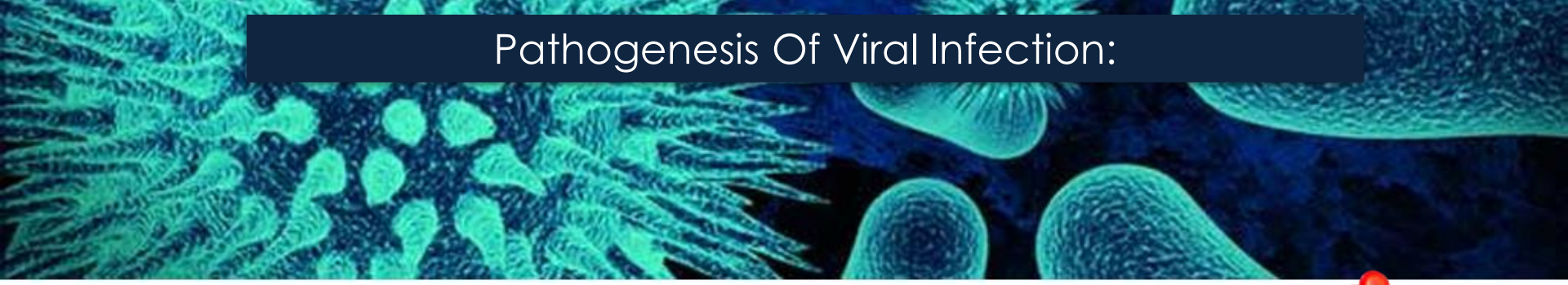
- Definition and levels of viral pathogenesis.
- Types of viral infections at cellular level.
- Pathogenesis at host level.
- The immune response to viral infection.
- The stages of viral infection.
- The types of viral infections at host level.

important:

RSV = Respiratory syncytial virus
HAV = Hepatitis A virus
HBV = Hepatitis B virus.
HCV = Hepatitis C virus
HIV = Human immunodeficiency virus
HPV = Human papillomavirus
HSV = Herpes simplex virus

HTLV = The human T-lymphotropic (leukemia) virus

YFV = Yellow Fever Virus
VZV = Varicella zoster virus



Pathogenesis Of Viral Infection:

Pathogenesis Of Viral Infection:

- Viral Disease At The Cellular Level (Cytopathogenesis):
  - Abortive
    "Vs Not Produced"
  - Productive
    "Vs Produced"
  - Non-productive
    "Vs Not Produced But Viral NA Present"
- Viral Disease At The Host Level:
  - Asymptomatic Infection
    "Most Common"
  - Persistent Infection:
    - Late Complication Of Acute Infection
    - Chronic Infection
    - Latent Infection
  - Acute Infection

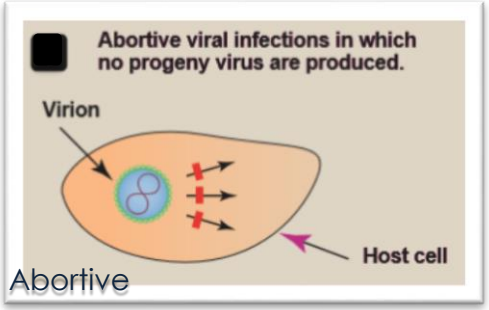
Extra:
Only viral nucleic acid is present, the virus itself is not produced and that is why it is called non-productive.

Pathogenesis Of Viral Infection:

1- Abortive Infection:

- Viruses don't complete the replication cycle.
- Due to: mutation, defective interfering particles & the action of IFNs.

(Extra: ifns or interferons are proteins released by animal cells, usually in response to the entry of a virus, which has the property of inhibiting virus replication.)



Abortive

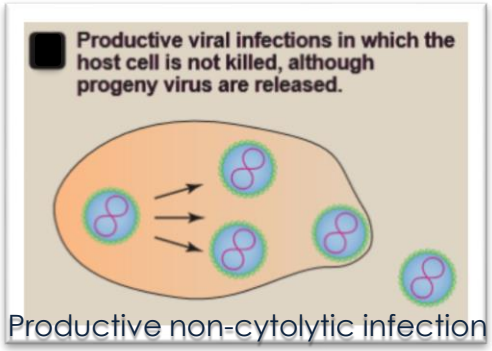
2- Productive Infection:

Non-cytolytic Infections:

- Viruses Replicate & Produce Progeny
- Viruses Releases By Cell Budding & Little Or No CPE
- Identified By Hemadsorption & Direct IF

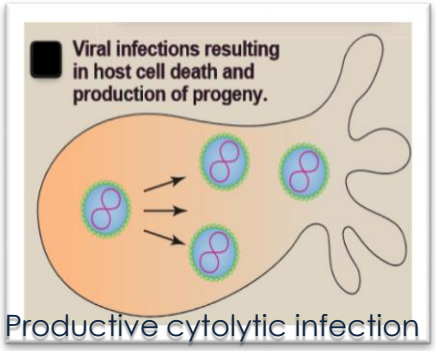
Cytolytic Infections:

- Virus Replicate & Produce Progeny (Progeny: Offspring)
- Cause Of Cell Death & Cytopathic Effects
- Inhibition Of Cellular Protein & NA Synthesis



Productive non-cytolytic infection

Hemadsorption is the adherence of red blood cells to other cells, particles, or surfaces



Productive cytolytic infection

Pathogenesis Of Viral Infection:

3- Non-productive Infections:

- Viruses infect cells that restrict or lack the machinery for transcribing viral genes.
- Viral genome is found either integrated into cell DNA or as a circular episome or both.

Latent infection:

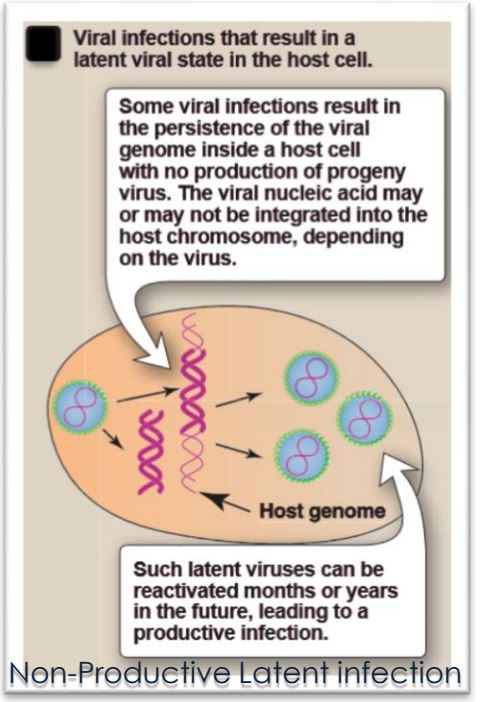
The cell retains its normal properties

There is limited expression of viral genes e.g. HSV

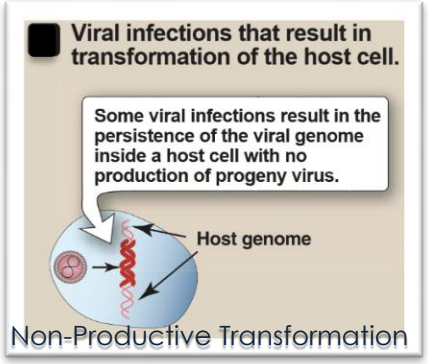
Transformation:

Cause tumor in animals & human and it can transform cell culture e.g. EBV, HPV & HTLV

Virus can stimulate uncontrolled cell growth **causing transformation** by: alternating the balance between growth activators & growth suppressors gene products.



Non-Productive Latent infection

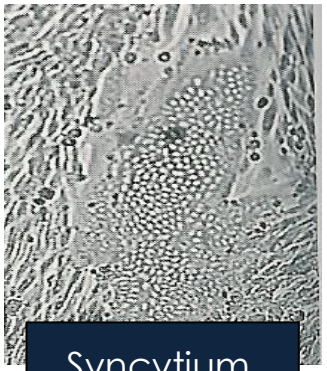


Non-Productive Transformation

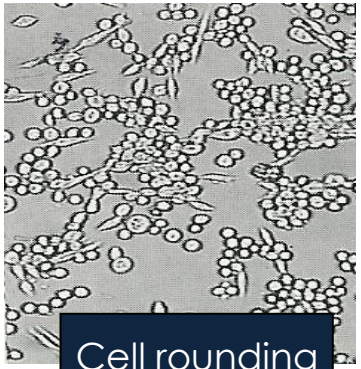
Cytopathic effects

Cytopathic effects
seen in several forms:

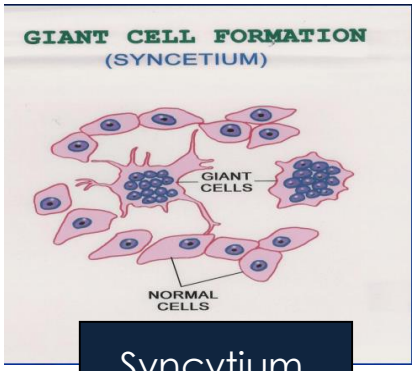
- Cell lysis
  "cell disintegration"
  (non-enveloped viruses)
- Cell rounding
  (enveloped)
- Syncytium formation
  "Cell fusion"
  Ex: Herpes Paramyxo Viruses
  Respiratory Syncytial virus (RSV)
- Inclusion Body formation



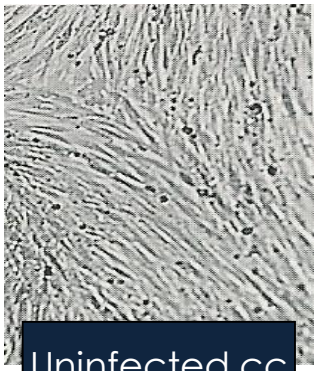
Syncytium



Cell rounding



Syncytium



Uninfected cc

Cytopathic effects: Inclusion

Takes a Place in:

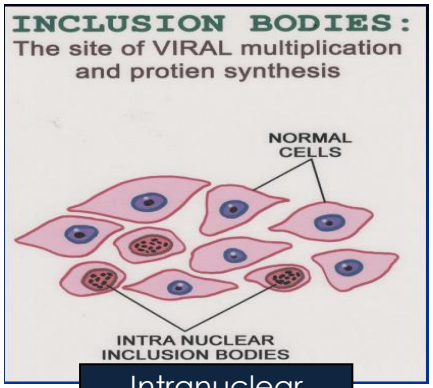
Intranuclear (DNA Vs):

- Protein synthesis and multiplication
- accrue in the nucleus. Ex: Herpes Vs.

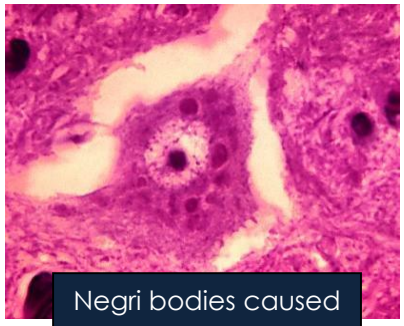
Intracytoplasmic (RNA Vs):

- Protein synthesis and multiplication accrue in the cytoplasm.
- Ex: Rabies Vs. it causes Negri bodies
- Ex: Cytomegalo Vs. It causes Owl's eye.

Takes a several forms:
1- Single/multiple
2- Small/large
3- Round/irregular

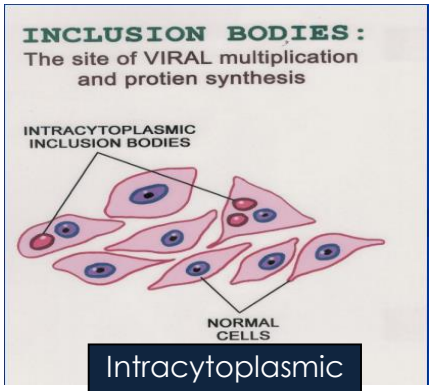


Intranuclear inclusions



Negri bodies caused by Rabie viruses

Owls eye inclusions by CMV VIRUS



Intracytoplasmic inclusions

❖ Cytopathic effects video.

Pathogenesis at Host Level

1-Transmission of the virus & its entry into the host.

2-Replication of the virus & damage to cells.

3-viruses remain localized or spread to other organs .

4-Viral shedding.

5. The immune response as
   -Host defense
   -Immunopathogenesis

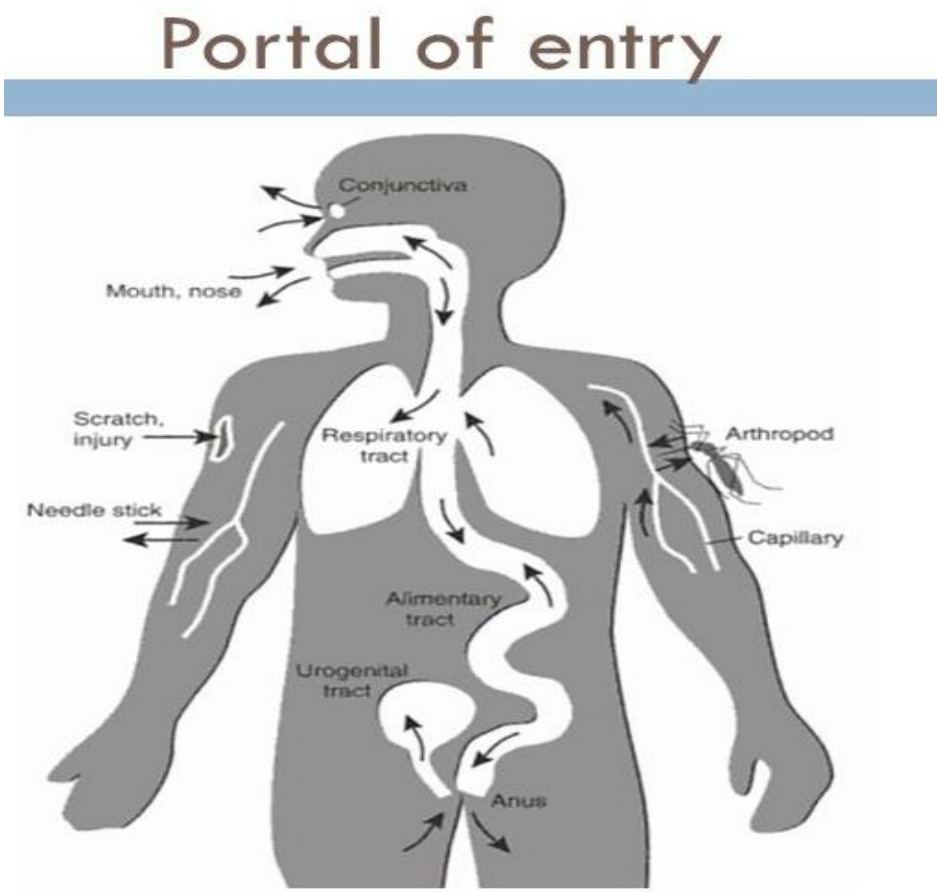
Pathogenesis at Host level

Transmission of the virus & its entry to the host:

1) Person to person:

Horizontal:
- Skin contact.
- Blood Respiratory route.
- Fecal - oral route.
- Genital contact.

Vertical:
- from the mother to her baby.
- During delivery through an infected birth canal.



2) Animal to person

Reservoir → Human (Rabies v.)

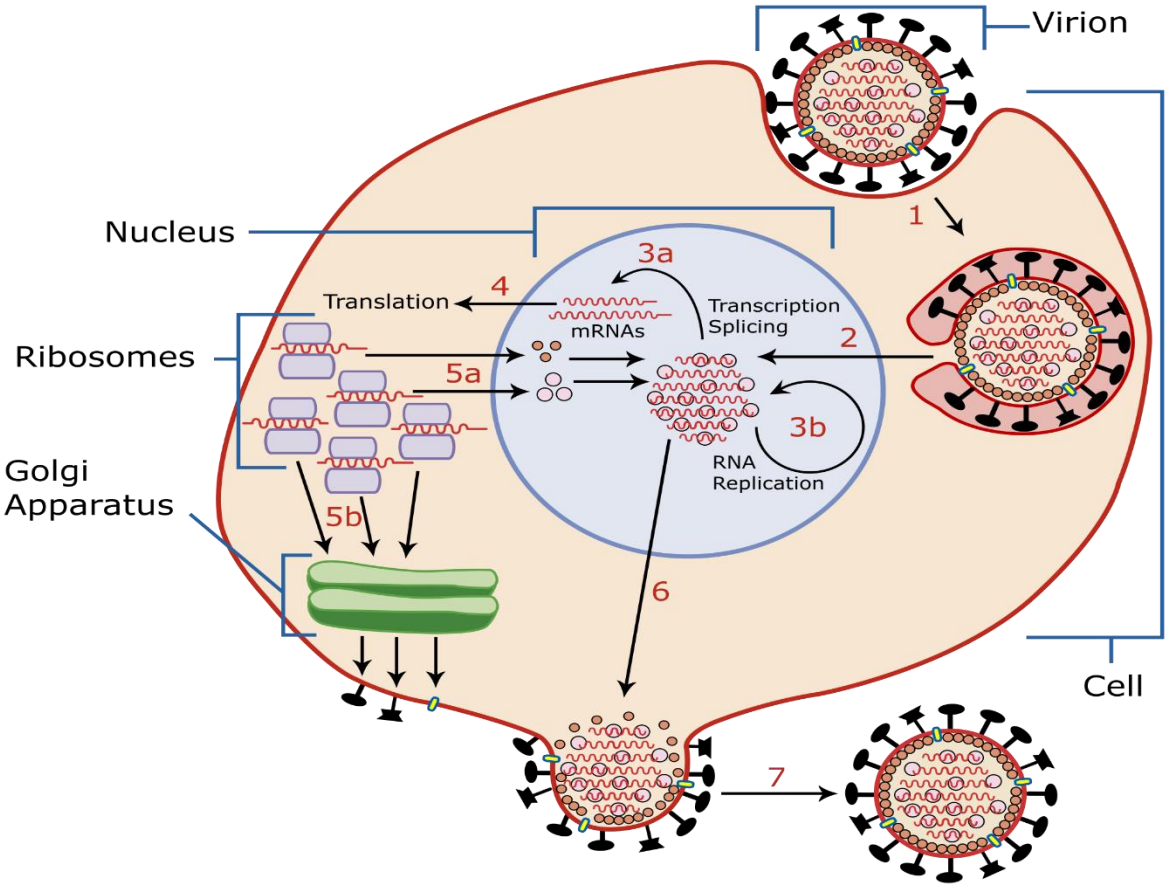
Reservoir → Human (YFV)

vector

Virus Shedding

Viral shedding refers to a type of spreading Mechanism of a virus through the body.

it is expulsion and release of virus progeny "off spring" following successful reproduction during a host-cell infection. Once replication has been completed and the host cell is exhausted of all resources in making viral progeny, the viruses may begin to leave the cell by several methods

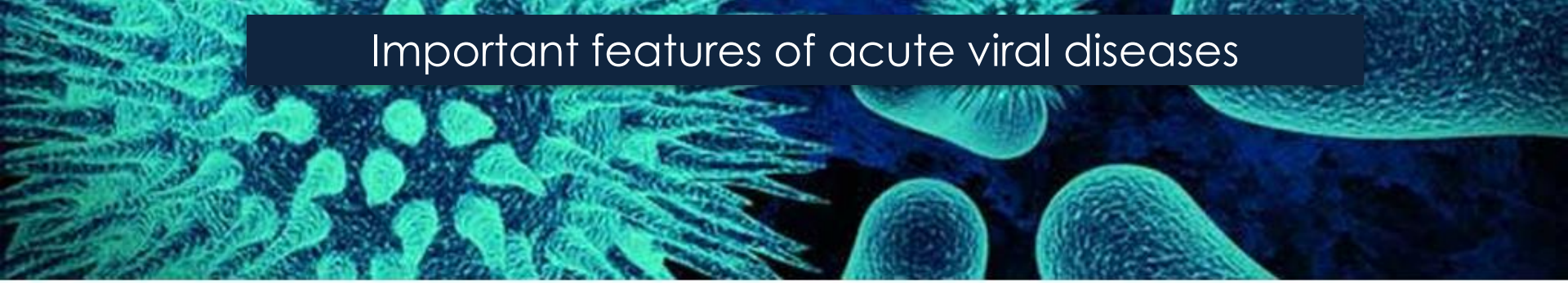


Common Routes of Human Infection by Viruses

Route of Entry	Virus	Disease (L/G)
-Skin		
Mild Trauma	HPV	Warts (L)
Injection (Blood)	HBV,HCV, HIV	Hepatitis B, Hepatitis C ,AIDS (G)
Bite of insect animal	Yellow fever virus Rabies virus	Yellow fever (G) Rabies (G)
-Respiratory tract	▪HSV-1 ▪Rhinovirus ▪RSV ▪Adenovirus ▪VZV ▪Measles virus	Gingivostomatitis (L) (URT) Common cold (L) (URT) Bronchiolitis (L) (LRT) Pneumonia (L) (LRT) Chickenpox (G) Measles (G)
-GIT	Rotavirus HAV Poliovirus	Diarrhea (L) Hepatitis A (G) Poliomyelitis (G)
-Genital tract	HSV-2 HBV HIV	Genital herpes (L) Meningitis (G) Encephalitis (G) Hepatitis B (G) AIDS(G)

Note: هذا الجدول موجود في سلايدات الدكتور عبدالكريم

Important features of acute viral diseases



	Local Infections	Generalized (systemic) infections
Example of disease	Rhinovirus	Measles
Site of Pathology	Portal of entry	Distant site
IP (incubation period)	Relatively short	Relatively long
Viremia (presence in the blood)	Absent	Present
Duration of immunity	Variable- may be short	Usually life long
Role of secretory AB (anti bodies) [IgA] in resistance	Usually important	Usually not important

The immune response to virus

The immune response acts as: Host defense – Immunopathogenesis.

- **Macrophages:**
APC, Phagocytosis and cytokines production.

- **Natural killer cells:**
Lysis of VICs.

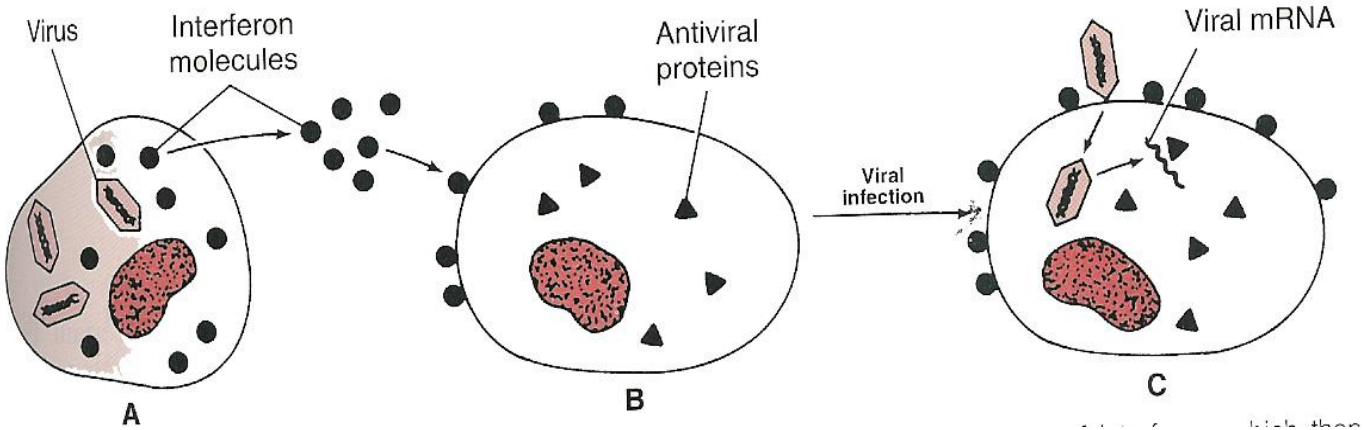
- **Cytokines:**

Interferons "INF":

- α, β IFN: inhibit the viral and the host cell mRNA translation
- γ IFN: stimulate phagocytosis and killing by macrophages and NK cells

Interleukin "IL":

- Stimulates AB production
- Activate T cells & CMI
- Suppress the IR



The immune response to virus by adaptive immunity

Cell-mediated Immunity "**CMI**":

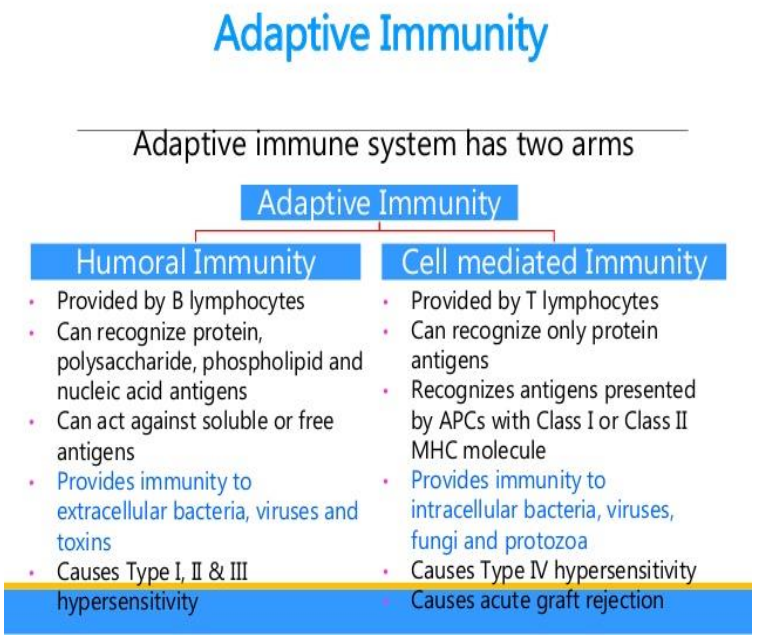
- Effective against intracellular viruses.
- Lysis of virally infected cells by CTC [CD8].

Humoral Immunity:

- Effective on extracellular viruses "viremia".
- Usually by neutralization(1).

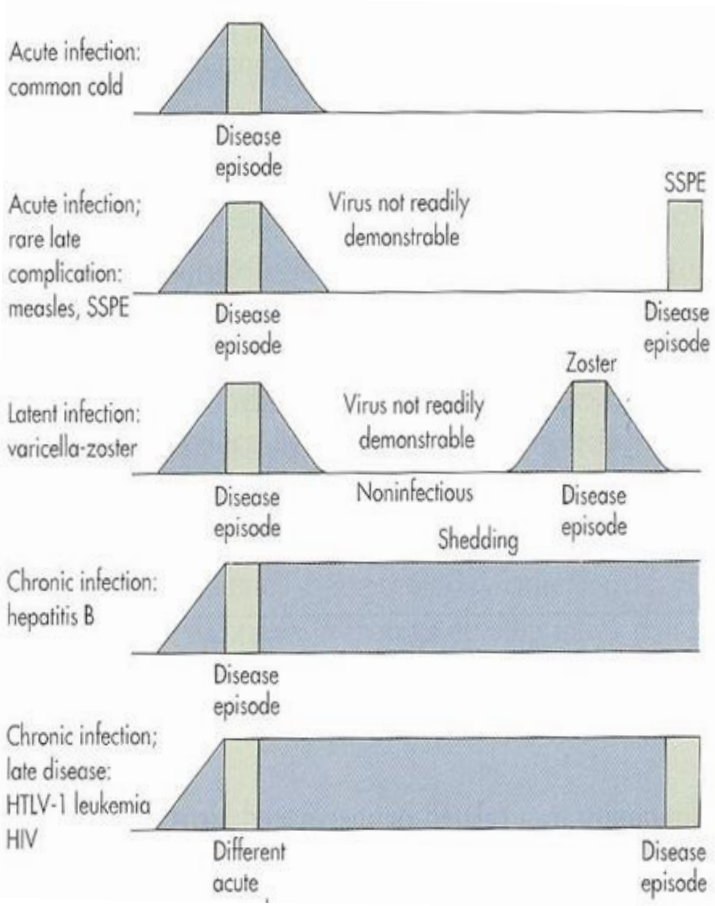
Stages of a typical viral infection:

1. The incubation period "IP".
2. Prodromal period "General symptoms".
3. The specific-illness period:
   The signs & symptoms of viral diseases are the result of cell killing by:
   • Inhibition of cellular macromolecular synthesis.
   • Immunologic attack "Immunopathogenesis" cytotoxic T cells. e.g. hepatitis (HAV.HBV.HCV).
4. The recovery period.



P.S: The cellular immunity is faster than the Humoral immunity

Types of viral infections at host level



- 1-Asymptomatic infection
- 2-Persistent infection
  - Late complication of acute infection
  - Latent infection
  - Chronic infection
- 3-Acute infection

Summary

- Viral pathogenesis
  - Viral diseases
    - Cellular level
      - Types of viral infection
        - Non-productive "Vs. not produced, But viral NA present"
          - Latent
          - Transformation
        - Productive "Vs. Produced
          - Cytolytic
          - Non-Cytolytic
        - Abortive — Vs. not produced
    - Host level
      - Types of viral infection
        - Asymptomatic infection
        - Acute infection
        - Persistent infection
      - Mechanisms of the disease
        - Transmission
          - Person to person
            - Horizontal transmission
            - Vertical transmission
          - Animal to person
        - Replication
        - Localized or spread
        - Viral shedding
  - Stages of viral infection
    - The incubation period "IP"
    - Prodromal period "symptoms"
    - The specific illness period
    - The recovery period
  - The immune response to virus
    - Macrophages — APC, Phagocytosis & cytokines production
    - Natural killer cells "NK" — Lysis of VICs
    - Cytokines
      - Interferons "IFNs"
        - α, β IFN: inhibit the mRNA translation
        - γ IFN: stimulate phagocytosis
      - Interleukin "IL"
        - Stimulate Ab production
        - Activate T cells & CMI
        - Suppress the IR
    - CMI — Effective against intracellular Vs
    - Humoral immunity — Effective against extracellular Vs.

Online Quiz

Just click here

Videos

-Immune response

-Viral pathogenesis steps

-natural killer cells

Books that could help you

-Medical Microbiology and Immunology
-Medical Microbiology.
-Lippincott's Illustrated Reviews: Microbiology

MiRobiology TEAM 435

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إن أصبنا فمن **الله** عز وجل، وإن أخطأنا فمن **أنفسنا والشيطان**