

Introduction to medical virology **“Viral Pathogenesis”**

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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.

Pathogenesis of viral infection

- ❖ Viral disease at the cellular level

- Cytopathogenesis

- ❖ Viral disease at the host level

- Mechanism of the disease

Cytopathogenesis:

The types of viral infections at cellular level

The effects on cells/
Type of Infection

Virus Production

➤ Abortive

Vs not produced

➤ Productive

- Cytolytic
- Non-cytolytic
[Persistent]

Vs Produced

Vs Produced

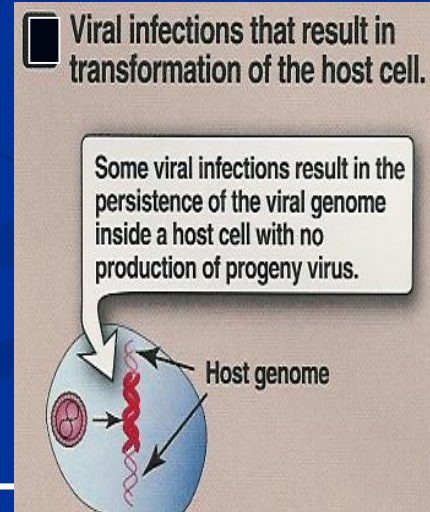
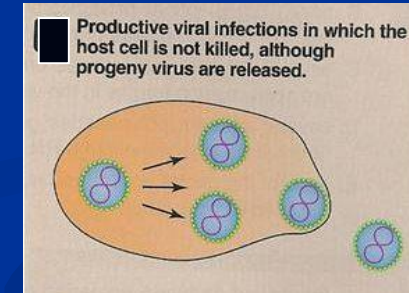
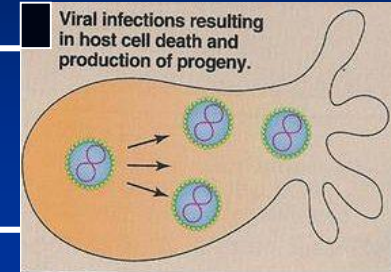
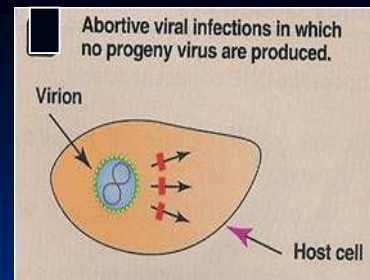
➤ Non-productive

Vs not Produced

- Latent [P_t]
- Transformation [P_t]

Viral NA present

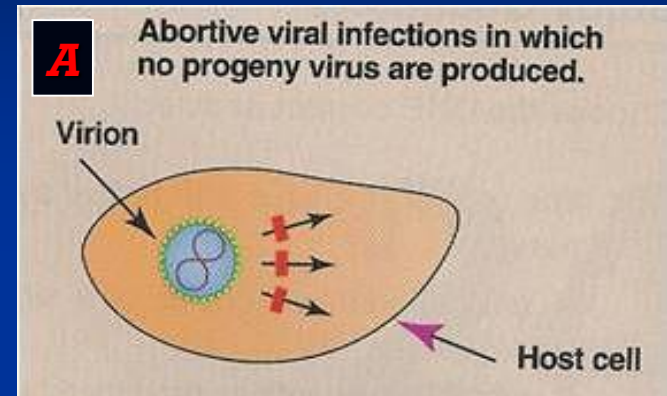
Viral NA present



The types of viral infections at cellular level

A) Abortive Infections:

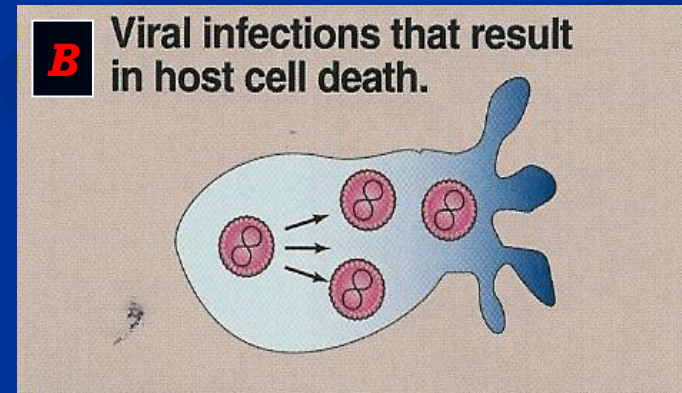
- Viruses don't complete the replication cycle
- Due to mutation, defective interfering particles & the action of IFNs



B) Productive Infections:

1. Cytolytic Infections

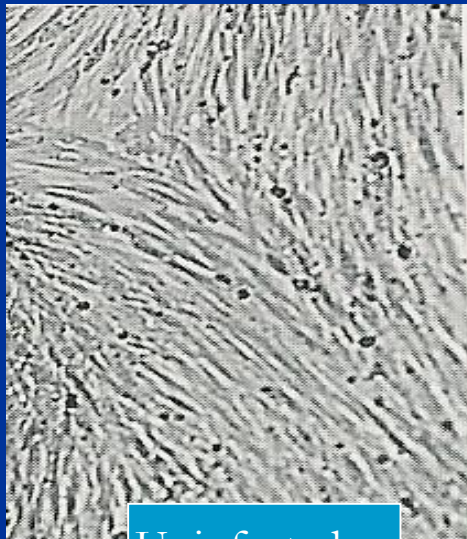
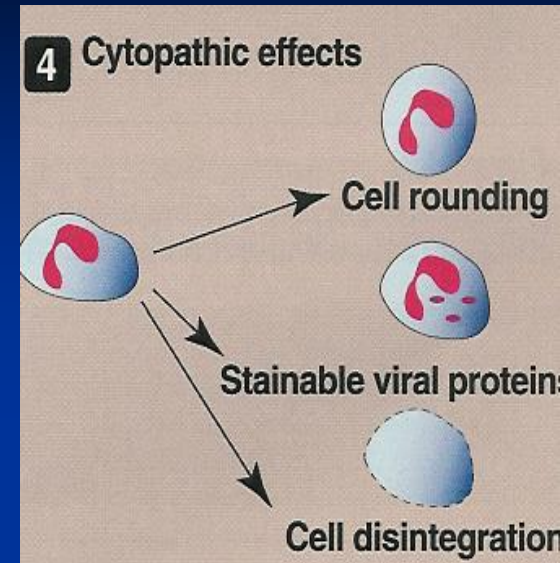
- Viruses replicate & produce progeny
- Cell death & Cytopathic effects [CPE]
- Inhibition of cellular protein & NA synthesis



Cytopathic Effects

■ CPE can take several forms:

1. Cell lysis
2. Cell rounding
3. Syncytium formation
4. Inclusion bodies formation



Uninfected cc



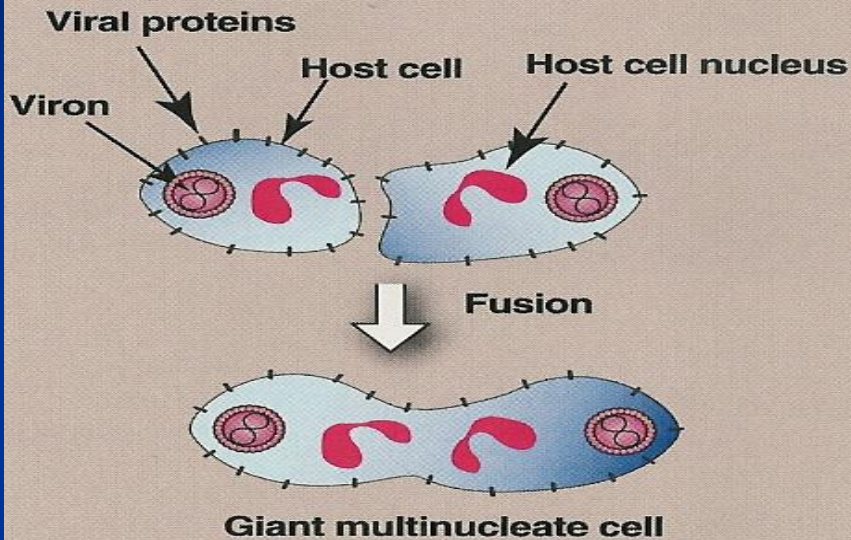
Cell rounding



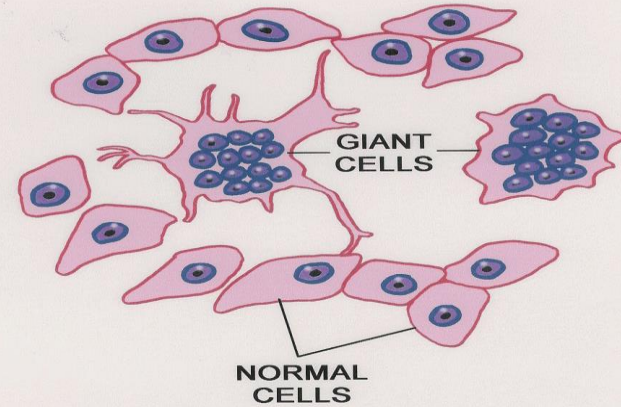
Syncytium

Syncytium formation

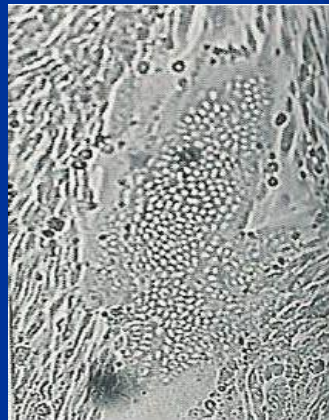
3 Viral infections that result in host cell fusion



GIANT CELL FORMATION (SYNCETIUM)



Herpes
paramyxoVs



Cc ;Syncytium (RSV)

Inclusion bodies formation

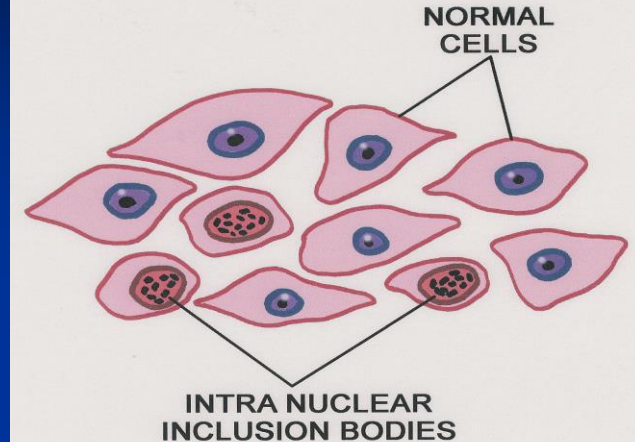
- ❖ **Site:**
 - Intranuclear [Herpes]
 - Intracytoplasmic [Rabies]

- ❖ **Take several forms:**

- Single/multiple
- Small/large
- Round/irregular

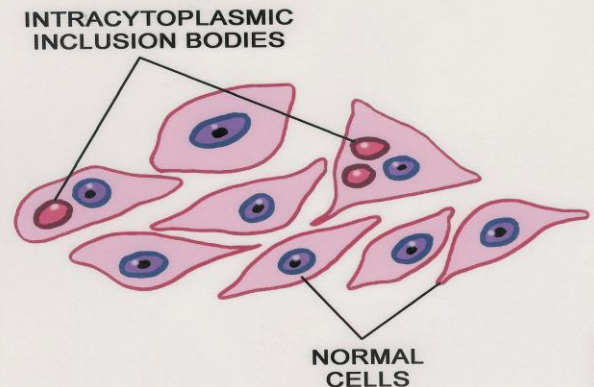
INCLUSION BODIES:

The site of VIRAL multiplication and protien synthesis

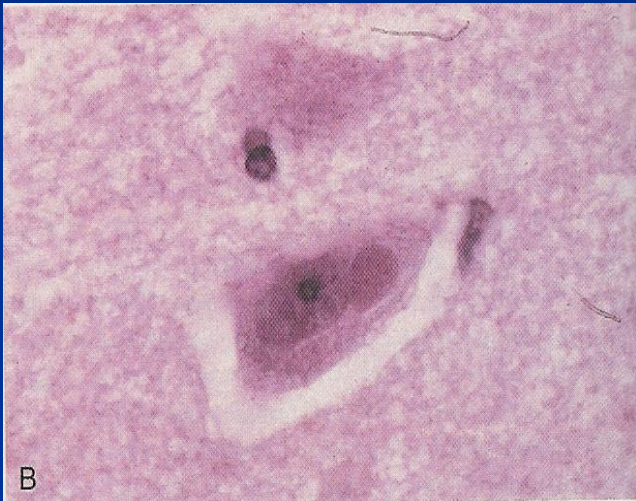


INCLUSION BODIES:

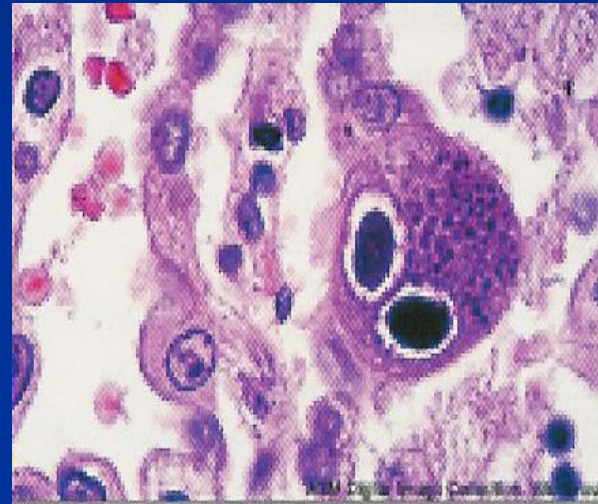
The site of VIRAL multiplication and protien synthesis



Inclusion bodies formation



Negri bodies caused by
Rabies virus



Owl's eye inclusions
caused by CMV

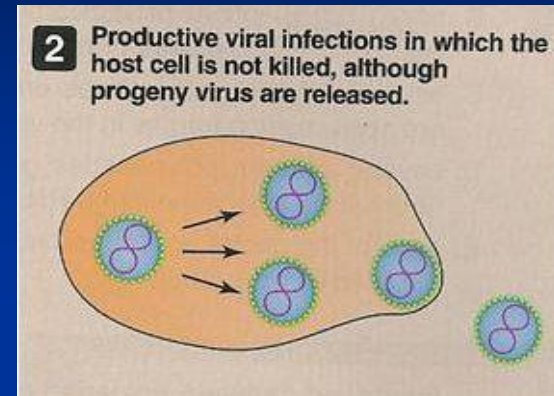
The types of viral infections at cellular level

B) Productive Infections:

1. Cytolytic Infections

2. Non-cytolytic infections :

- Viruses replicate & produce progeny
- Vs released by cell budding & little or no CPE
- Identified by hemadsorption & direct IF



Infl. A – Hemadsorption (MK)



The types of viral infections at cellular level

C) Non-productive Infections:

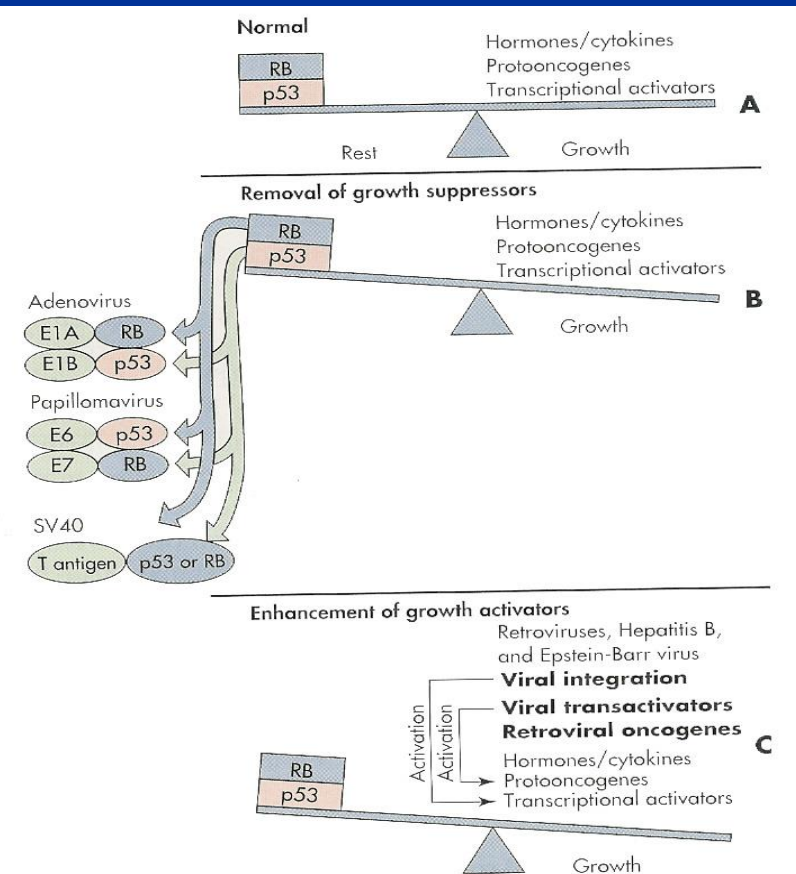
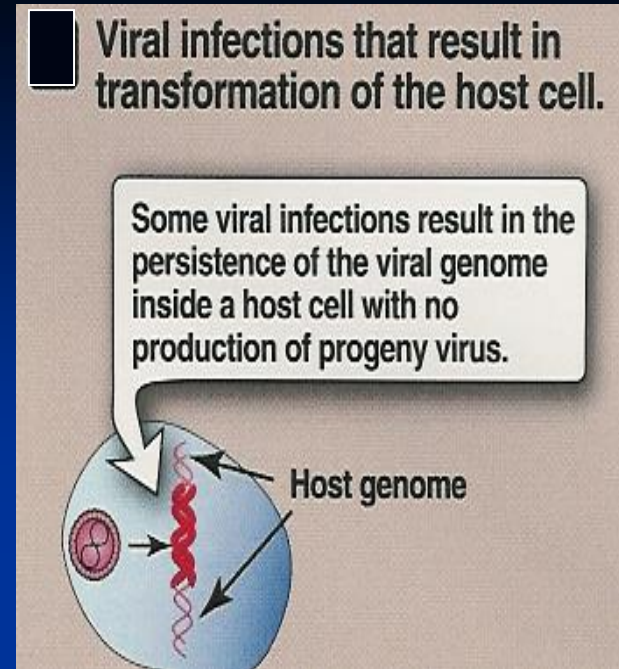
- Vs infect cells that restrict or lack the machinery for transcribing viral genes.
- Viral genome is found either integrated into cell DNA or as a circular episome or both.

1) Latent Infection:

- Persistent infection b/c
there is limited expression of viral genes
- The cell retains its normal properties
- Ex: HSV

2) Transformation:

- Ex ; EBV, HPV and HTLV
- Cause tumor in animals & H and can transform cell culture.



Vs can stimulate uncontrolled cell growth causing Tf by alternating the balance between growth activators & growth suppressors gene products

Pathogenesis at Host Level

1. Transmission of the virus & its entry into the host.
2. Replication of the virus & damage to cells
3. Vs remain localized or spread to other organs
4. Viral shedding
5. The immune response as
 - Host defense
 - Immunopathogenesis

Transmission

1. *Person to person*

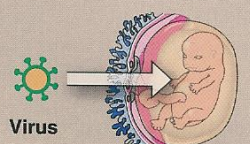
a) Horizontal transmission

- Skin contact , Blood
- Respiratory route
- Fecal - oral route
- Genital contact

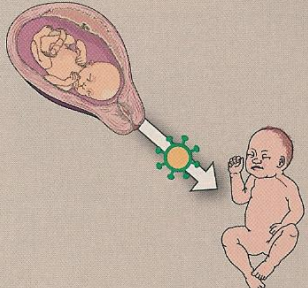
b) Vertical transmission

2. *Animal to person*

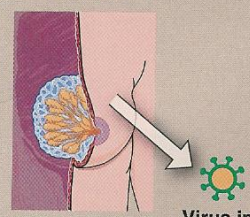
1 In utero by transplacental spread



2 During delivery through an infected birth canal



3 After birth by ingestion of breast milk



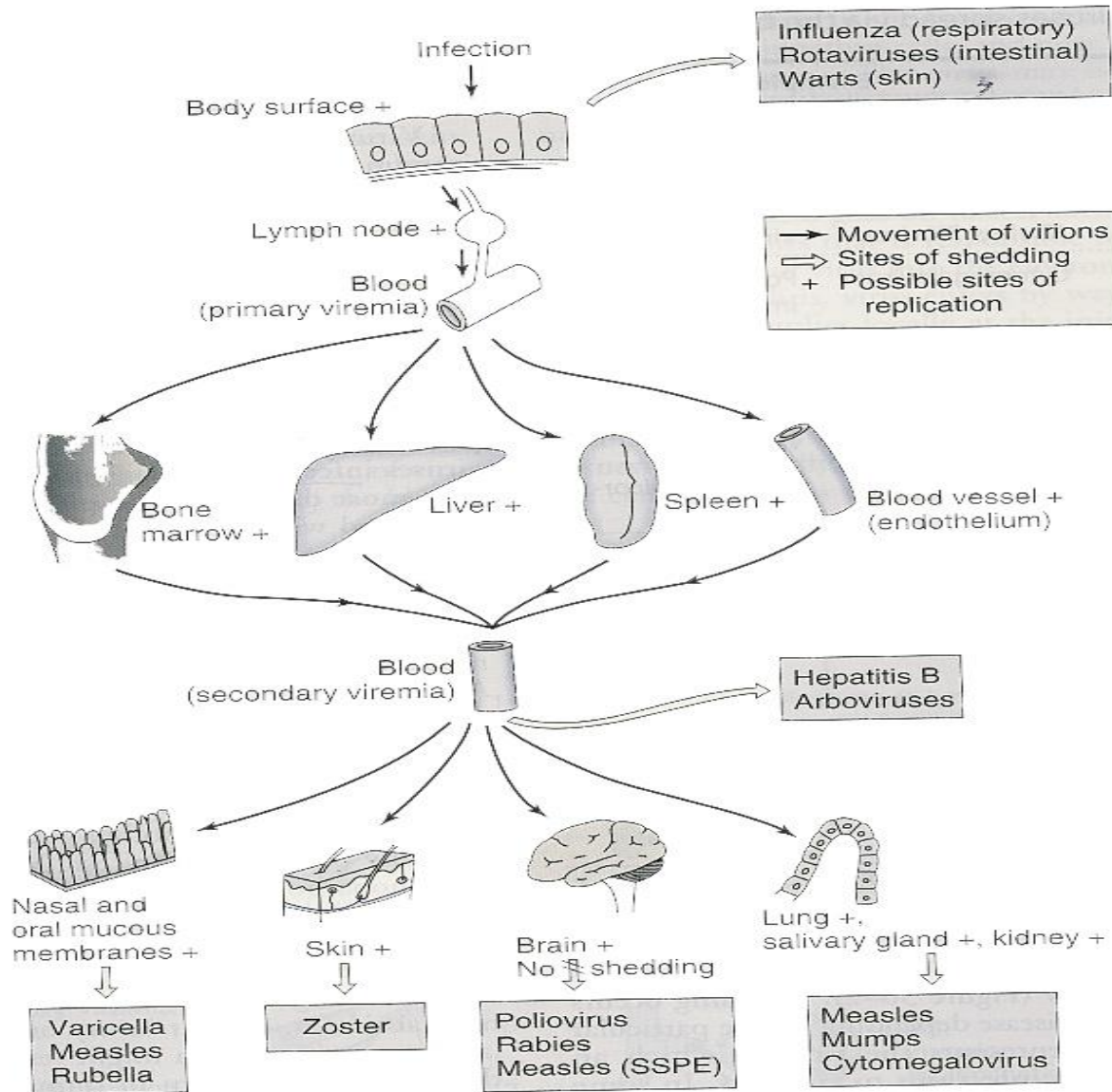
B Some viruses transmitted mother to infant

Herpes simplex virus types 1 and 2
Human cytomegalovirus
Human immunodeficiency virus
Rubella virus

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	<ul style="list-style-type: none"> ▪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	Genital herpes (L) Meningitis (G) Encephalitis (G)
	HBV HIV	Hepatitis B (G) AIDS(G)

Mechanisms of spread of virus through the body

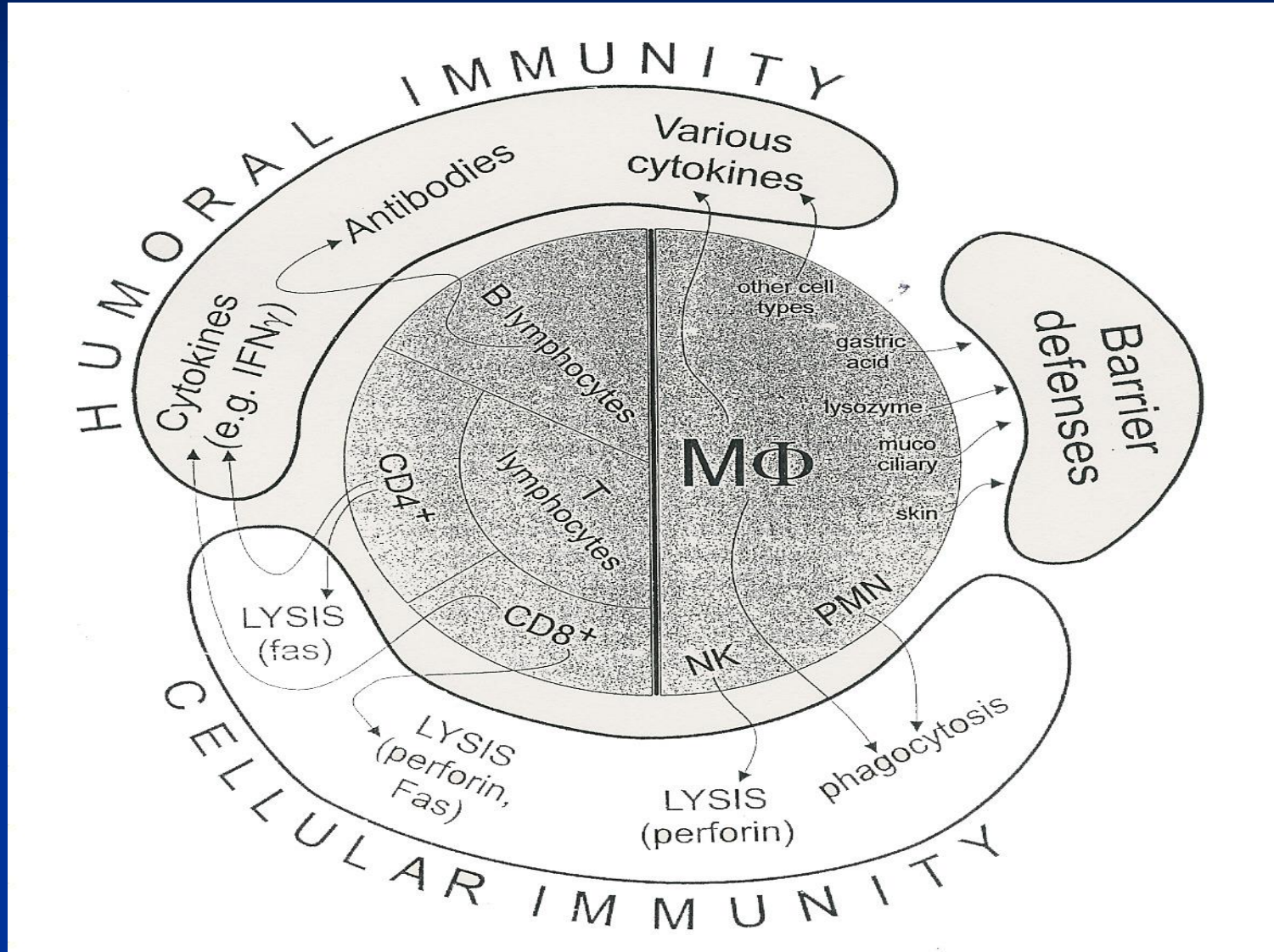


Virus shedding

Important features of Acute Viral Diseases

	<i>Local Infections</i>	<i>Systemic Infections</i>
<i>Ex. of specific Disease</i>	<i>Rhinovirus</i>	<i>Measles</i>
<i>Site of Pathology</i>	<i>Portal of entry</i>	<i>Distant site</i>
<i>IP</i>	<i>Relatively short</i>	<i>Relatively long</i>
<i>Viremia</i>	<i>Absent</i>	<i>Present</i>
<i>Duration of Immunity</i>	<i>Variable- may be short</i>	<i>Usually life long</i>
<i>Role of Secretory AB [IgA] in resistance</i>	<i>Usually important</i>	<i>Usually not important</i>

The immune response to virus



The immune response to virus

❖ *Macrophages:*

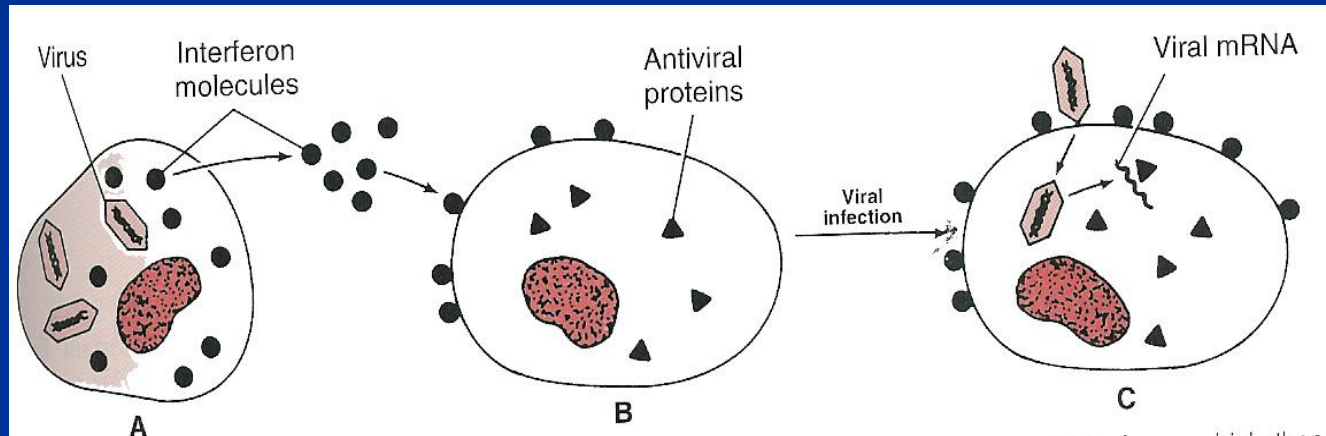
APC, Phagocytosis, Cytokines production

❖ *Natural killer (NK) cells :*

Lysis of VICs

❖ *Cytokines:*

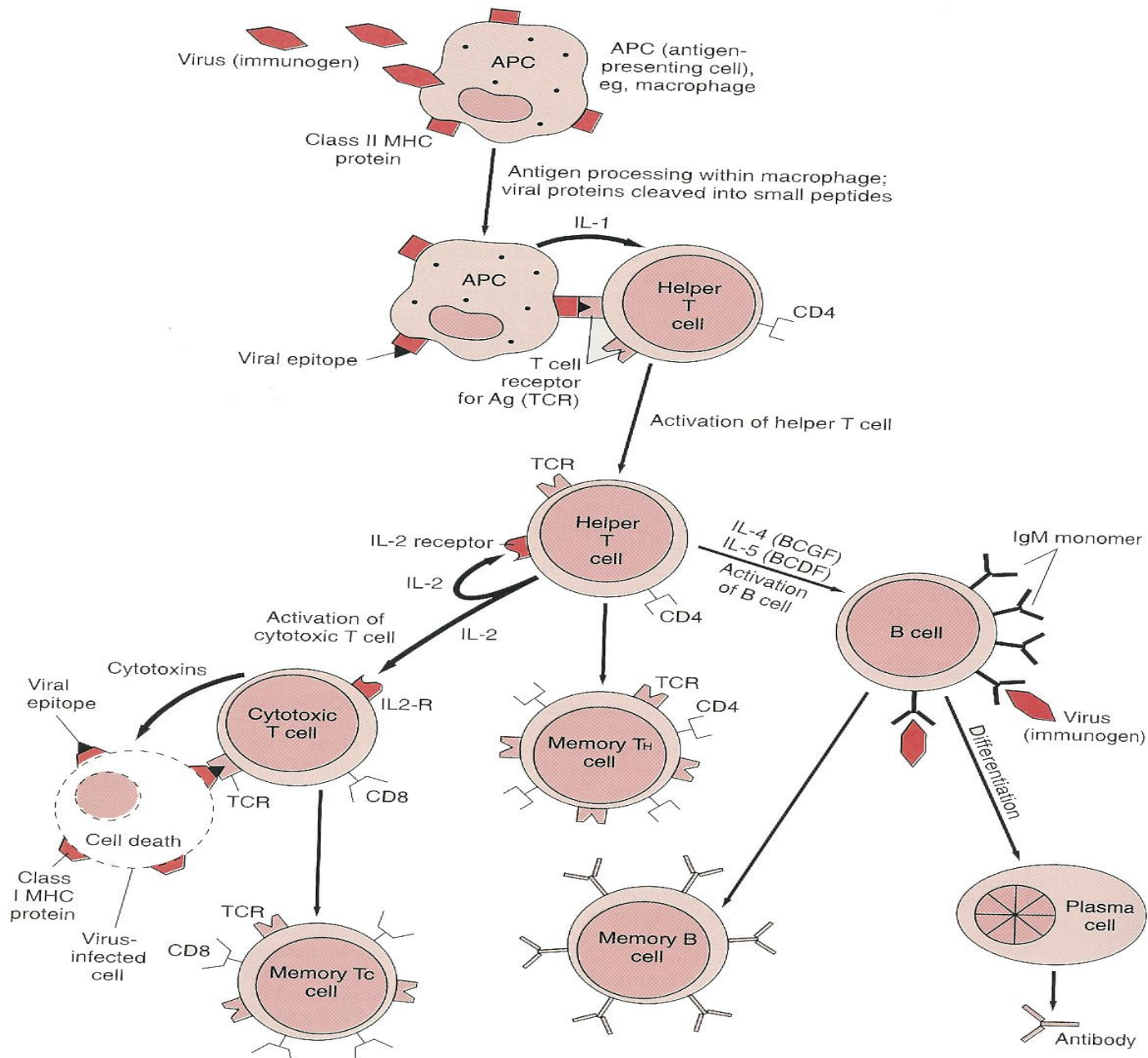
➤ Interferons (IFN)



- α , β IFN \longrightarrow inhibit the viral and the host cell mRNA translation
- γ IFN \longrightarrow stimulate phagocytosis and killing by macrophage & NK cells

➤ Interleukin (IL)

- Stimulate Ab production
- Activate T cells & CMI
- Suppress the IR



The immune response to virus

❖ *CMI:*

- Effective against **intracellular** viruses
Lysis of virally infected cells by CTCs [CD8]

❖ *Humoral Immunity:*

- Effective on **extracellular** viruses [viremia]
 - Neutralization

The stages of a typical viral infection:

1. The incubation period
2. Prodromal period
3. The specific-illness period:

The signs & symptoms of viral diseases are the result of Cell killing by:

A) Inhibition of cellular macromolecular synthesis

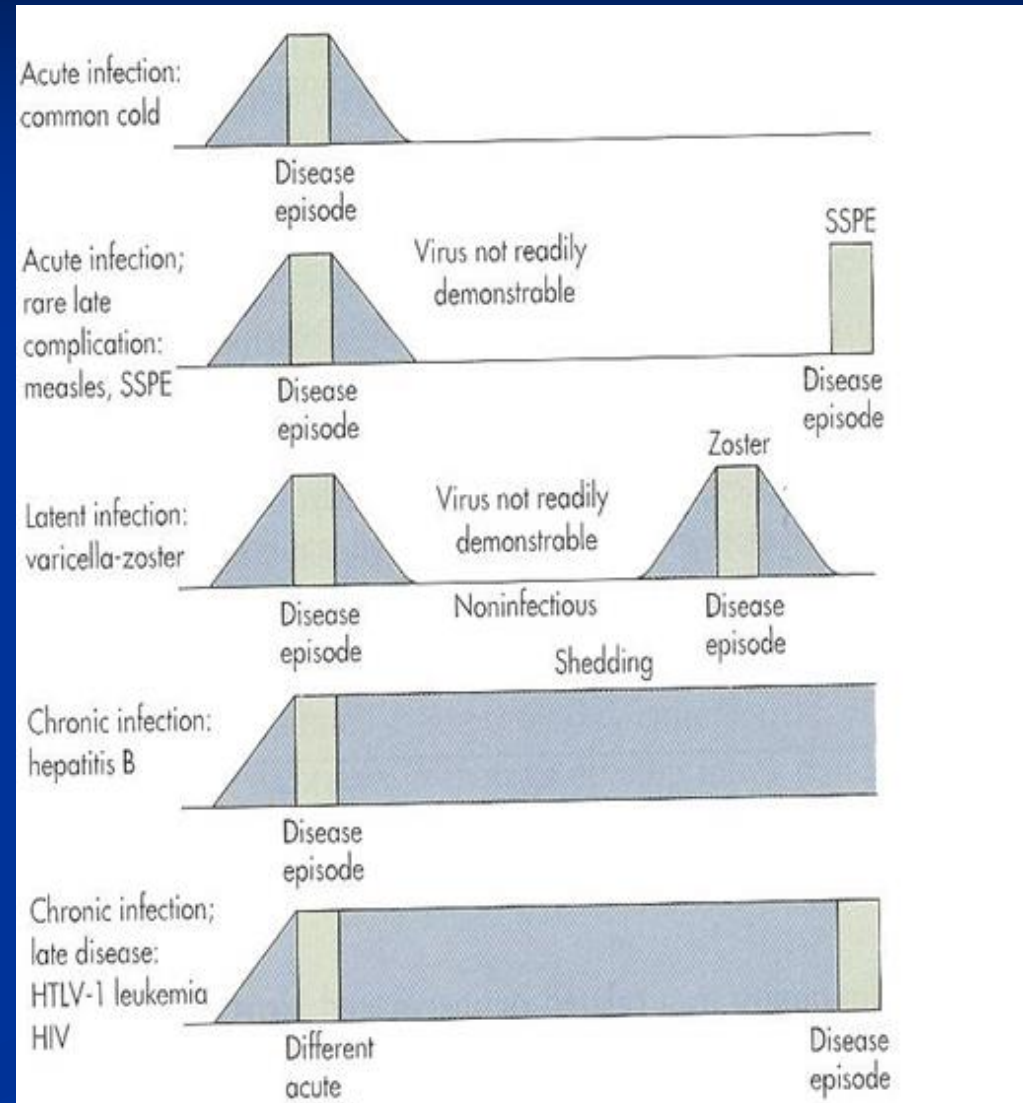
B) Immunologic attack (Immunopathogenesis)

Cytotoxic T cells e.g. Hepatitis (HAV, HBV,HCV)

4. The recovery period

Types of viral infections at host level:

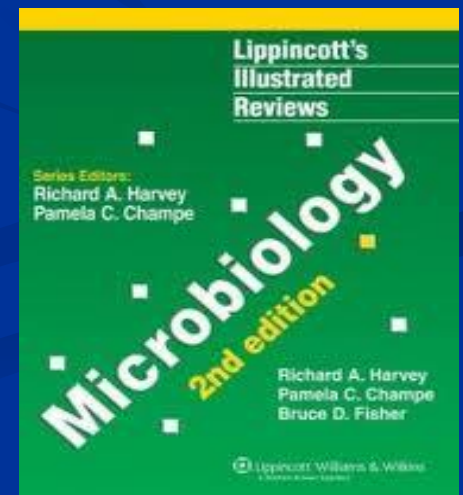
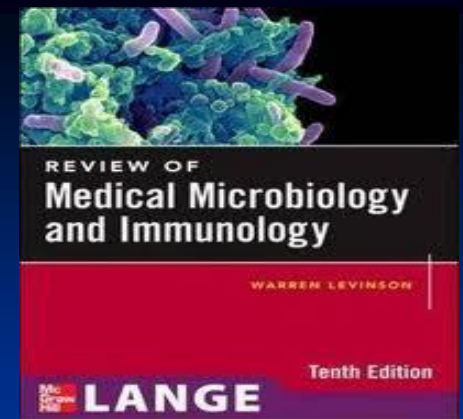
1. Asymptomatic infection
2. Acute infection
3. Persistent infection
 - Late complication of acute infection
 - Latent infection
 - Chronic infection



Reference books

& the relevant page numbers

- **Medical Microbiology and Immunology**
By: Warren Levinson .
10th Edition, 2008.
Pages;221-232
- **Medical Microbiology.**
By: David Greenwood ,Richard C.B. Slack
John F Peutherer and Mike Barer.
17th Edition, 2007.
Pages;80,90-92
- **Lippincott's Illustrated Reviews: Microbiology**
By: William A. Strohl ,Harriet Rouse &
Bruce D. Fisher
2nd Edition, 2007 .
Pages;15-17,242-243.



Questions ?