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.

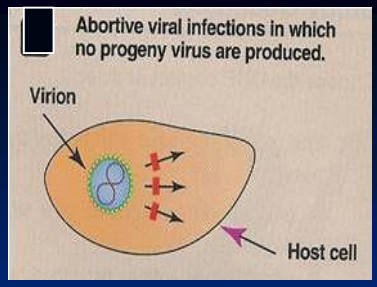
Pathogenesis of viral infection

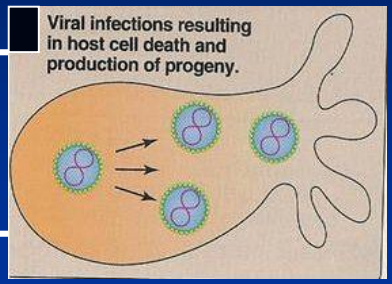
- Viral disease at the cellular level
  - Cytopathogenesis
- Viral disease at the host level
  - Mechanism of the disease

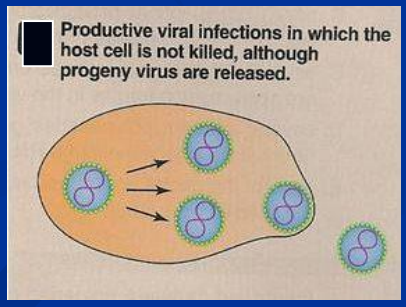
Cytopathogenesis:

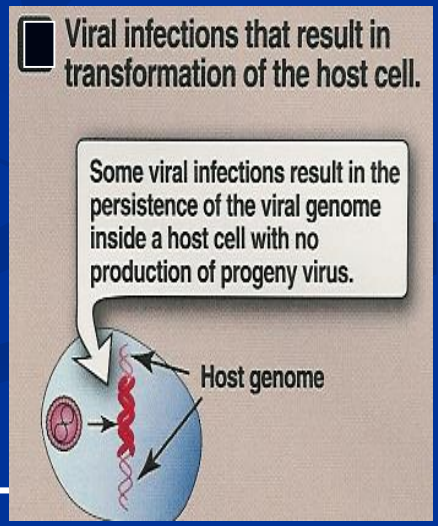
The types of viral infections at cellular level

The effects on cells/ Type of Infection	Virus Production
Abortive	Vs not produced
Productive	
▪ Cytolytic	Vs Produced
▪ Non-cytolytic [Persistant]	Vs Produced
Non-productive	Vs not Produced
▪ Latent [P_t]	Viral NA present
▪ Transformation [P_t]	Viral NA present





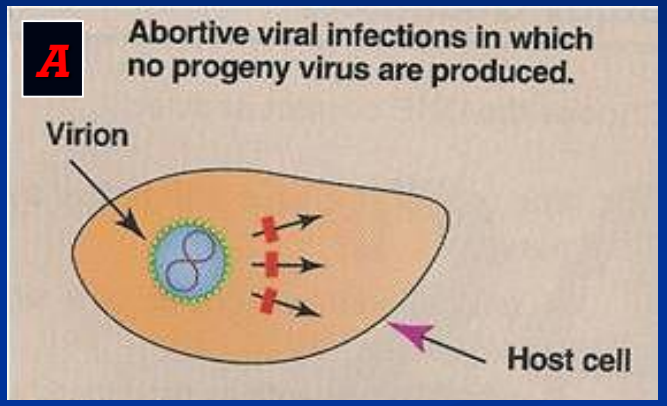




The types of viral infections at cellular level

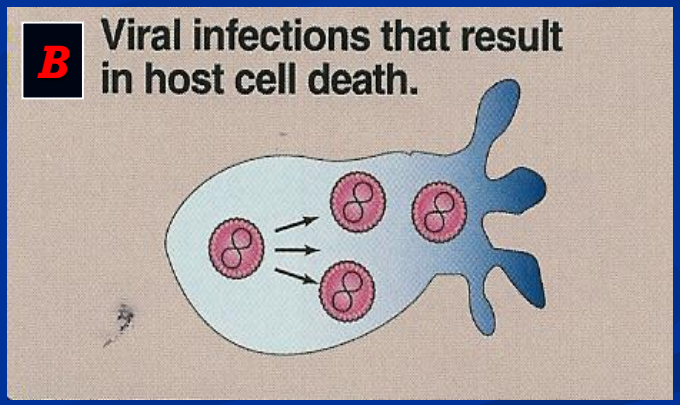
A) Abortive Infections:

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



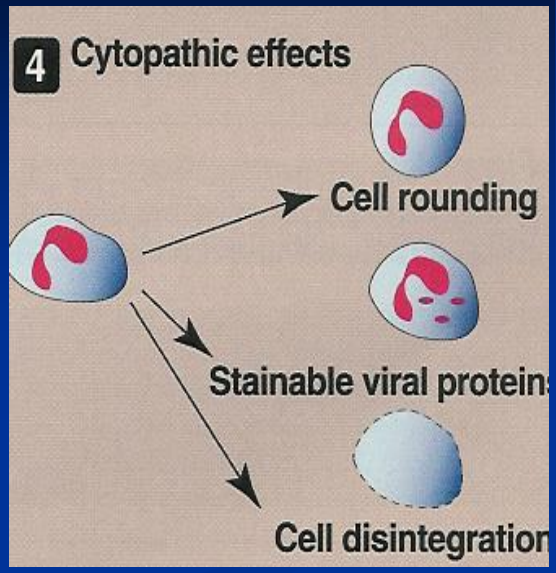
B) Productive Infections:

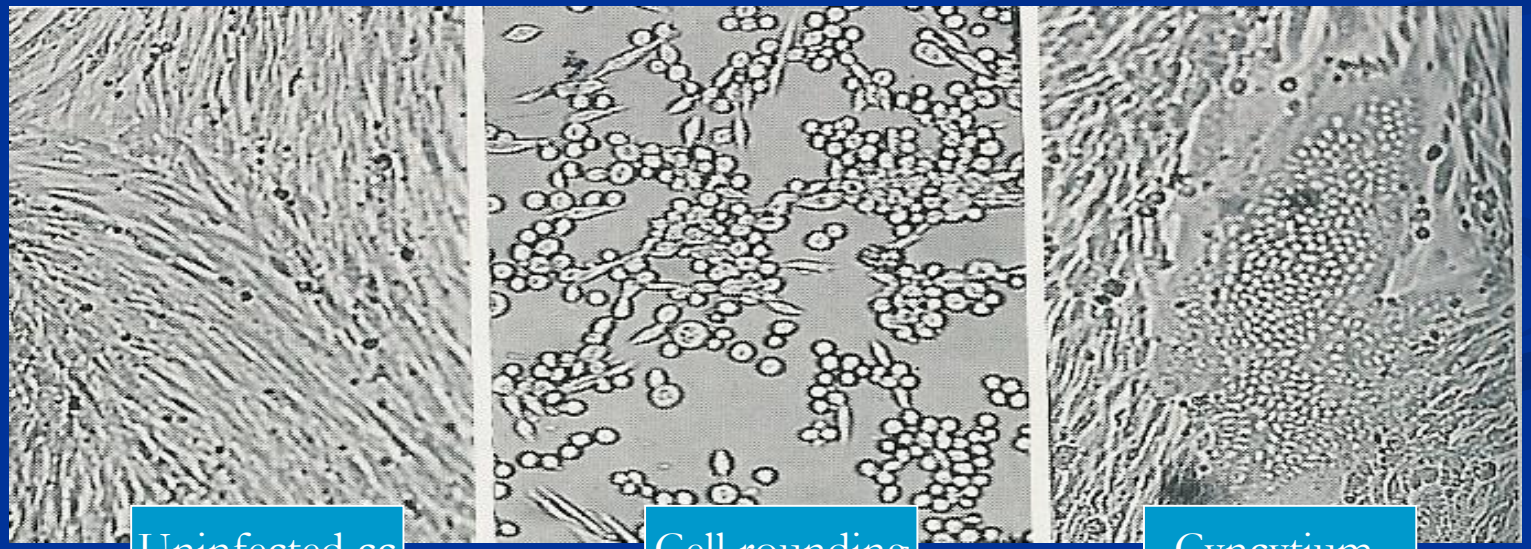
1. Cytolytic Infections
   - Viruses replicate & produce progeny
   - Cell death & Cytopathic effects [CPE]
   - Inhibition of cellular protein & NA synthesis



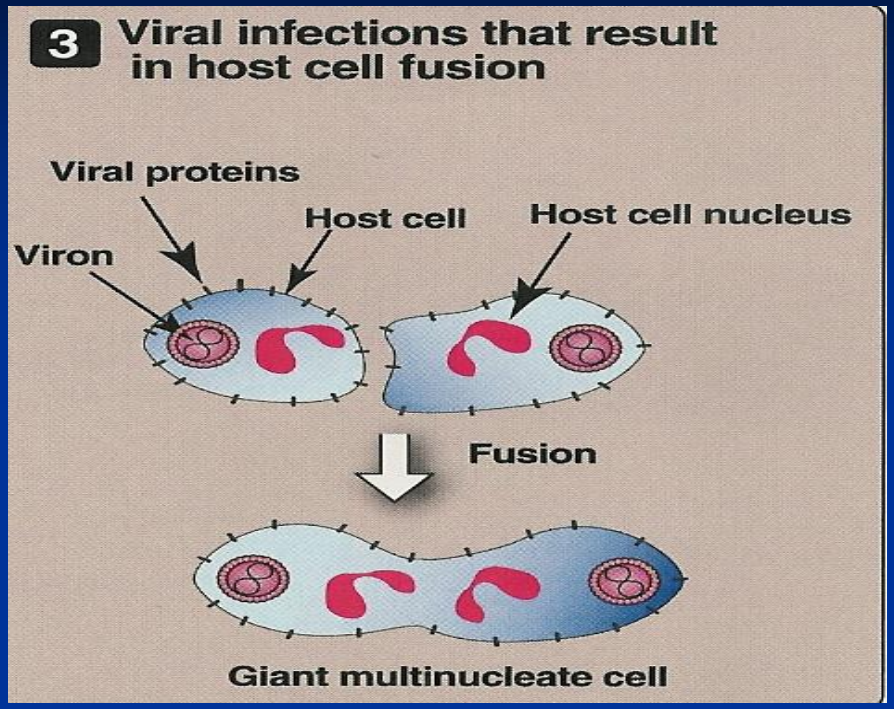
Cytopathic Effects

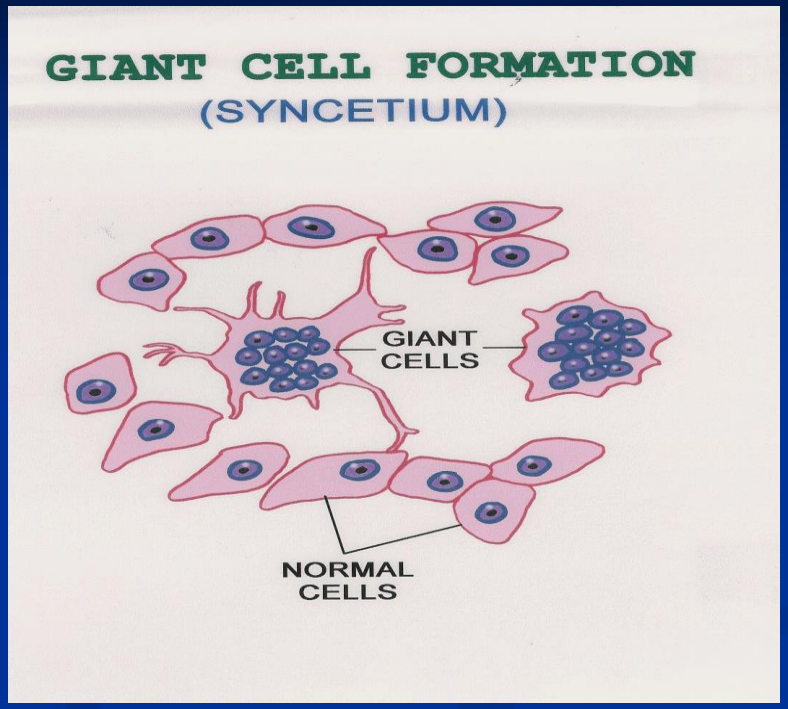
- CPE can take several forms:
  1. Cell lysis
  2. Cell rounding
  3. Syncytium formation
  4. Inclusion bodies formation





Syncytium formation





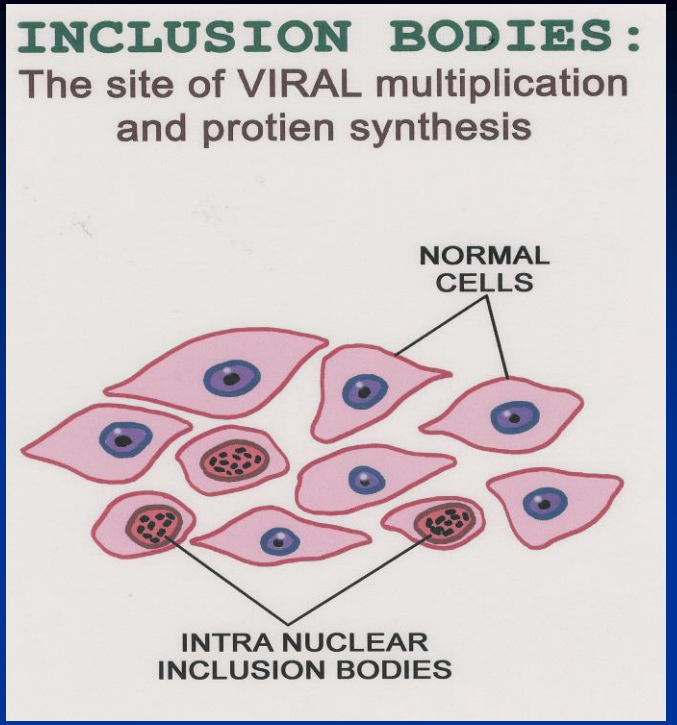
Herpes
paramyxoVs

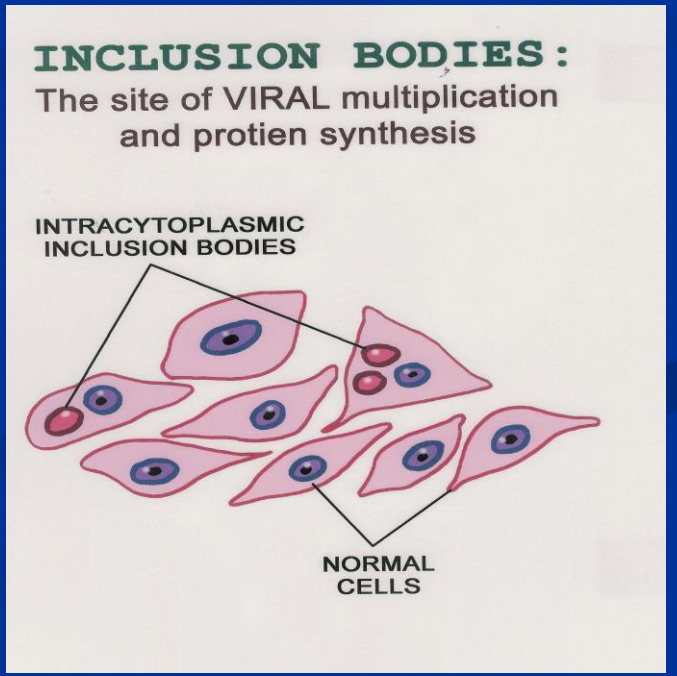
Cc ;Syncytium (RSV)

Inclusion bodies formation

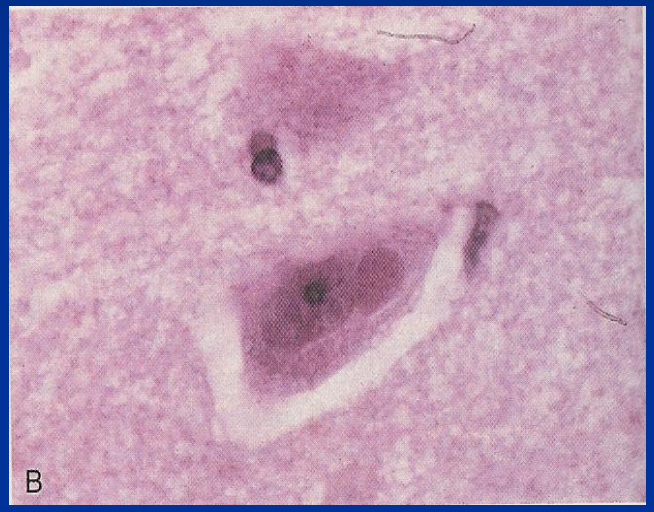
- Site:
  - Intranuclear [Herpes]
  - Intracytoplasmic [Rabies]

- Take several forms:
  - Single/multiple
  - Small/large
  - Round/irregular





Inclusion bodies formation



Negri bodies caused by Rabies virus

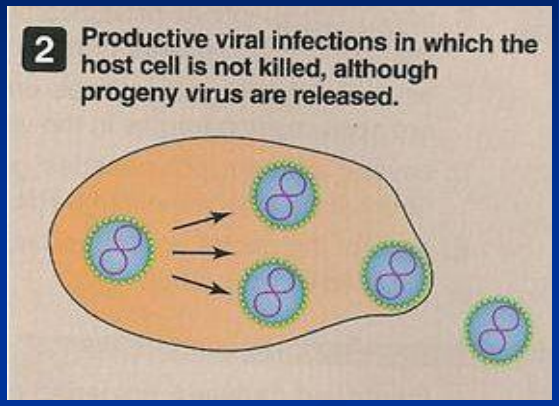
Owl’s eye inclusions caused by CMV

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

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:

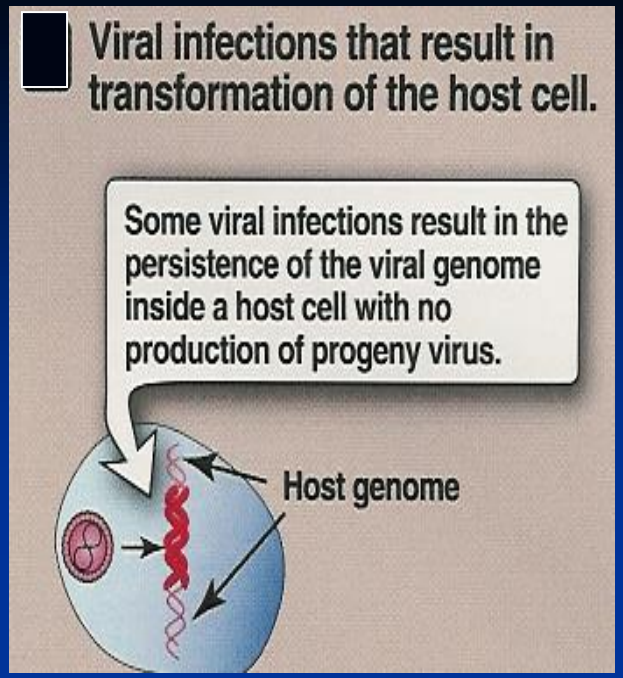
- Persistent infection b/c

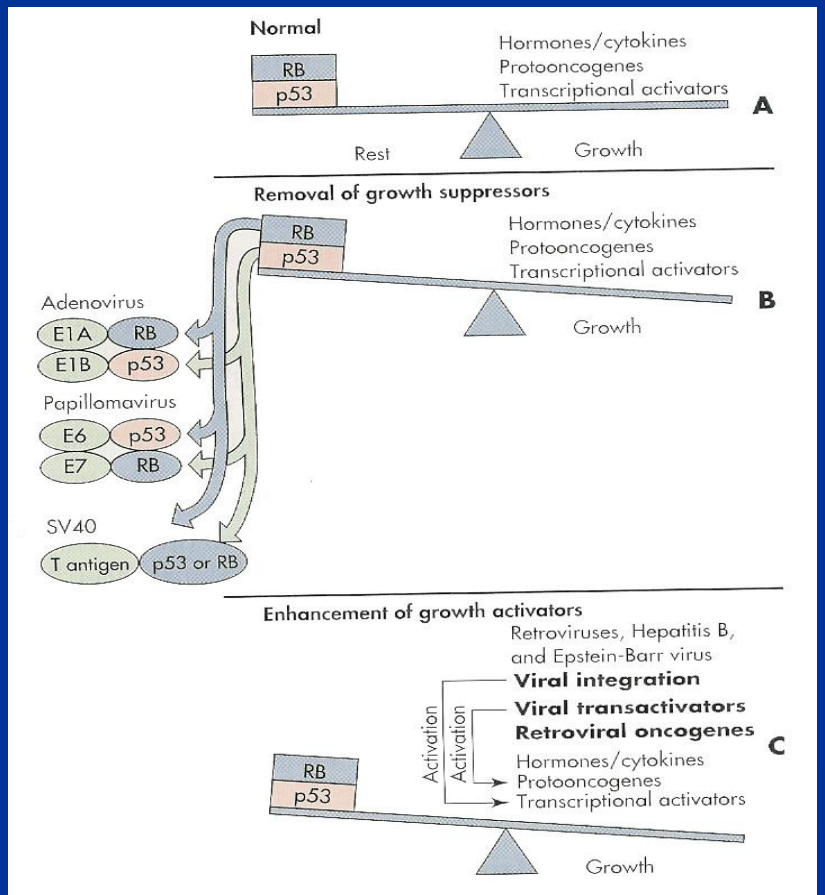
there is limited expression of viral genes

- 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

Cytopathogenesis:

The types of viral infections at cellular level

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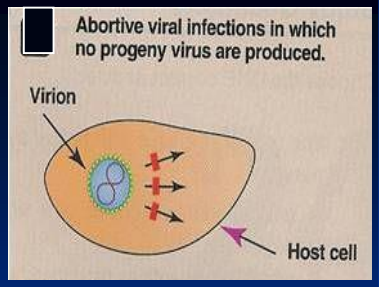
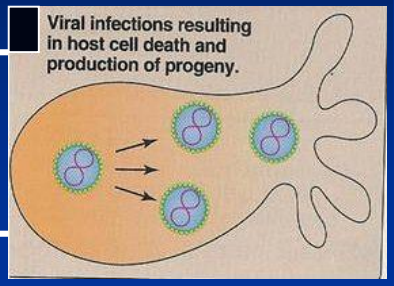
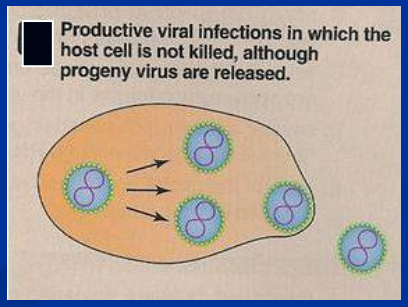
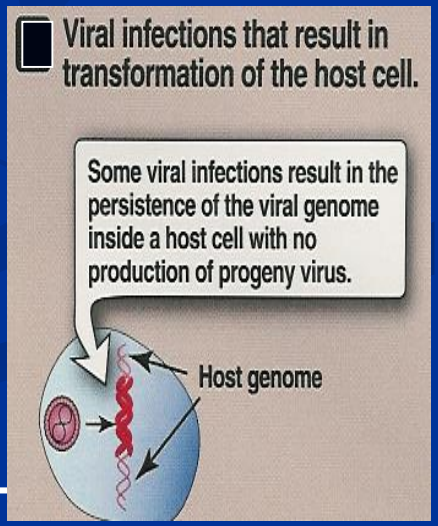








Pathogenesis at Host Level

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

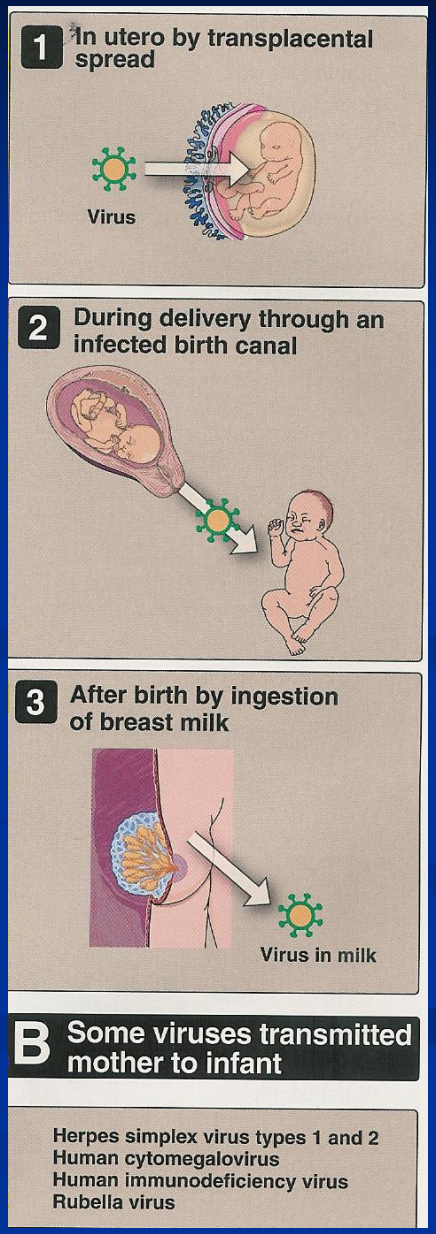
   Host defense

   Immunopathogenesis

Transmission

1. **Person to person**
   a) Horizontal transmission
      - Skin contact , Blood
      - Respiratory route
      - Fecal - oral route
      - Genital contact
   b) Vertical transmission

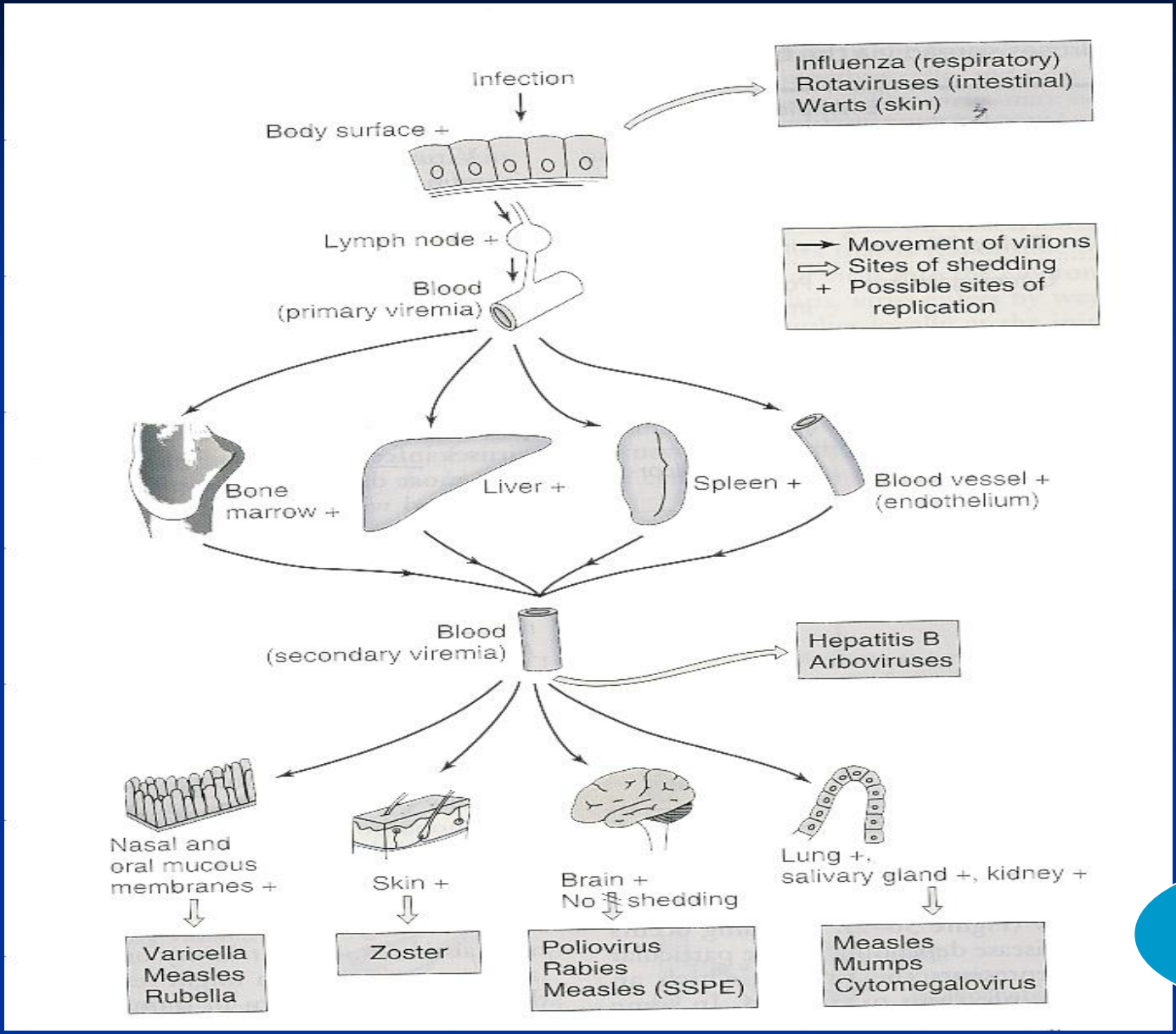
2. **Animal to person**



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	Yellow fever virus	Yellow fever (G)
animal	Rabies virus	Rabies (G)
Respiratory tract	▪HSV-1	Gingivostomatitis (L) (URT)
	▪Rhinovirus	Common cold (L) (URT)
	▪RSV	Bronchiolitis (L) (LRT)
	▪Adenovirus	Pneumonia (L) (LRT)
	▪VZV	Chickenpox (G)
	▪Measles virus	Measles (G)
GIT	Rotavirus	Diarrhea (L)
	HAV	Hepatitis A (G)
	Poliovirus	Poliomyelitis (G)
Genital tract	HSV-2	Genital herpes (L)
		Meningitis (G)
		Encephalitis (G)
	HBV	Hepatitis B (G)
	HIV	AIDS(G)

Mechanisms of spread of virus through the body

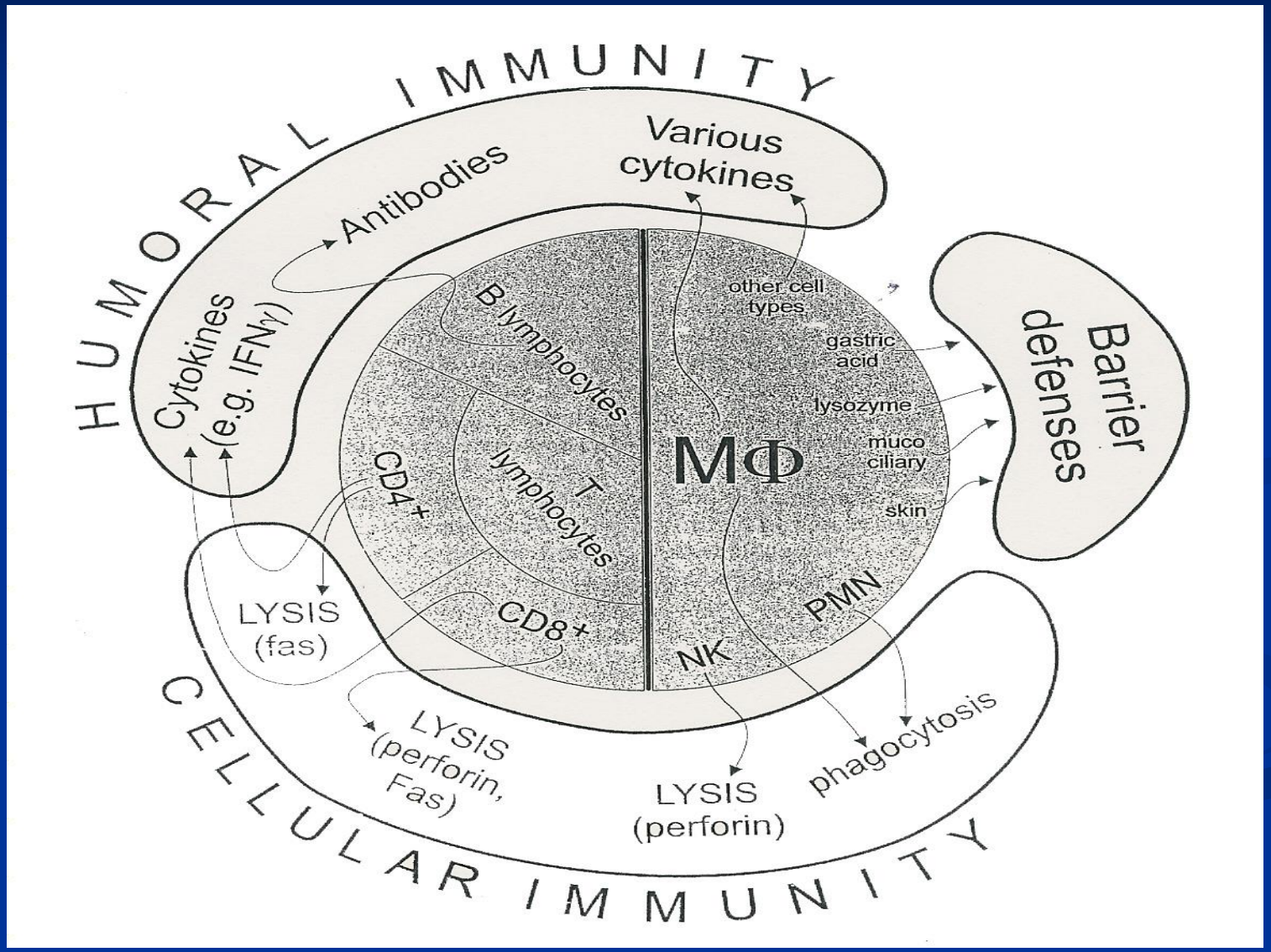


Virus shedding

Important features of Acute Viral Diseases

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

The immune response to virus



The immune response to virus

- ***Macrophages:***

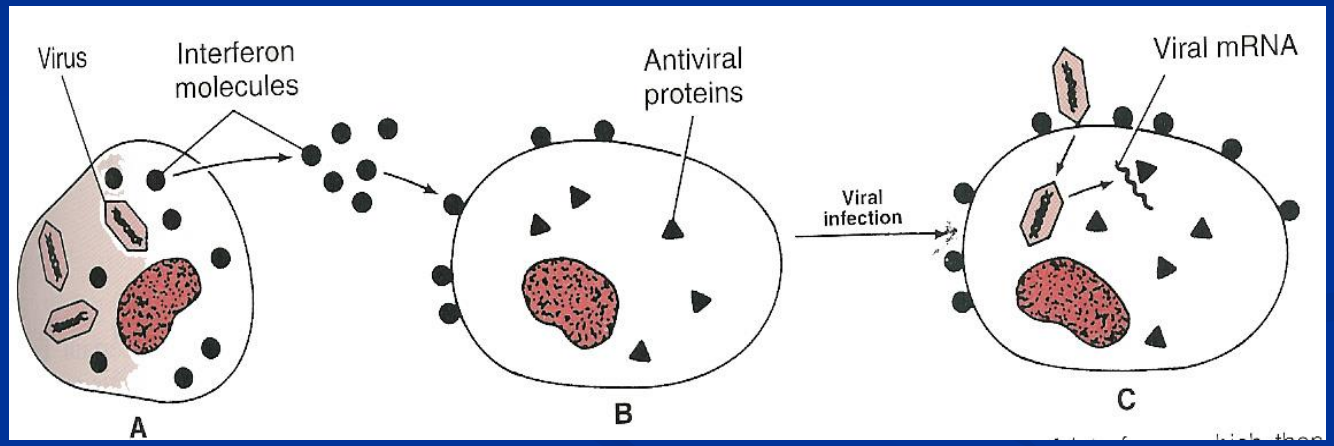
  APC, Phagocytosis, Cytokines production

- ***Natural killer (NK) cells :***

  Lysis of VICs

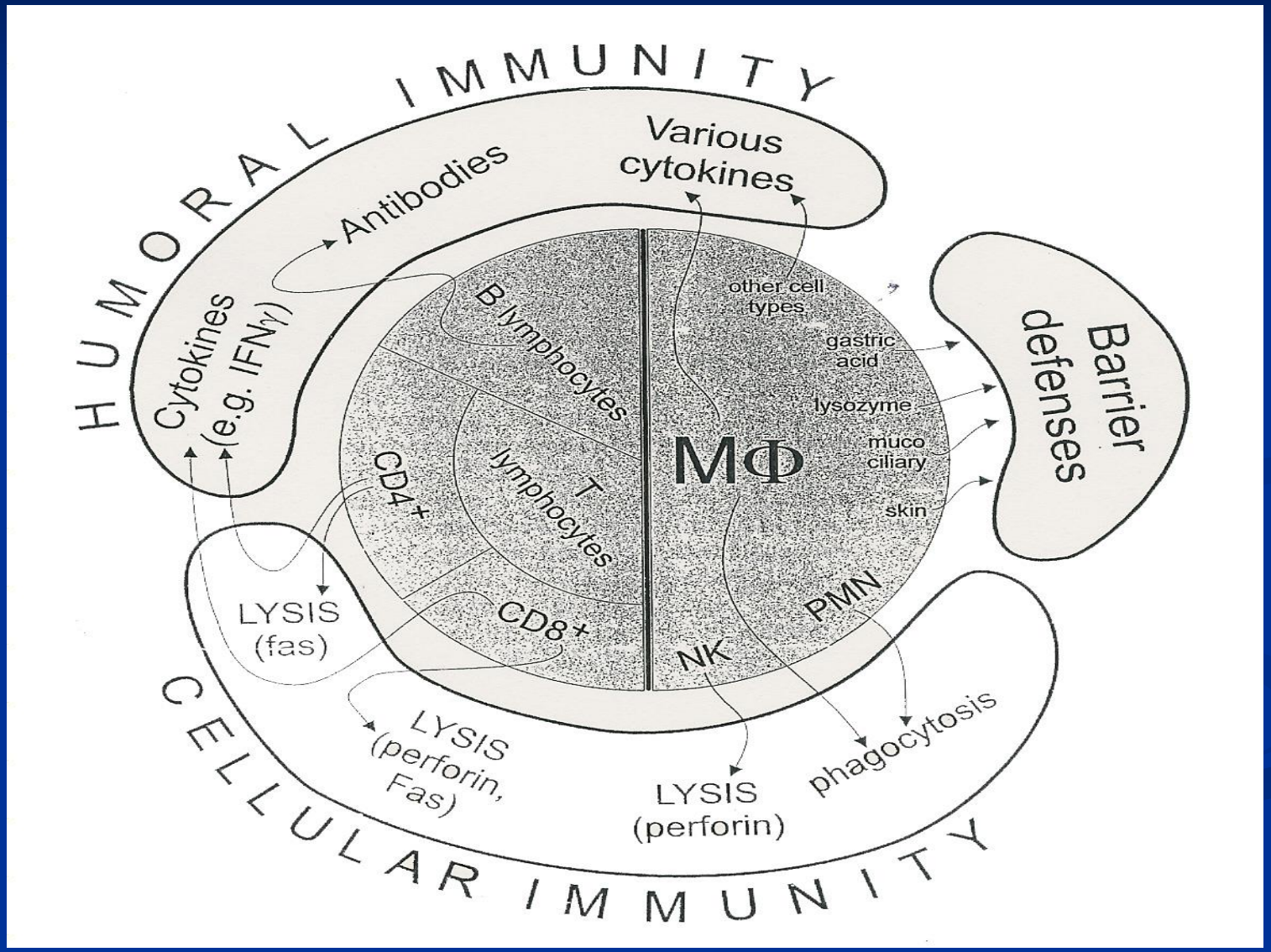
- ***Cytokines:***

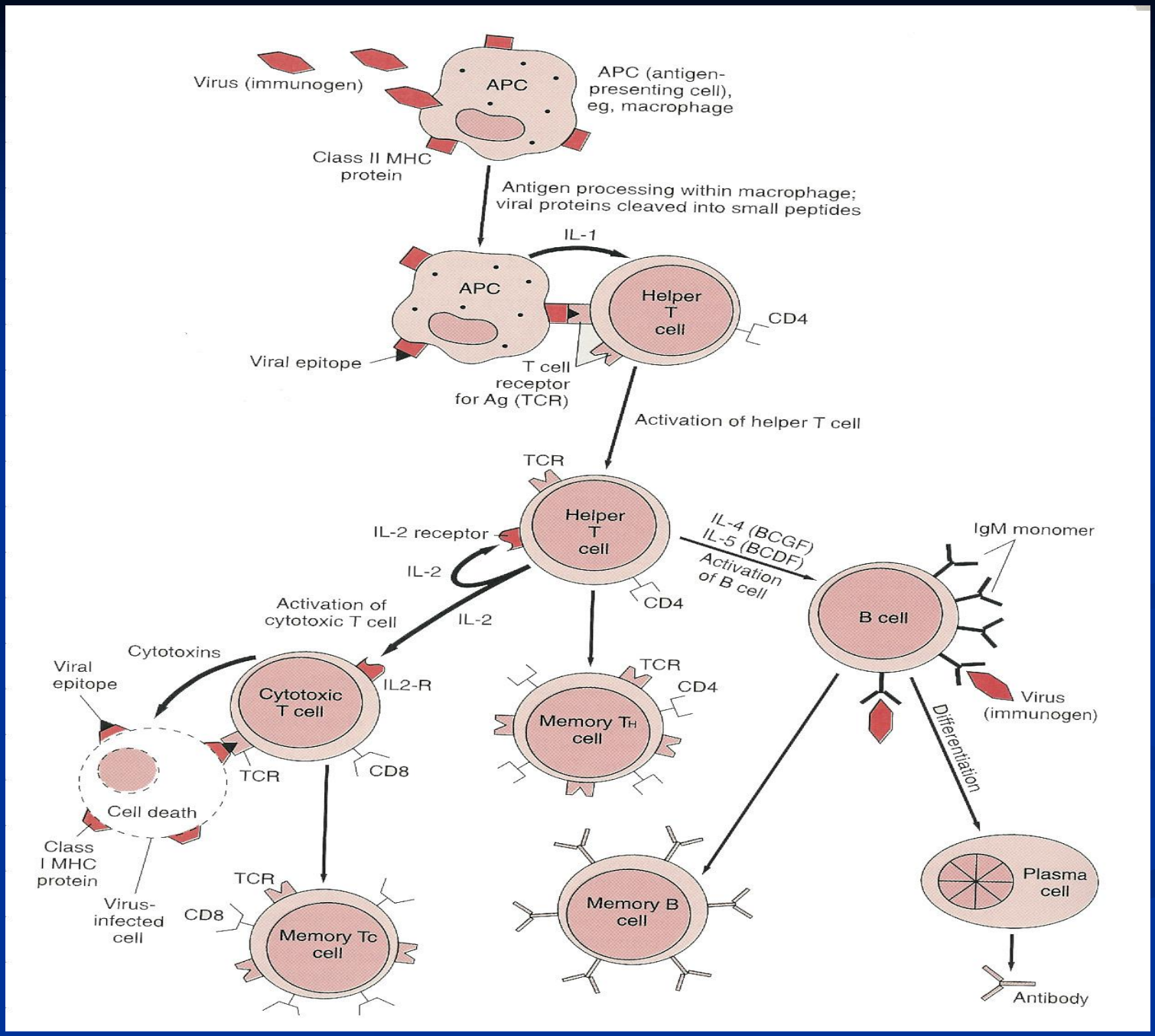
  - Interferons (IFN)



  - α , β IFN → inhibit the viral and the host cell mRNA translation
  - γ IFN → 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




Virus (immunogen)
APC
APC (antigen-presenting cell), eg, macrophage
Class II MHC protein
Antigen processing within macrophage; viral proteins cleaved into small peptides
IL-1
APC
Helper T cell
CD4
Viral epitope
T cell receptor for Ag (TCR)
Activation of helper T cell
TCR
Helper T cell
IL-2 receptor
IL-2
CD4
IL-4 (BCGF)
IL-5 (BCDF)
Activation of B cell
IgM monomer
B cell
Activation of cytotoxic T cell
IL-2
Cytotoxins
Viral epitope
Cytotoxic T cell
IL2-R
TCR
CD8
Cell death
Class I MHC protein
Virus-infected cell
TCR
CD4
Memory TH cell
Virus (immunogen)
Differentiation
TCR
CD8
Memory Tc cell
Memory B cell
Plasma cell
Antibody

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

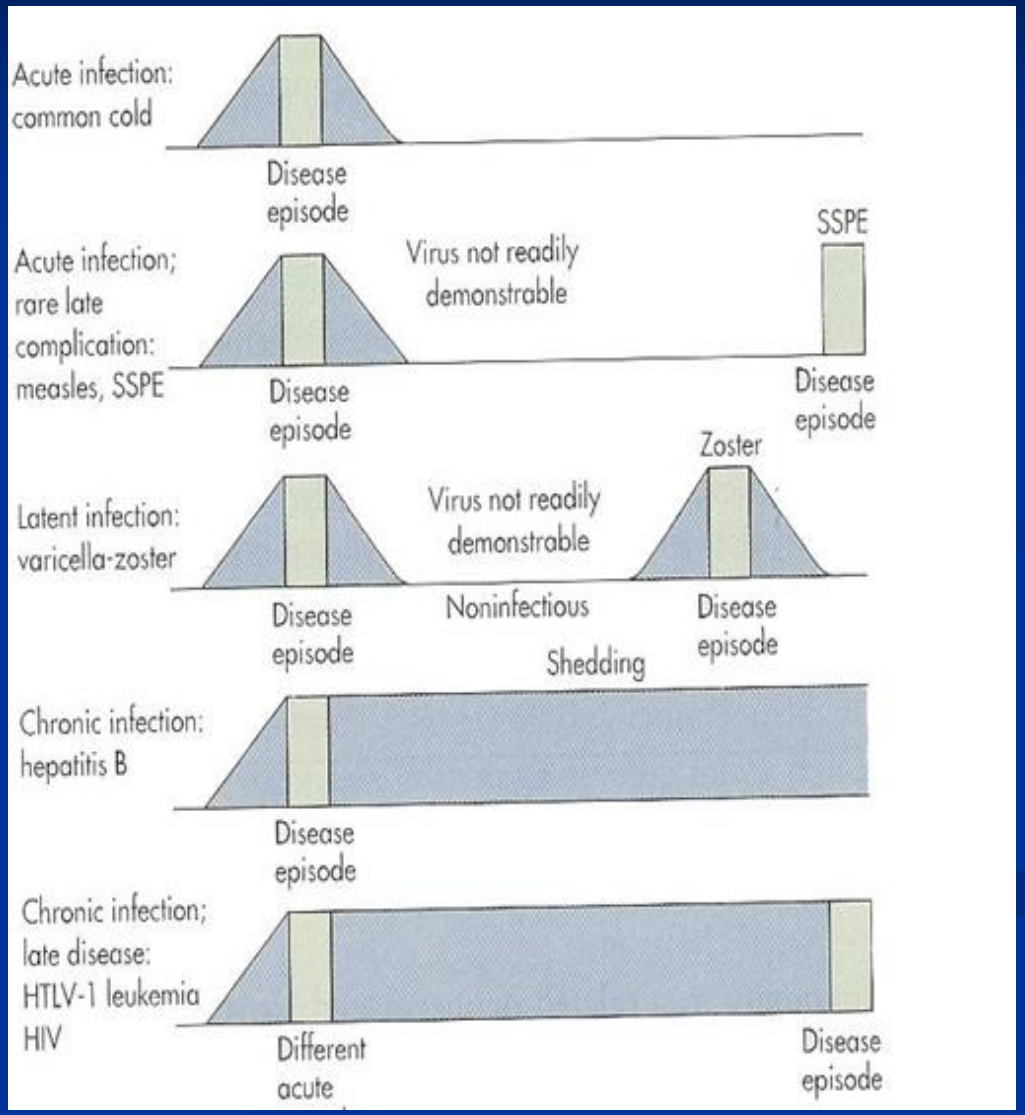
   B) Immunologic attack (Immunopathogenesis)

   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



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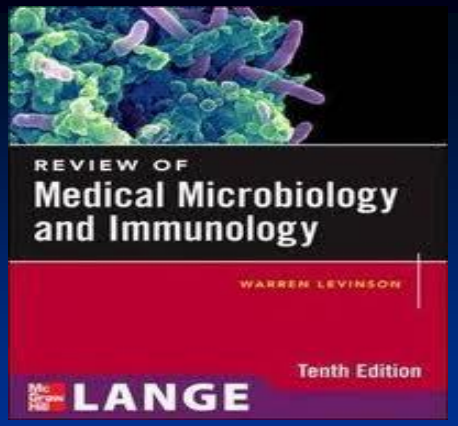

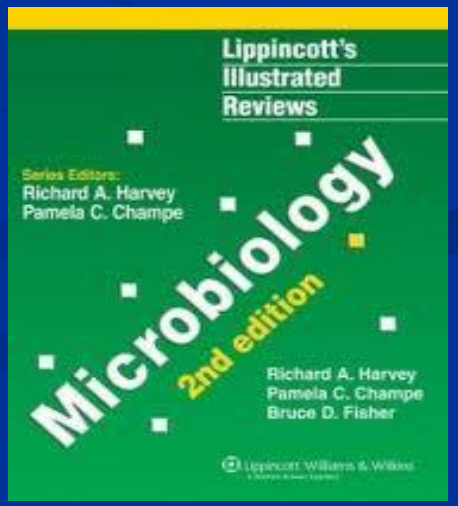

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