بسم الله الرحمن الرحيم

Pathogenesis of viral infection

(Foundation Block , Microbiology : 2015)

By: Dr.Malak M. El-Hazmi

OBJECTIVES

- *definition and levels of viral pathogenesis.*
  cellular level.
  host level.
- *The immune response to viral infection.*
- *The stages of viral infection.*
- *The types of viral infections at host level.*

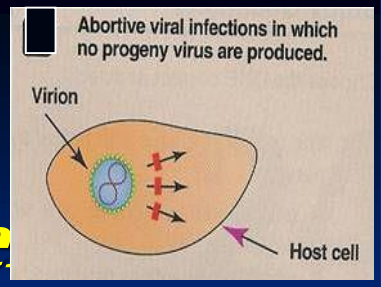
Pathogenesis of viral infection

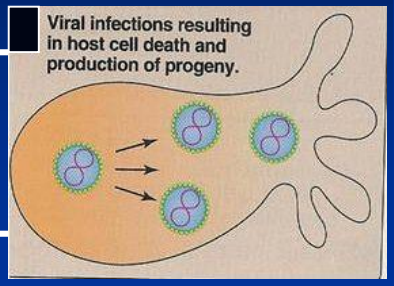
- Viral disease at the cellular level
  - Cytopathogenesis
- Viral disease at the host level
  - Mechanism of the disease

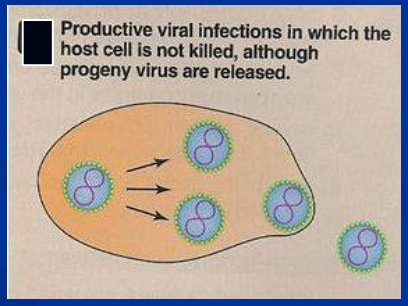
Cytopathogenesis:

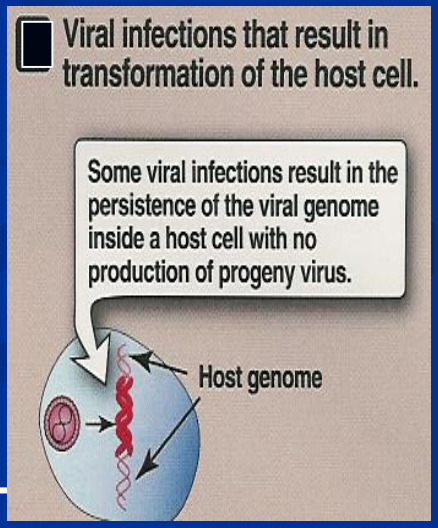
The types of viral infections at cellular leve

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





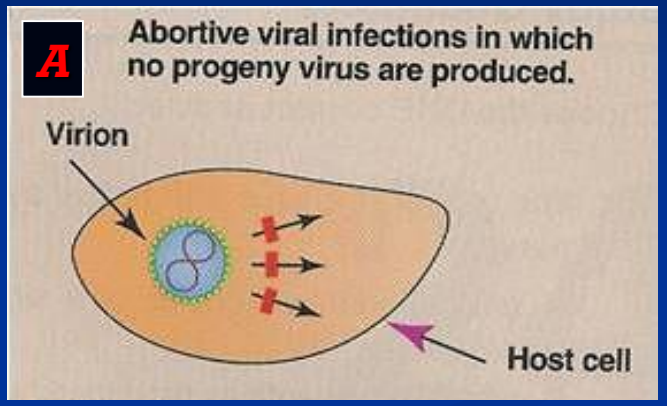




The types of viral infections at cellular level

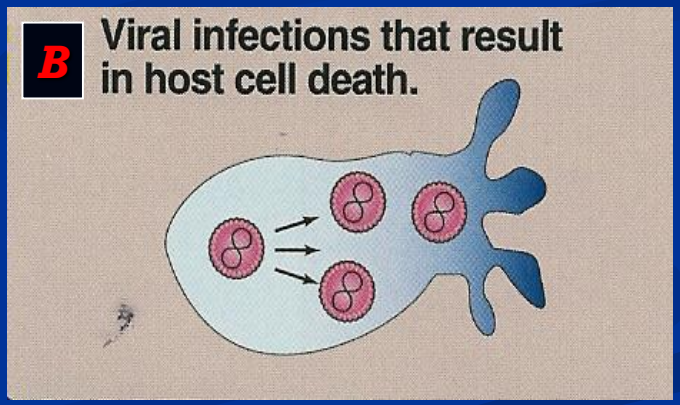
A) Abortive Infections:

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



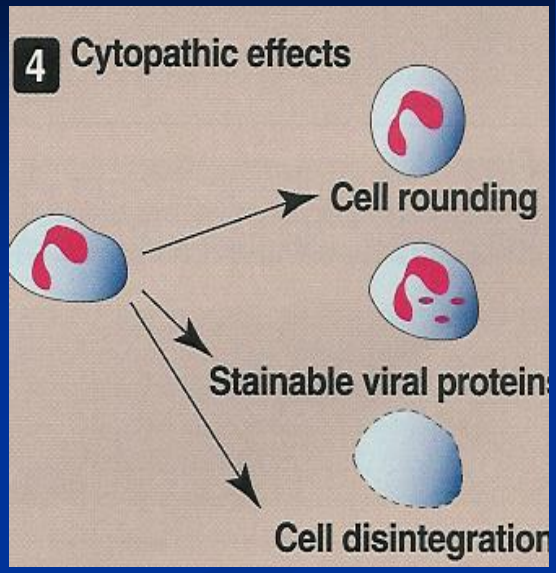
B) Productive Infections:

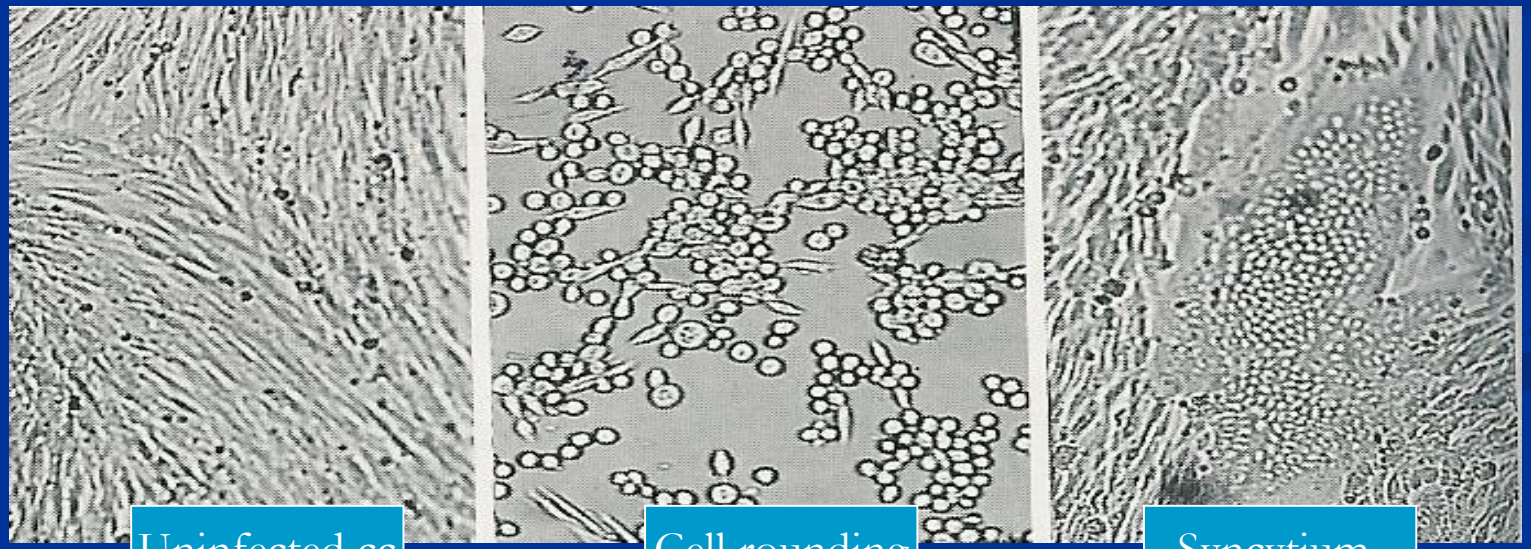
1. Cytolytic Infections
   - Viruses replicate & produce progeny
   - Cell death & Cytopathic effects [CPE]
   - Inhibition of cellular protein & NA synthesis



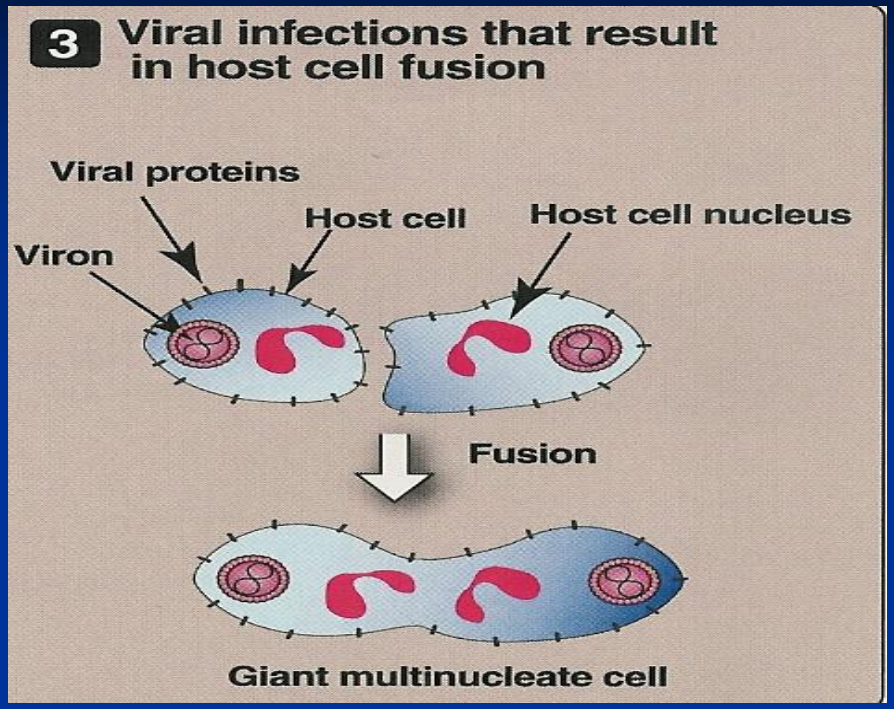
Cytopathic Effects

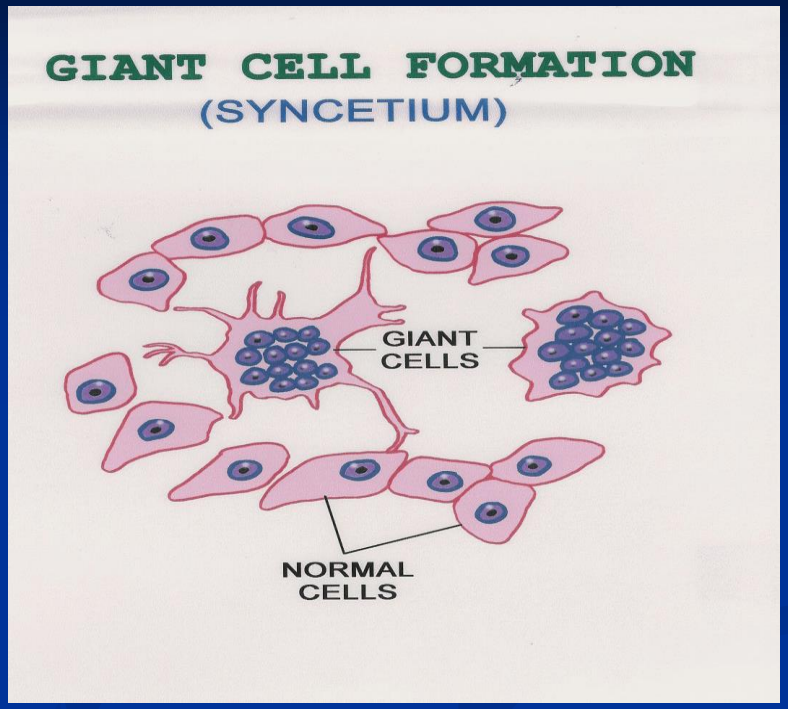
- CPE can take several forms:
  1. Cell lysis
  2. Cell rounding
  3. Syncytium formation
  4. Inclusion bodies formation

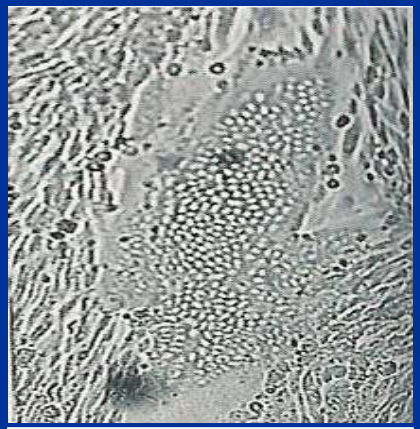




Syncytium formation





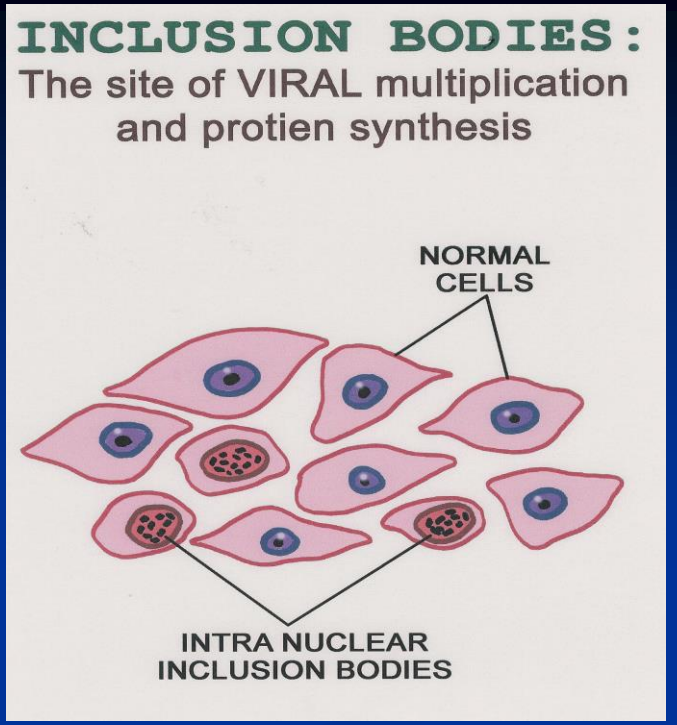


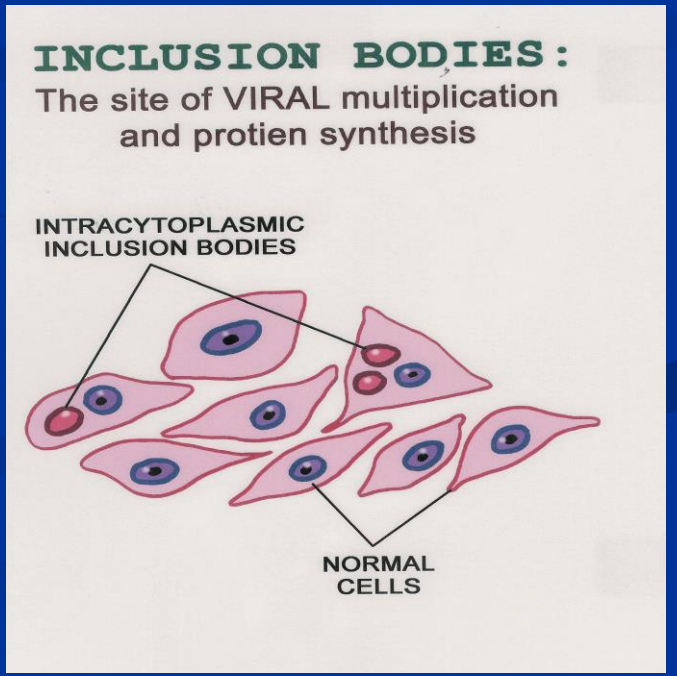
Syncytium

Inclusion bodies formation

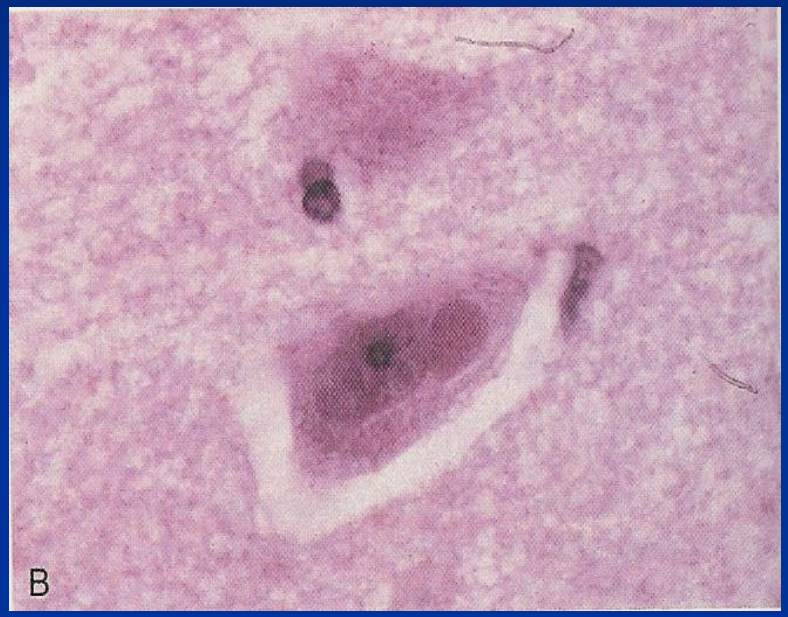
- Site:
  - Intranuclear [Herpes]
  - Intracytoplasmic [Rabies]

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

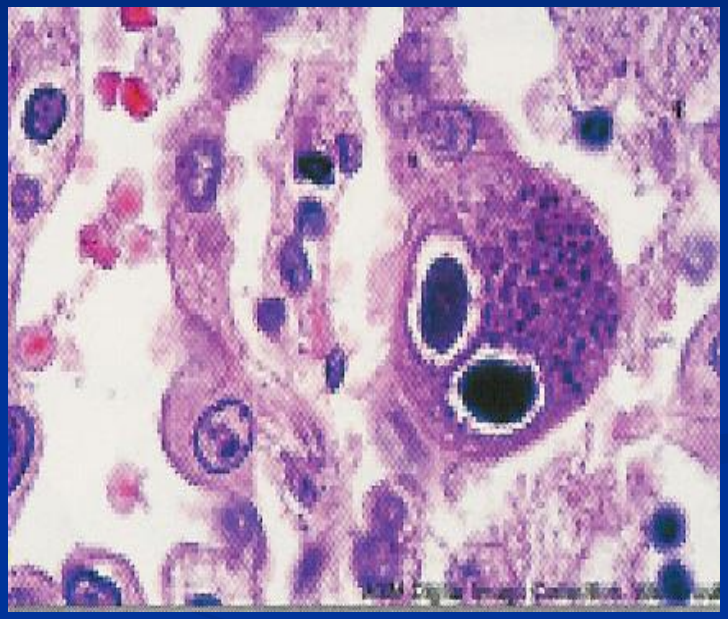




Inclusion bodies formation



Negri bodies caused by Rabies virus



Owl's eye inclusions caused by CMV

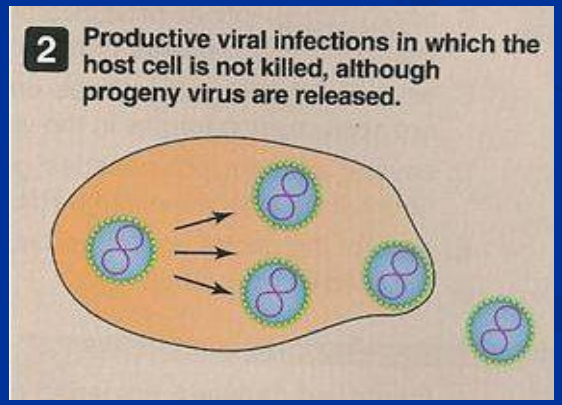
The types of viral infections at cellular level

B) Productive Infections:

1. Cytolytic Infections

2. Non-cytolytic infections :

- Viruses replicate & produce progeny
- Vs released by cell budding & little or no CPE



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 inf b/c

there is limited expression of viral genes

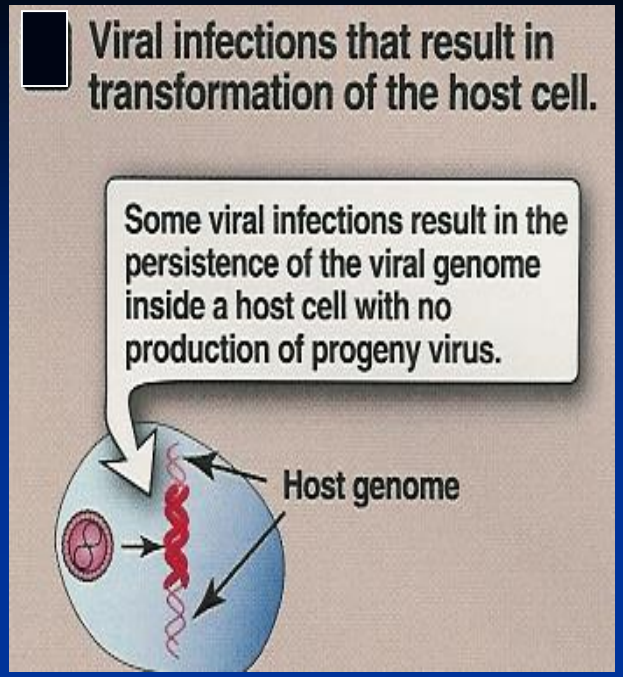
- Ex: HSV

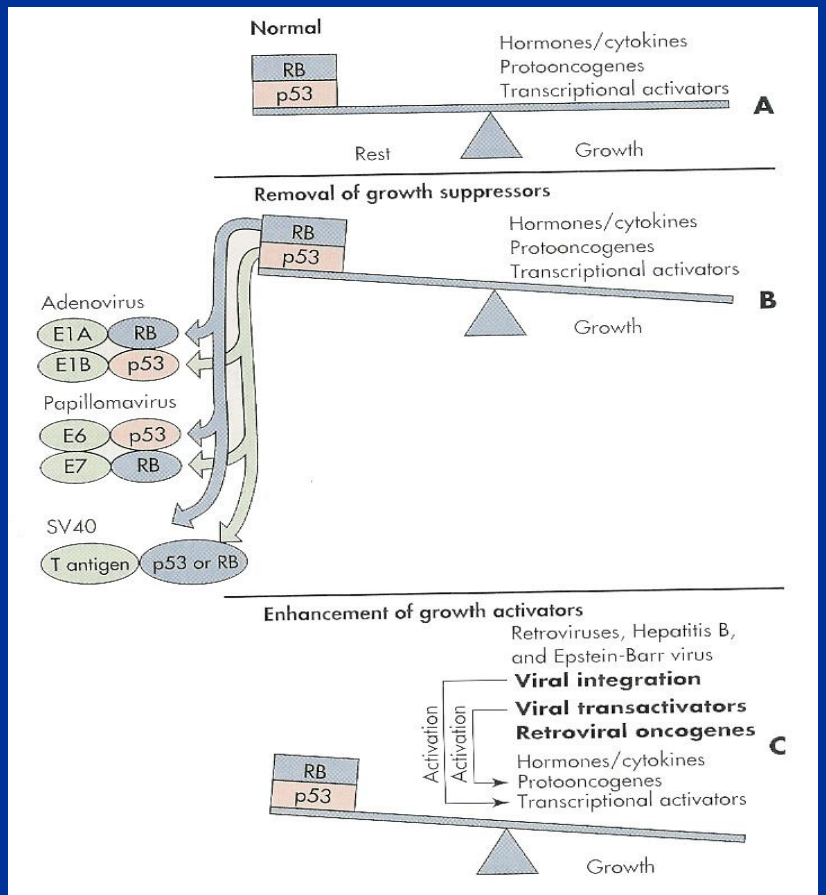
2) Transformation:

Transformation:

- Ex ; EBV, HPV and HTLV
- Cause tumor in animals & H

  and can transform cell culture



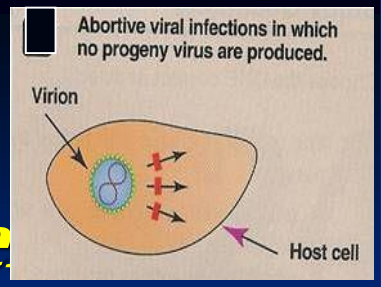


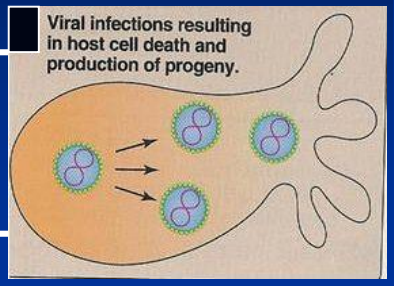
Vs can stimulate uncontrolled cell growth causing Tf by alternating the balance between growth activators & growth suppressors gene products

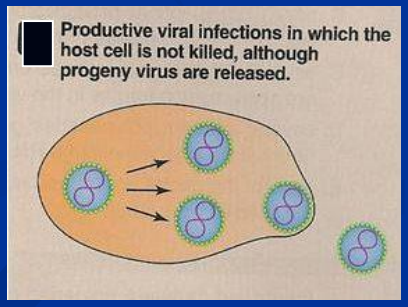
Cytopathogenesis:

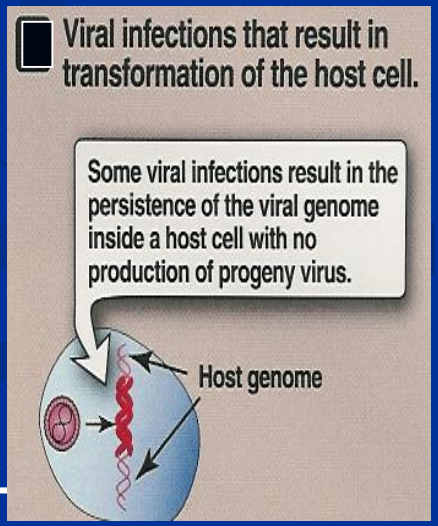
The types of viral infections at cellular leve

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









Pathogenesis at Host Level

- Transmission of the virus & its entry into the host.
- Replication of the virus
- Vs remain localized or spread to other organs
- Viral shedding

- The immune response as
  - Host defense
  - Immunopathogenesis

Transmission

1. Person to person

a) Horizontal transmission

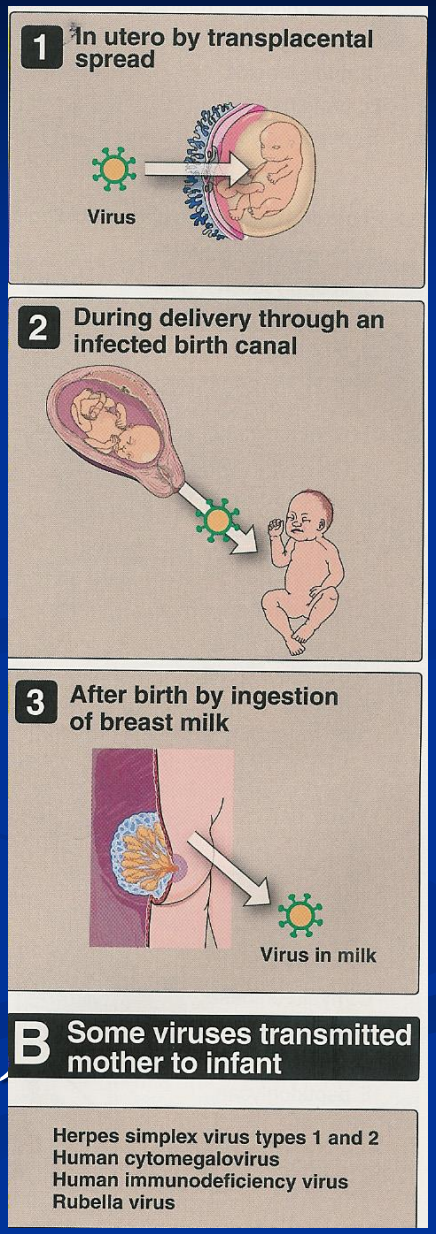
- Skin contact , Blood
- Respiratory route
- Fecal - oral route
- Genital contact

b) Vertical transmission

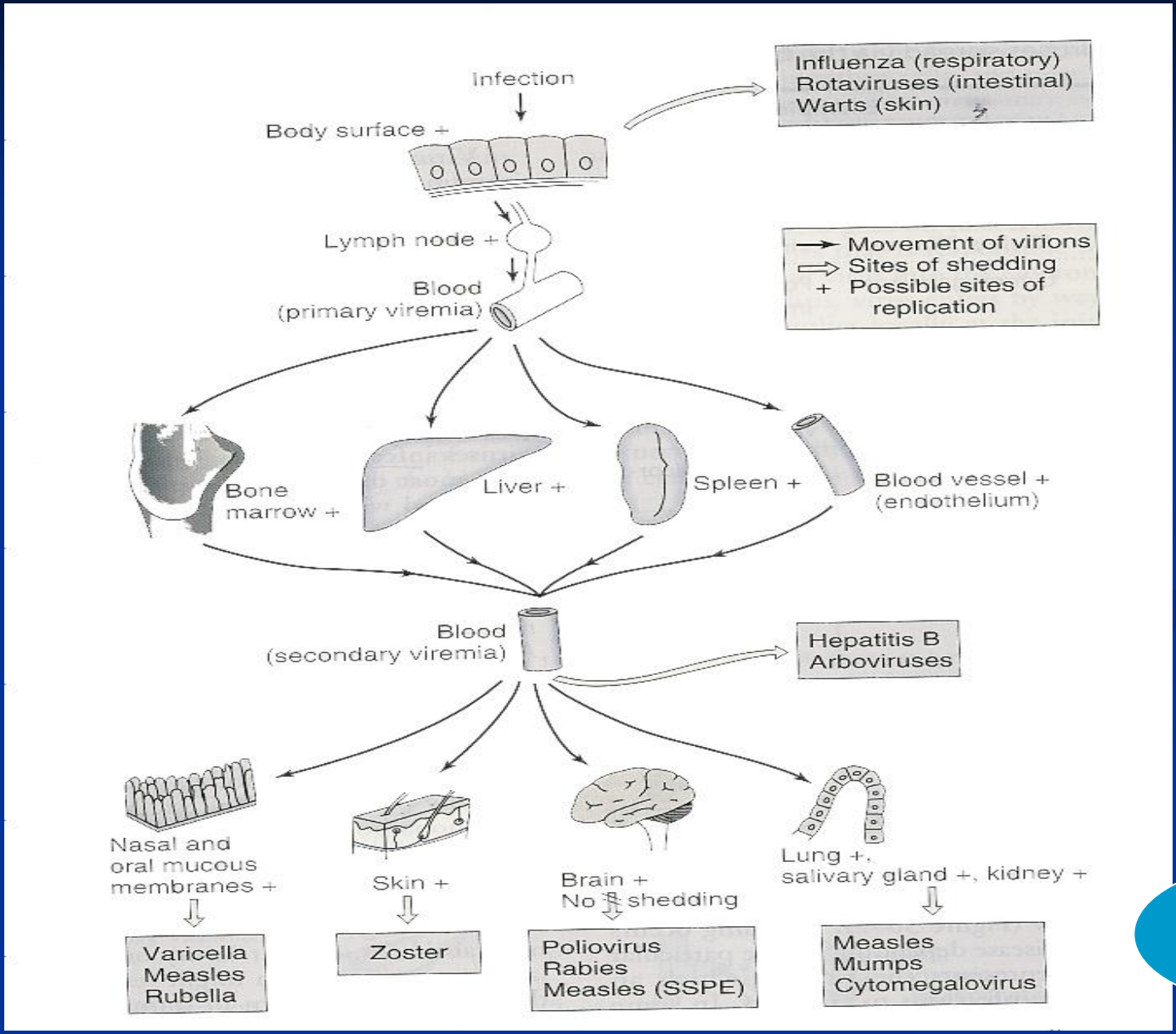
2. Animal to person

Reservoir → Human (Rabies v.)

Reservoir → vector → Human (YFV)



Mechanisms of spread of virus through the body

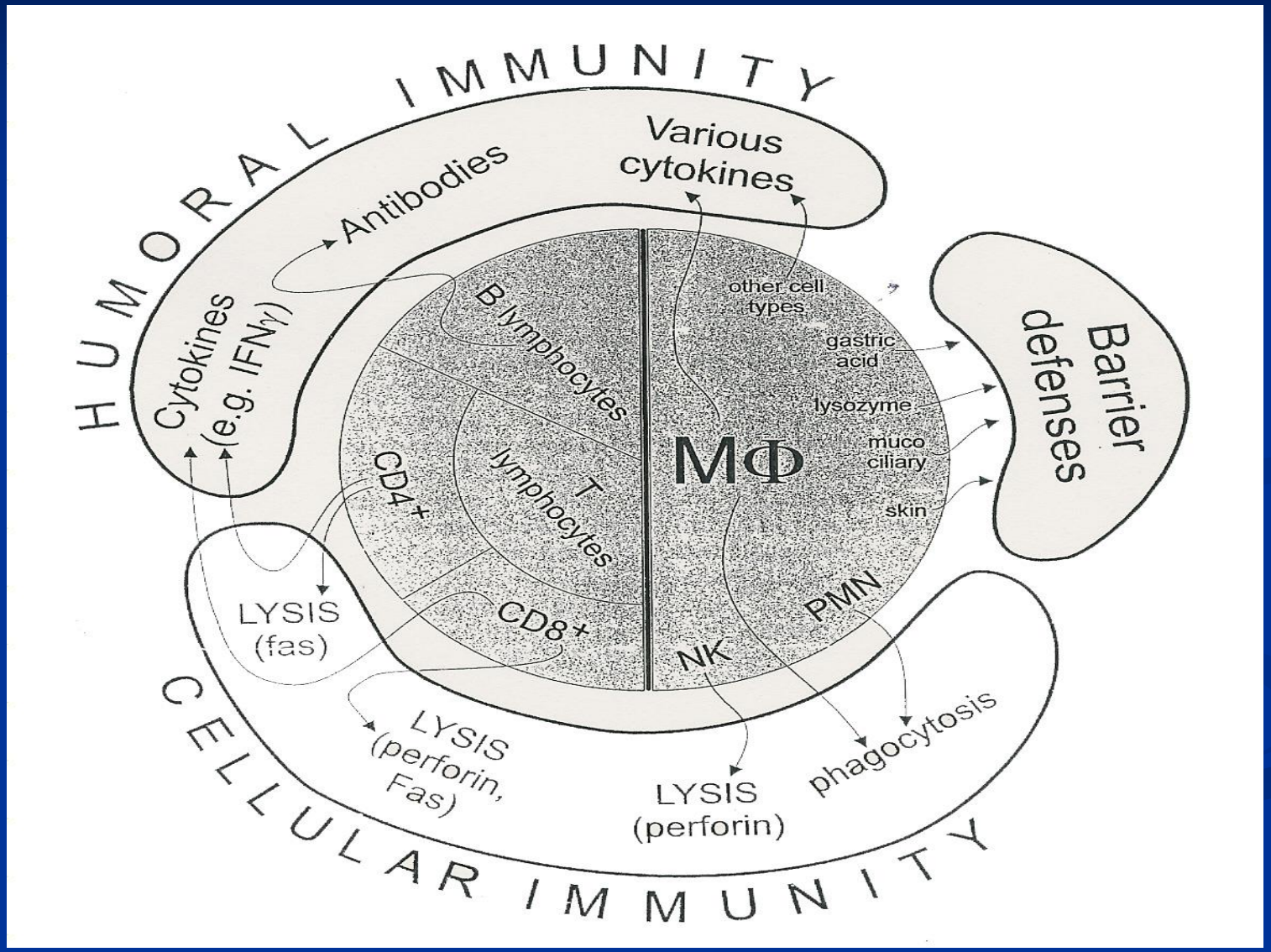


Virus shedding

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



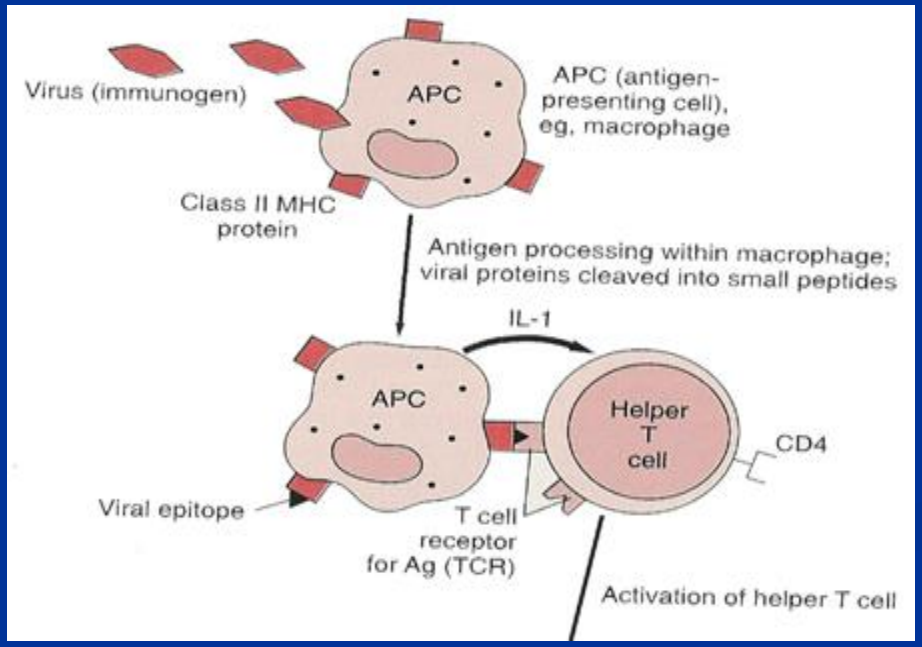
The immune response to virus

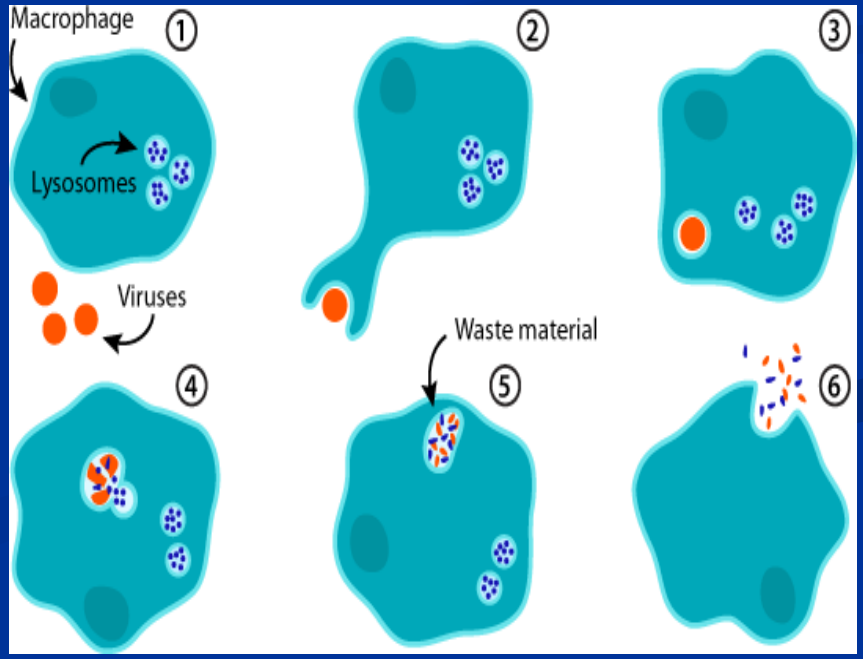
- Natural killer (NK) cells :

  Lysis of VICs

- Macrophages:

  APC, Cytokines production ,Phagocytosis





The immune response to virus

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

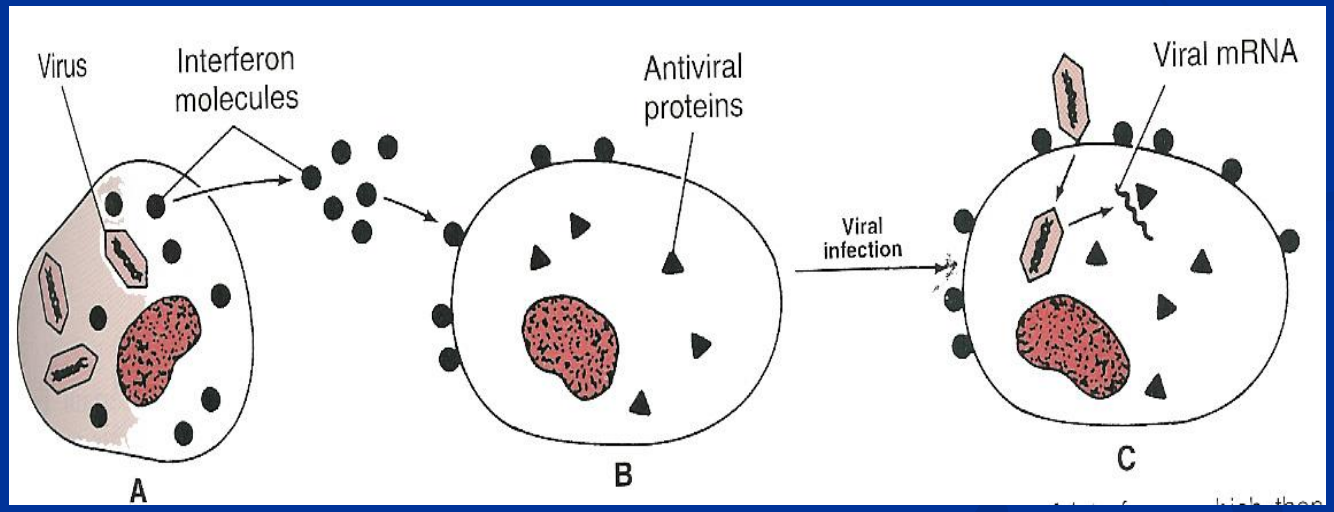
  Lysis of VICs

- ***Macrophages:***

  APC, Phagocytosis , Cytokines production

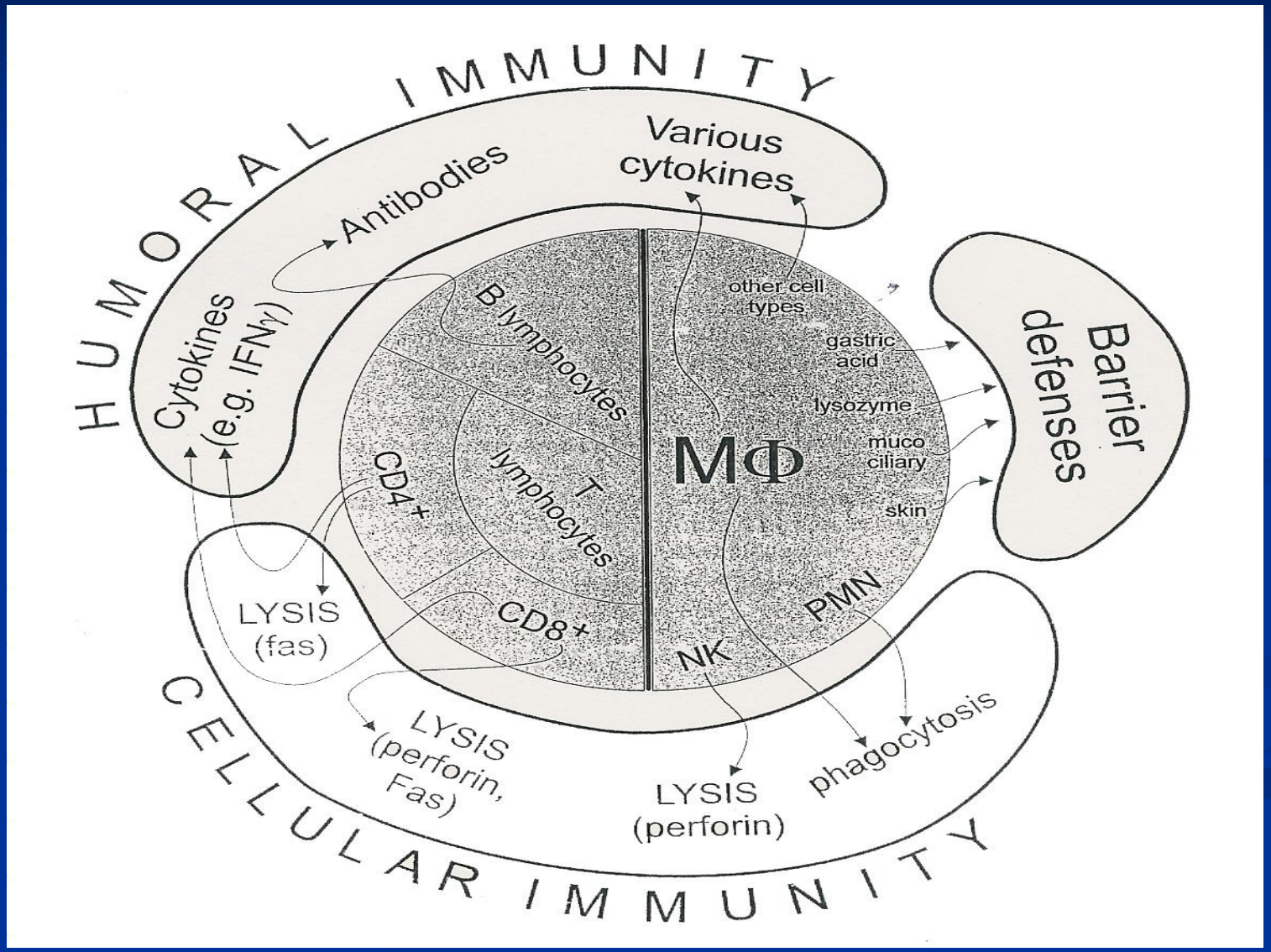
- ***Cytokines:***

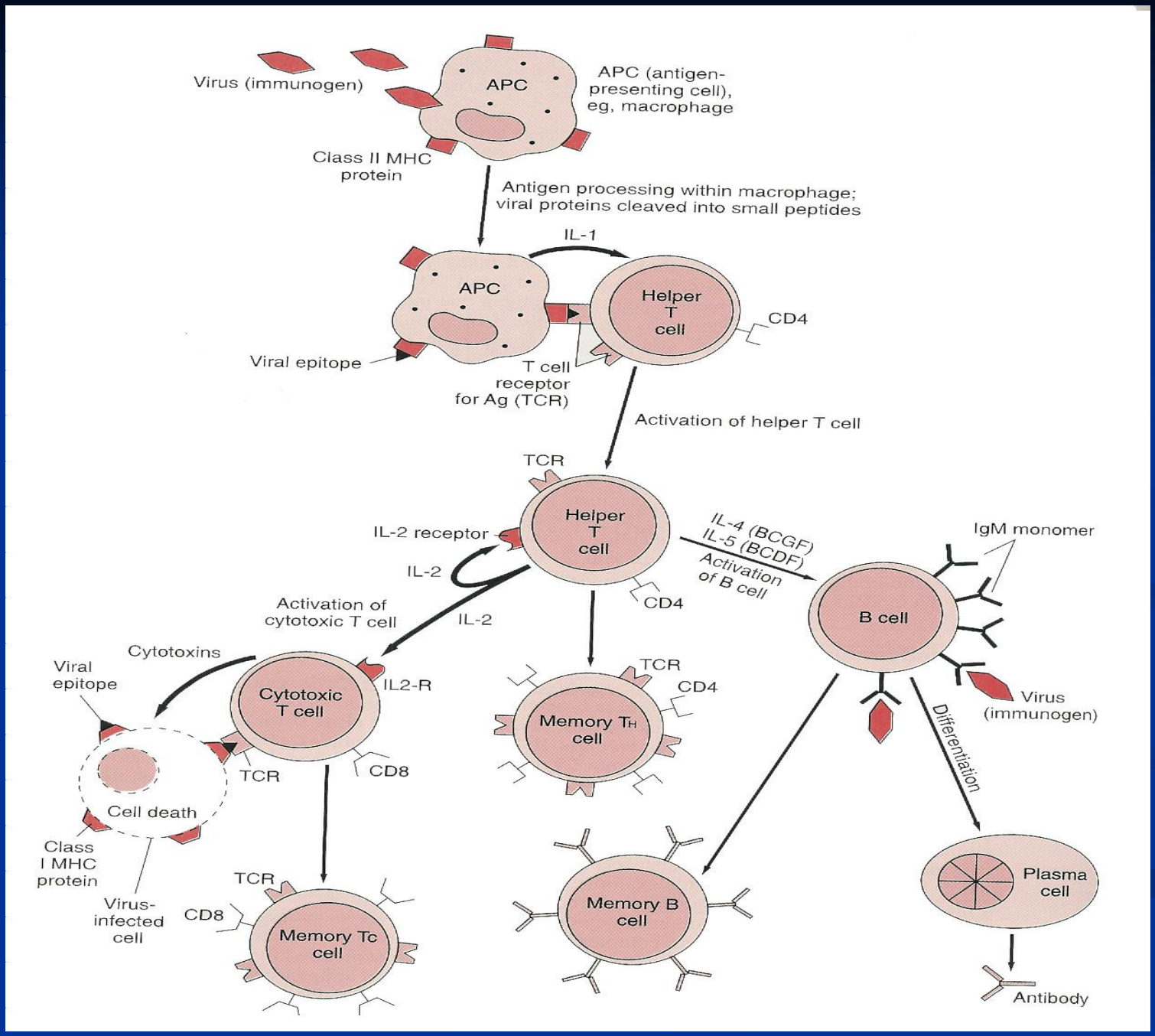
  - Interferons (IFN)



- α , β IFN → inhibit viral translation
- γ IFN → stimulate phagocytosis and killing by macrophage & NK cells

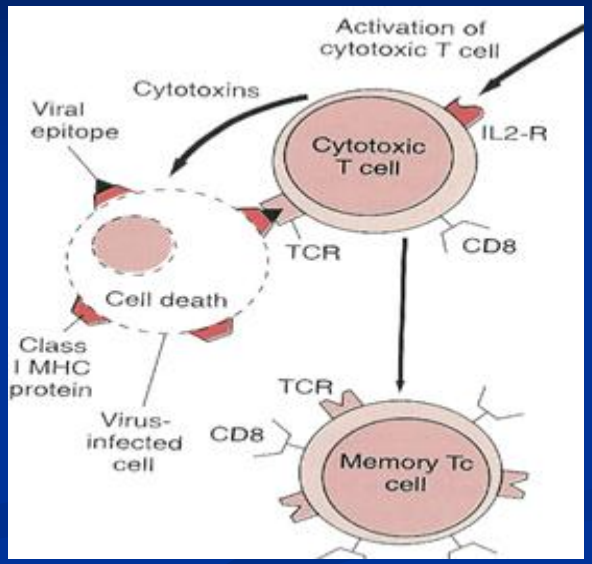
The immune response to virus



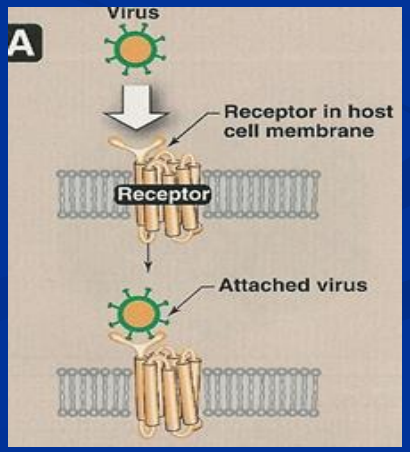

Virus (immunogen)
APC
APC (antigen-presenting cell), eg, macrophage
Class II MHC protein
Antigen processing within macrophage; viral proteins cleaved into small peptides
IL-1
APC
Helper T cell
CD4
Viral epitope
T cell receptor for Ag (TCR)
Activation of helper T cell
TCR
Helper T cell
IL-2 receptor
IL-2
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

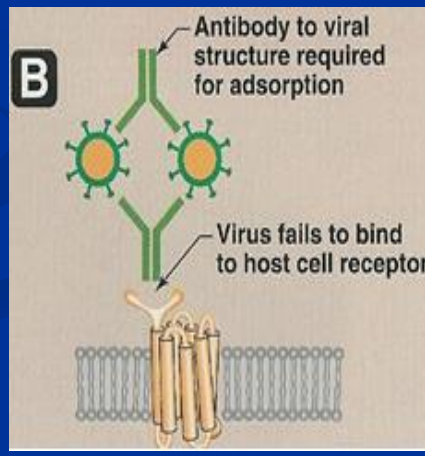
The immune response to virus

- **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

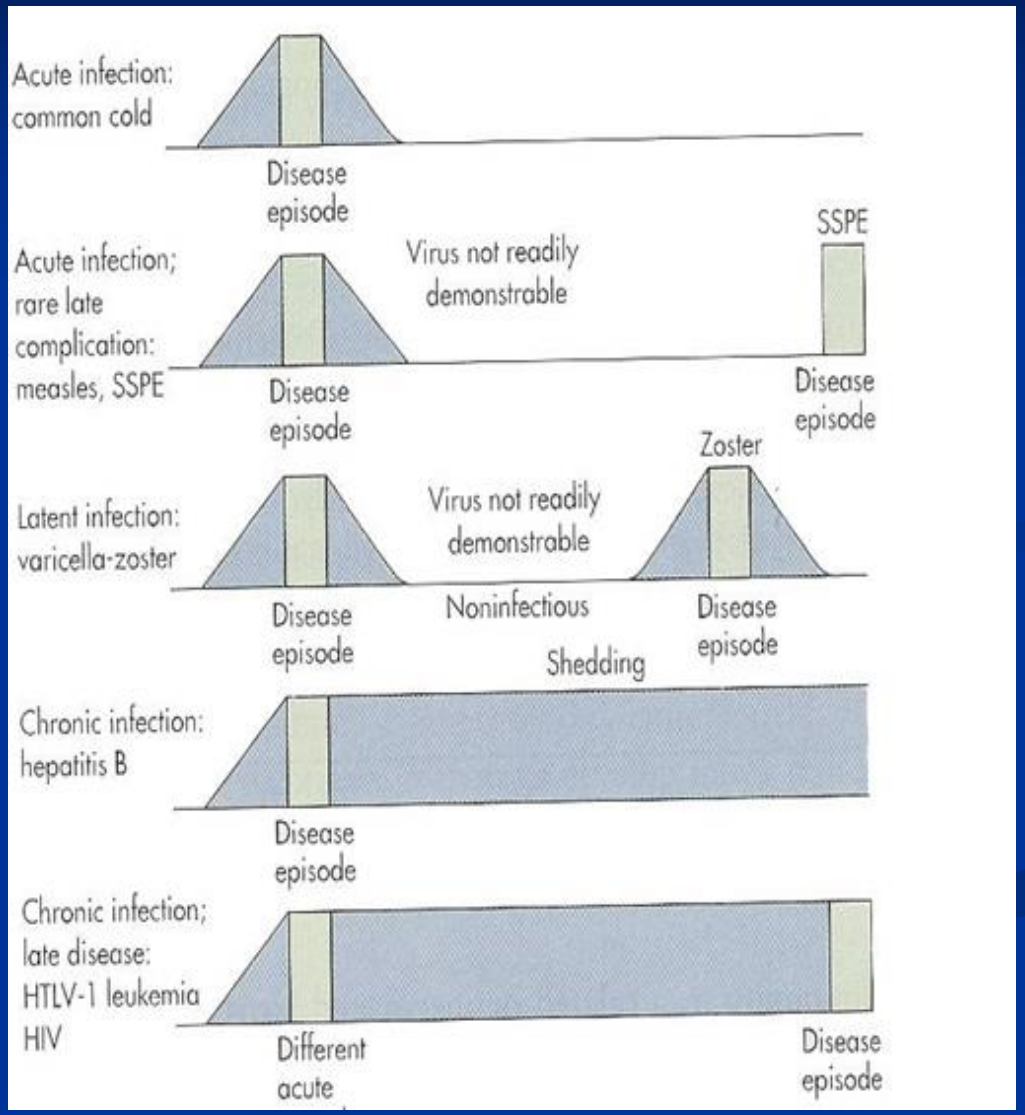
   B) Immunologic attack (Immunopathogenesis)

   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. Persistant infection
   - Late complication of acute infection
   - Latent infection
   - Chronic infection



- **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

من سلك طريقا يلتمس فيه علما سهل الله له طريقا إلى الجنة وإن الملائكة لتضع أجنحتها رضا لطالب العلم وإن طالب العلم يستغفر له من في السماء والأرض حتى الحيتان في الماء وإن فضل العالم على العابد كفضل القمر على سائر الكواكب، إن العلماء هم ورثة الأنبياء إن الأنبياء لم يورثوا دينارا ولا درهما إنما ورثوا العلم فمن أخذه أخذ بحظ وافر

الراوي: أبو الدرداء المحدث: الألباني - المصدر: صحيح ابن ماجه - الصفحة أو الرقم: 183
خلاصة حكم المحدث: صحيح

تميم التميمي
سلسلة التصاميم الدعوية 2011
www.tameem.net

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

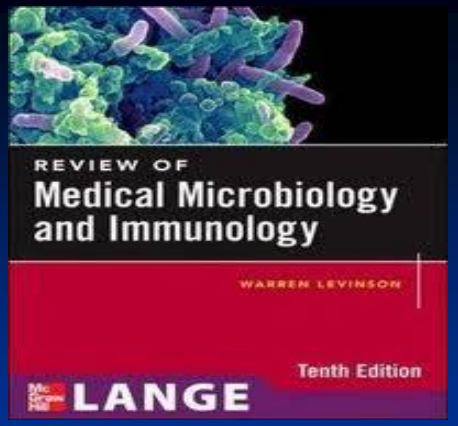
- Lippincott's Illustrated Reviews: Microbiology

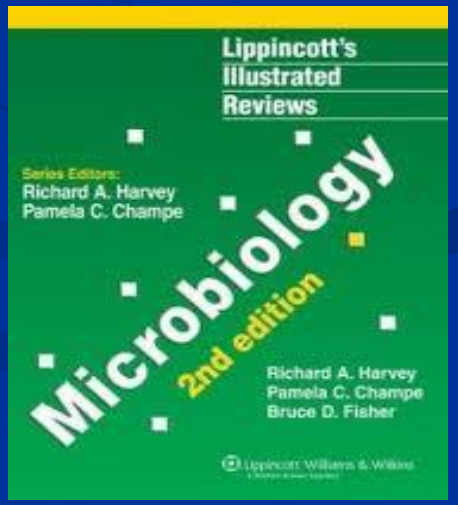
  By: William A. Strohl ,Harriet Rouse &

  Bruce D. Fisher

  2nd Edition, 2007 .

  Pages;15-17,242-243.





Thank you