

2021-2022

# **Immunodeficiency**

**(2 of 2)**

# Acquired (secondary) immunodeficiencies

- More common
- Many causes such as therapy, cancer, sarcoidosis, malnutrition, infection & renal disease
- The most common of which is therapy-related

# AIDS, epidemiology

- AIDS was first described in the United States
- Largest number is in Africa
- Major routes of transmission:
  - Sexual contact
  - Parenteral inoculation
  - From infected mothers to their newborns
  - 10%...unknown risk factors

# AIDS, 5 major risk groups

- Men who have sex with men
- Heterosexual contacts of members of other high-risk groups
- IV drug abusers
- Recipients of blood and blood components
- Hemophiliacs, especially those who received large amounts of factor VIII or IX concentrates before 1985

\*1%: in children

...90% by vertical transmission

# AIDS, epidemiology, cont'd

- Sexually transmitted diseases increase risk of infection
- Measures to decrease transmission by blood products transfusion:
  - antibody screening
  - antigen screening
  - heat treatment of clotting factor concentrates
  - nucleic acid testing
- In gonorrhea, chlamydia and chorioamnionitis:
  - ↑ in inflammatory cells carrying the virus

# AIDS, epidemiology, cont'd

- Needle stick injury....



Visit [https://web.stanford.edu/group/parasites/ParaSites2006/Leish\\_vaccine/Links%20and%20References.html](https://web.stanford.edu/group/parasites/ParaSites2006/Leish_vaccine/Links%20and%20References.html) for references

# AIDS, etiology

- HIV

...of lentivirus family

- HIV-1 and HIV-2

 More common

- Infectious particle: 2 RNA strands within a protein core surrounded by a lipid envelope derived from infected host cells but containing viral proteins

# AIDS, etiology...cont'd

- Life cycle:

Infection of cells → production of viral DNA → its integration into host genome → expression of viral genes → production of viral particles

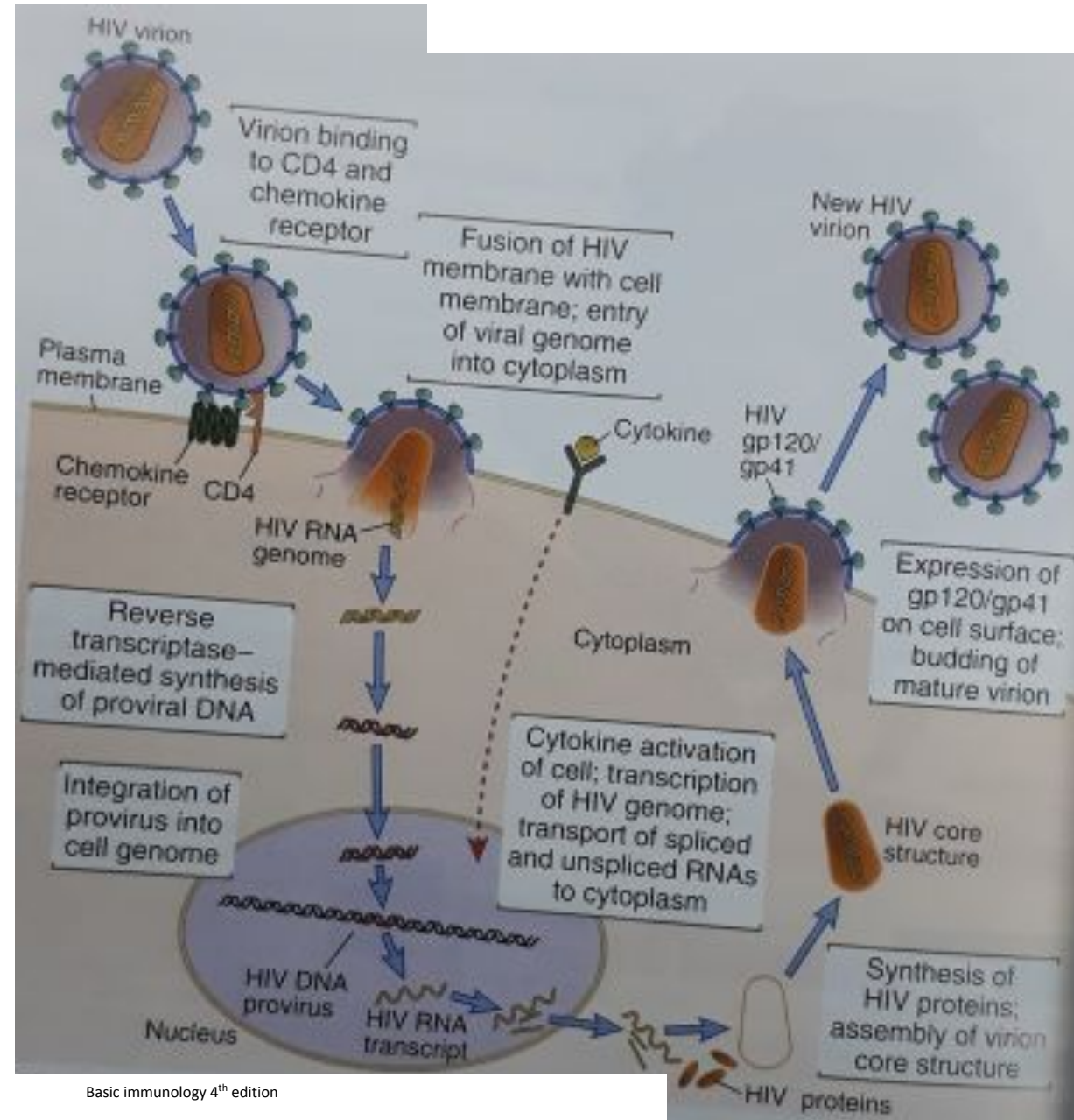
- Major envelope glycoprotein: gp120



Binds to CD4, CXCR4, or CCR5



# AIDS, etiology...cont 'd



# AIDS, pathogenesis

- It infects mainly CD4+ T cells...progressive destruction of these cells

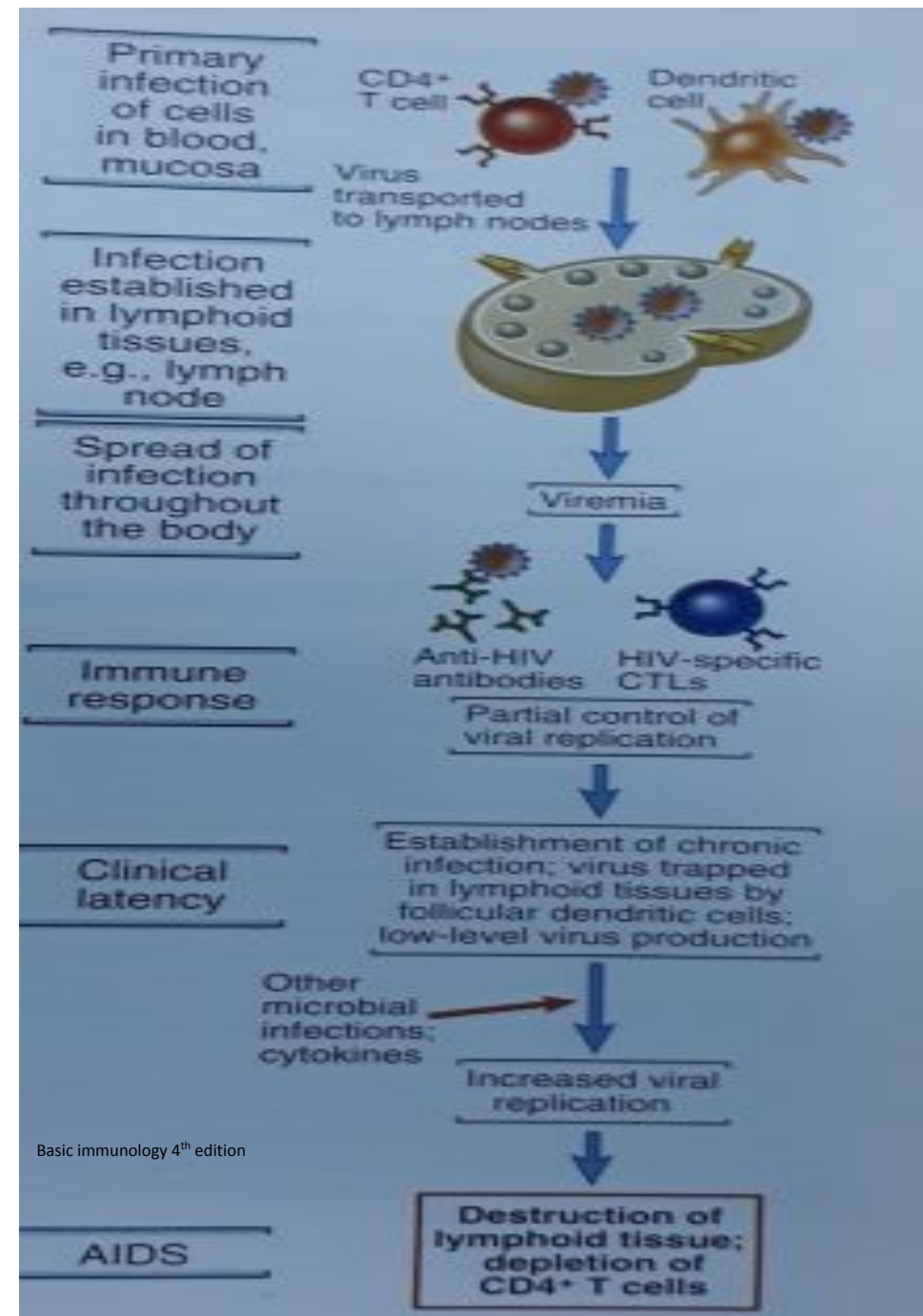


May also infect macrophages and dendritic cells

- Latent → reactivation → progressive destruction of cells...

AIDS development over many years

# AIDS, pathogenesis...cont'd



# Clinical features of HIV infection

- Early after HIV infection: mild acute illness

Fever and malaise due to initial viremia  
...see slide #15



- The illness subsides within a few days...enters the clinical latency period  
...during this latency: -progressive loss of CD4+ T cells in lymphoid tissues  
-progressive destruction of lymphoid tissue

architecture



- Eventually: the blood CD4+ T cell count begins to decline

# Clinical features of HIV infection, cont'd

- When the count  $< 200$  cells/mm<sup>3</sup>...AIDS (susceptibility to infections)



- If not given treatment:

-infections by intracellular microbes →  
-viruses  
-Pneumocystis jiroveci  
-atypical mycobacteria

-infections by extracellular bacteria → defective helper T cell-dependent antibody responses

...also defective CTL function against  
viruses

# Clinical features of HIV infection, cont'd

-susceptibility to cancers caused by oncogenic viruses



- B cell lymphomas
- Kaposi sarcoma

-patients with advanced AIDS: wasting syndrome (cachexia)

-dementia...infection of microglial cells (macrophages)

# Clinical features of HIV infection, cont'd

- Infected patients produce antibodies & CTLs against HIV Ags early in disease

e.g., gp120

...limit the early acute HIV syndrome...but do not prevent progression

...the virus rapidly mutates the region of gp120

...CTLs are not much effective because the virus

↓ expression of MHC I in infected cells

Immune responses against HIV may paradoxically ↑ the spread  
...Ab-coated viral particles may gain entry through Fc receptors on FDCs & macrophages in lymphoid organs

Even if CTLs are able to kill infected cells, phagocytes may become infected when they clear the dead cells

# The elite controllers

- They are long-term nonprogressors
- They control the infection without therapy
- Some...deletion of CCR5 gene
- Certain HLA alleles...HLA-B57 & HLA-B27



# Therapy

- HAART = highly active antiretroviral therapy

...by blocking the activity of viral reverse transcriptase, protease, and integrase



but

- The virus can undergo mutations
- Reservoirs of latent virus are not eradicated by these drugs

**Thank  
You**