

# Pathophysiology of Acquired Immunodeficiency Syndrome

PHCL 415  
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# Learning Objectives

- Characterize the modes, factors, & preventative measures associated with human immunodeficiency virus (HIV) transmission
- Describe the molecular characteristics of the HIV virus
- Describe the HIV replication life cycle
- Understand how HIV infection is diagnosed
- Recognize the clinical presentation of primary HIV infection

# Outline

- HIV, AIDS & CD4+
- Classification
- Clinical course
- Opportunistic infections
- Signs & symptoms
- Disorders due to AIDS

# Introduction

# Characteristics of AIDS

- Profound immunosuppression
- Associated opportunistic infections
- Malignancies
- Wasting
- Central nervous system degeneration

# AIDS Epidemic & Transmission

- Caused by HIV infection
- Occurs worldwide
- No cure
- Transmitted through blood, semen, vaginal fluids, and breast milk
- Not spread by casual contact or insects
- Infectious, even if the person is asymptomatic

# Cells Affected by the HIV Virus

- A subset of lymphocytes called CD4+ T lymphocytes (also known as T helper cells or CD4+ T cells)
- Macrophages
- Dendritic cells

# Function of CD4+ T Cells

- Necessary for normal immune function
- Recognize foreign antigens
- Help activate antibody-producing B lymphocytes
- Orchestrate cell-mediated immunity
- Influence the phagocytic function of monocytes and macrophages



# Life Cycle of The HIV

1. Attachment of the HIV virus to CD4+ receptor
2. Internalization and uncoating of the virus with viral RNA and reverse transcriptase
3. Reverse transcription produces a mirror image of the viral RNA and double-stranded DNA molecule
4. Integration of viral DNA into host DNA using the integrase enzyme

# Life Cycle of The HIV

5. Transcription of the inserted viral DNA to produce viral messenger RNA
6. Translation of viral messenger to create viral polyprotein
7. Cleavage of viral polyprotein into individual viral proteins that make up the new virus
8. Assembly and release of the new virus from the host cell

# Three Phases of HIV

- Primary infection phase
- Chronic asymptomatic or latency phase
- Overt AIDS phase

# CDC HIV/AIDS Classification System

- The clinical importance of the CD4+ cell count in the categorization of HIV-related clinical conditions
  - Category 1: >500 cells/ $\mu$ L
  - Category 2: 200 to 499 cells/ $\mu$ L
  - Category 3: <200 cells/ $\mu$ L

# Question

- Which of the following cell types is most problematic in the development of AIDS?
  - a) CD4+ cells
  - b) Macrophages
  - c) Dendritic cells
  - d) Neutrophils

# Answer

- a) CD4+ cells: These memory cells are primarily affected in AIDS
- b) Macrophages
- c) Dendritic cells
- d) Neutrophils

# Clinical Course of HIV

- Typical progressors: 60–70% acquire AIDS 10–11 years after infection.
- Rapid progressors: 10–20% progress rapidly and acquire AIDS in less than 5 years.
- Slow progressors: 5–15% do not progress to AIDS for more than 15 years.
- Long-term nonprogressors: 1% have been infected for at least 8 years, are antiretroviral naive, have high CD4+ cell counts and usually very low viral loads.

# Consequences of CD4+ Death

- Opportunistic infections
- Malignant tumors
- Nervous system manifestations
- Wasting syndrome
- Metabolic disorders



# Opportunistic Infections Affecting AIDS

- **Bacterial opportunistic infections**

- Bacterial pneumonia, tuberculosis, Salmonella, Mycobacterium avium-intracellulare complex (MAC)

- **Fungal opportunistic infections**

- Candidiasis, coccidiomycosis, cryptococcosis, histoplasmosis

# Opportunistic Infections Affecting AIDS

- **Protozoal opportunistic infections**
  - Cryptosporidiosis, isosporiasis, pneumocystiasis, toxoplasmosis
- **Viral infections**
  - Cytomegalovirus (CMV), herpes, progressive multifocal leukoencephalopathy (PML)

# Most Common Opportunistic Infections Affecting AIDS

- Pneumocystis jiroveci pneumonia
- CMV
- Oropharyngeal or esophageal candidiasis (thrush)
- Infections caused by MAC

# Signs & symptoms

# Signs & Symptoms of Acute HIV Infection

- Fever
- Fatigue
- Rash
- Headache
- Lymphadenopathy
- Pharyngitis

# Signs & Symptoms of Acute HIV Infection

- Arthralgia
- Myalgia
- Night sweats
- Gastrointestinal problems
- Aseptic meningitis
- Oral or genital ulcers

# Disorders associated with aids

# Respiratory Manifestations Associated With AIDS

- PCP
- Pulmonary tuberculosis (TB)
- CMV, MAC
- *Toxoplasma gondii*
- *Cryptococcus neoformans*
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*
- *Legionella pneumophila*
- Kaposi sarcoma



# Diseases of the Gastrointestinal Tract Associated With AIDS

- Diarrhea or gastroenteritis
  - *Cryptosporidium parvum*
- Esophagitis
  - Esophageal candidiasis (thrush)
  - CMV infection
  - Herpes simplex virus infection

# Nervous System Manifestations Associated With AIDS

- AIDS dementia complex (ADC)
- Toxoplasmosis
- PML
  - These disorders can affect the peripheral or central nervous system

# Cancers & Malignancies Associated With AIDS

- Kaposi sarcoma
- Non-Hodgkin lymphoma
- Noninvasive cervical carcinoma

# Wasting Syndrome

- **Factors that contribute to wasting**
  - Anorexia
  - Endocrine dysfunction
  - Malabsorption
  - Cytokine dysregulation
- **Characteristics**
  - Involuntary weight loss of at least 10% of baseline body weight, presence of diarrhea, more than two stools per day, chronic weakness and fever

# Metabolic and Morphologic Disorders Associated With HIV

- Lipodystrophy and mitochondrial disorders
- Hypercholesterolemia
- Hypertriglyceridemia
- Insulin resistance
- Impaired glucose tolerance

# Transmission & Prevention

# Transmission

- Intravenous drug use
- Risky/unsafe sexual behavior

# Prevention

- Personalized risk assessment
- Prevention plan
- Education
- Behavioral intervention



# Diagnosis

# Diagnosis

- Laboratory methods to determine infection
  - HIV antibody test
  - Western blot test
  - OraSure test
  - Polymerase chain reaction (PCR)
- Clinical methods to evaluate the progression of the disease

# Question

- The signs and symptoms of an AIDS infection are due to \_\_\_\_\_.
- a) The secondary infection
- b) HIV action on the hypothalamus
- c) The body's response against the virus

# Answer

- a) The secondary infection: Signs and symptoms are due to the secondary infection and to the remaining immune system actions against the infection
- b) HIV action on the hypothalamus
- c) The body's response against the virus

# References

- Pharmacotherapy: A Pathophysiologic Approach, 7e
- Pathophysiology of Disease: An Introduction to Clinical Medicine, 6e
- Applied Therapeutics: The Clinical Use of Drugs, 9e

Thank You

Hope you enjoyed this part of the  
course