



# **Opportunistic Infections: A Brief Overview**



# Objectives

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1. Briefly describe the natural history and immunology of HIV
2. Define the term *opportunistic Infection (OI)*
3. Describe why people living with HIV/AIDS are susceptible to OIs
4. Describe the correlation between CD4 cell counts and OIs
5. Name the general pathogens causing OIs



# HIV

- Discovered in the early 1980s, but was around before that
  - Called a retrovirus → medicines used against it are called “antiretrovirals”
- Attacks several types of cells, but most importantly uses the CD4 cell
  - Invades the CD4 cell
  - Tricks the CD4 cell to make more HIV
  - Then kills the CD4 cells
- Produces billions (1,000,000,000’s) of viruses a day
  - Can measure how many viruses are present: “viral load”



# Natural History

- HIV gains entry into CD4 cells and multiplies inside them, eventually destroying them.
- As CD4 cell count decreases and viral load increases, the immune defences are weakened.
- People infected with HIV eventually become vulnerable to special infections, called “opportunistic” infections.
- Without ARV treatment, HIV progresses to symptomatic disease and AIDS and death



# Natural History of HIV Infection

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## Seroconversion

- Infection with HIV, antibodies develop

## Asymptomatic

- No signs of HIV, immune system controls virus production

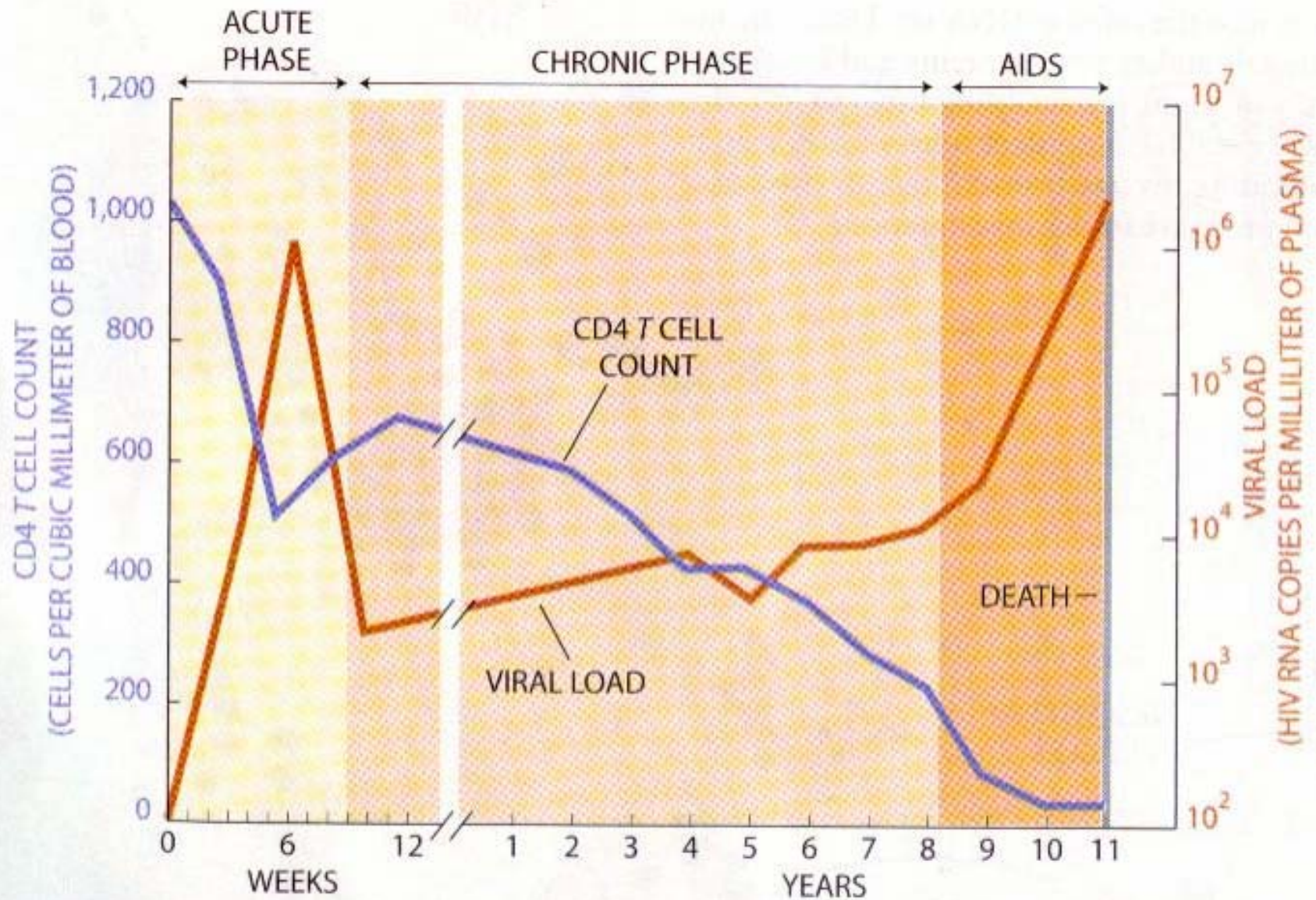
## Symptomatic

- Physical signs of HIV infection, some immune suppression

## AIDS

- Advanced immune suppression, opportunistic infections, end-stage disease

# Clinical Course of HIV Infection



SOURCE: Anthony Fauci et al. in *Annals of Internal Medicine*, Vol. 124; 1996



# War analogy

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- Immune system: Military
- CD4 cells: Generals/soldiers
- HIV: Enemies



# The Invasion

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- When HIV (the enemy) first enters the body, it uses the body's OWN generals to reproduce itself
- Makes many, many more enemies
  - May be over a million (1,000,000) viruses in each ml of blood!
- Kills many soldiers and generals
- May make a person sick with flu-like symptoms: “acute retroviral syndrome”



# Seroconversion / Acute HIV Infection

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- Clinical manifestations resolve as antibodies to the virus become detectable in patient's serum.
- Patients then enter a stage of asymptomatic infection lasting months to years.



# Win, Lose or Draw?

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- So now, there are plenty of enemies and plenty of soldiers
  - We can count them: “viral load”, “CD4 count”
  - Seems on the outside like there is a “draw”
    - But plenty of warfare is taking place
- Slowly, but surely, the enemy kills off more of the soldiers
  - May take 8-10 years in adults who newly got infected for them to get seriously ill
    - Some people are rapid progressors (3-5 years)
    - Others are long-term non-progressors (may take 15 years or longer)
    - Called “latent phase”



# Latent Stage

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- During this stage, level of virus in blood is very low
- Generally lasts for five years or more
- See gradual immune depletion over time
- Patients are usually symptom-free
- CD4 count may be above 500 to start and then will drop



# Latent Stage

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- As the CD4 cell count drops, infections commence and persist or increase
- Over time, mild infections, particularly of skin and mucosal surfaces, start to appear
- Examples include skin rashes and oral thrush



# Meanwhile....

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- The military is protecting the body against all disease-causing organisms
- Because there are plenty of soldiers, these other organisms don't cause many problems
  - If given the chance, they *would* cause problems, but can't because the soldiers are patrolling the body
  - Example: ordinary people may not try to rob a bank when there is a lot of security around, but if there is no security, then some might try



# Waiting for the right opportunity

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- But when HIV kills enough soldiers, those other organisms can now attack the body
  - Called “*opportunistic infections*” because they wait around for the right *opportunity* to cause disease
    - Wait for there to be too few soldiers (CD4 cells) to protect the body
    - Examples: thrush, TB, cryptococcal meningitis, oesophageal candidiasis, PCP
  - These organisms can kill the person if not treated



# AIDS

- Advanced Immune Depletion (CD4 cell  $<200$ / mL) or having ever had WHO stage IV illnesses.
- Viral loads tend to increase, and patients become less able to work or perform other normal functions
- Patients are at high risk for more opportunistic infections
  - Opportunistic infections are the main reason why patients with AIDS die!
- Antiretroviral medication should be started if patient is ready



# WHO Clinical Classification System

- Stage I:** Asymptomatic, generalized lymphadenopathy
- Stage II:** Weight loss <10%, prurigo, fungal nail infection, herpes zoster, recurrent URTIs
- Stage III:** Weight loss > 10%, chronic diarrhea or fever, oral candidiasis /HL, pulmonary TB, severe bacterial infections
- Stage IV:** AIDS-defining illnesses: e.g HIV wasting syndrome, PCP, brain toxoplasmosis, candida oesophagitis, extra-pulmonary TB, CMV retinitis, Kaposi's sarcoma, non-Hodgkins lymphoma and/or performance score 4: bedridden >50% of the day during the last month



# The Empire Strikes Back

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- If, somehow, you could give the few remaining soldiers some weapons, things will likely get better
- Weapons: antiretrovirals!!!
  - Military first needs training on how to use these weapons
  - ARV training, adherence training, etc.
- Now, the few remaining soldiers can fight off the increasing numbers of enemies



# Recruiting more soldiers

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- Enemies: now dead *or hiding*
- Military can now recruit more soldiers and train more generals
- The other “opportunistic” organisms that caused problems when there weren’t many soldiers, now can’t cause problems there are more soldiers to protect the body

# OI overview



- Individuals with HIV/AIDS acquire diseases that also affect otherwise healthy people
  - May have more severe course, however
- Individuals with HIV/AIDS may also acquire diseases that would not cause disease in otherwise healthy people
  - They are susceptible because of weakened immune system
  - **Opportunistic infections** – infections that would not cause disease in an otherwise healthy person



# OI Overview

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People with HIV/AIDS are especially susceptible to OIs due to:

- Suppression of their immune system
- Psychological stress, which can influence the immune system
- Depletion of nutritional status



# Opportunistic Infections

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- May be the initial presentation of HIV
  - May have otherwise ignored or not had previous symptoms
  - May not have wanted VCT or thought it was even necessary
- Are often signs of immunologic deterioration
  - Tend to occur as CD4 counts drop
  - In children < 1 year of age, may get opportunistic infections with “normal” CD4 counts



# Opportunistic infections

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- May need closer follow-up if OIs occur
- Prevention and treatment of disease may prolong life and improve a patient's quality of life
- Response to ARVs will prevent most OIs
  - If OIs occur while on ARVs, think about poor adherence and/or resistance



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***Opportunistic infections are the main reason why people with HIV die!***



# Where do OI's come from?

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- Organisms exist in environment, but normal immune system can combat infection
- Feces: human and/or animal
  - Cryptosporidium, Isospora, Toxoplasma
- Soil (cryptococcus, cryptosporidium)



## Where do OI's come from? Cont'd

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- Water (cryptosporidium)
- Raw, undercooked meat (toxoplasma)
- Some regional distributions as well
- Others exist everywhere (PCP)



# OI Exposure prevention

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- VERY IMPORTANT, VERY IMPORTANT
  - Meats and poultry – cook thoroughly
  - Fruits and vegetables – wash well
  - If clean water not available, boil water first
- Other preventive actions
  - Wash hands often – can prevent cryptosporidium, isospora, toxoplasmosis
  - Avoid contact with ill persons if possible
  - Avoid animal feces



## Brief Overview, continued

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- Co-infections with pathogens such as TB and malaria increase the HIV viral burden and thus accelerate the disease progression.
- Uganda is an example of a situation in which high quality HIV care services were offered early in the epidemic---this seems to have resulted in many HIV- positive persons living well, despite a lack of access to ART.

- Many people with HIV/AIDS first learn that they are HIV infected when they are diagnosed with an OI
- The natural history of HIV involves a progressive loss of CD4 T lymphocytes
- As the CD4 level *declines*, the risk of contracting OIs *increases*
- OIs may be bacterial, viral, fungal, or protozoal

# Brief Overview

- Major causes of HIV-related diseases in selected Africa countries are depicted in the graphic:

## Major Causes of HIV-related disease in selected African countries

