



---

# **The Biology and Natural History of HIV infection**

**Presented: Tropical and Travel Medicine  
Course**

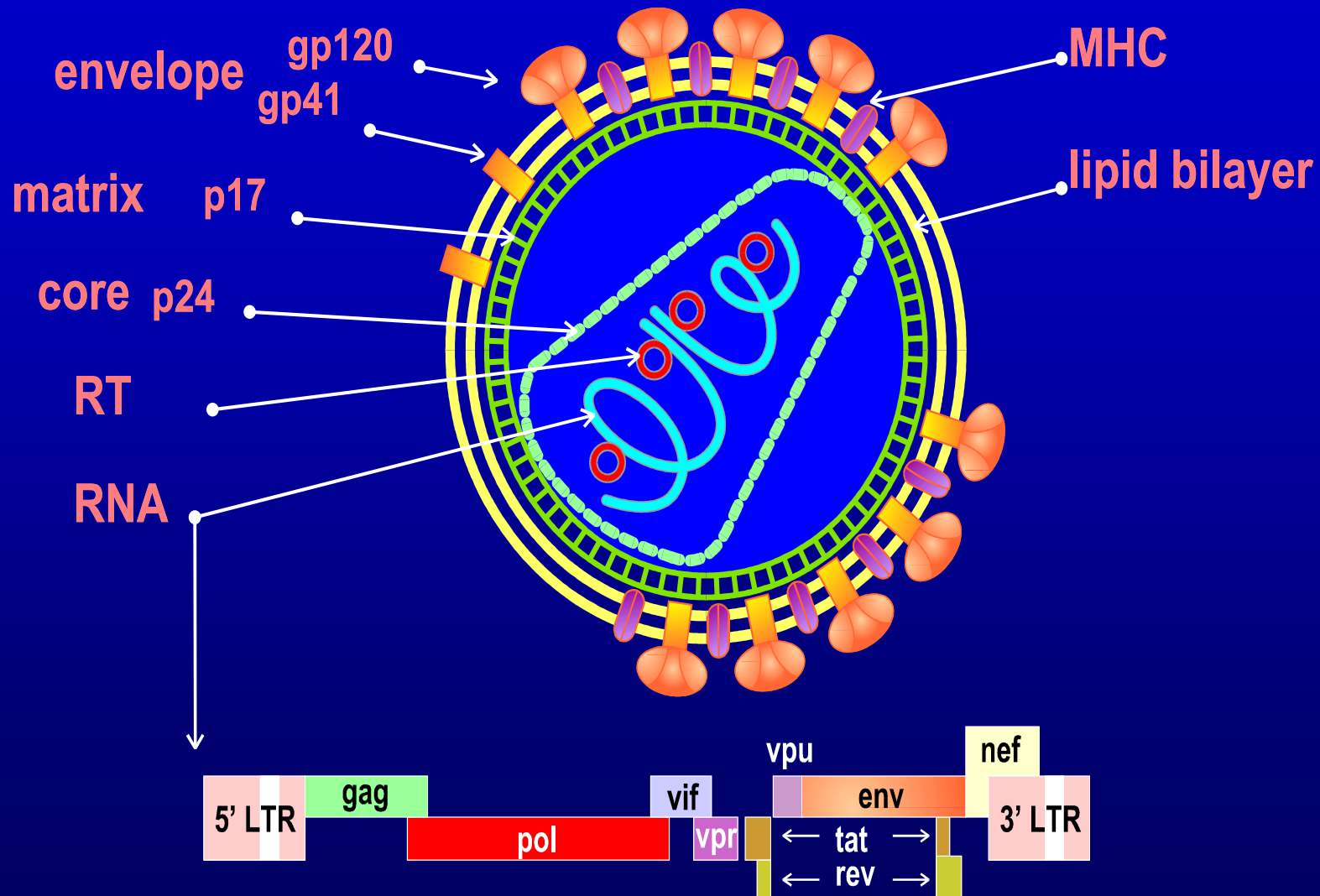
**Jullu, Boniphace – IHI**

**26/AUGUST/2008**

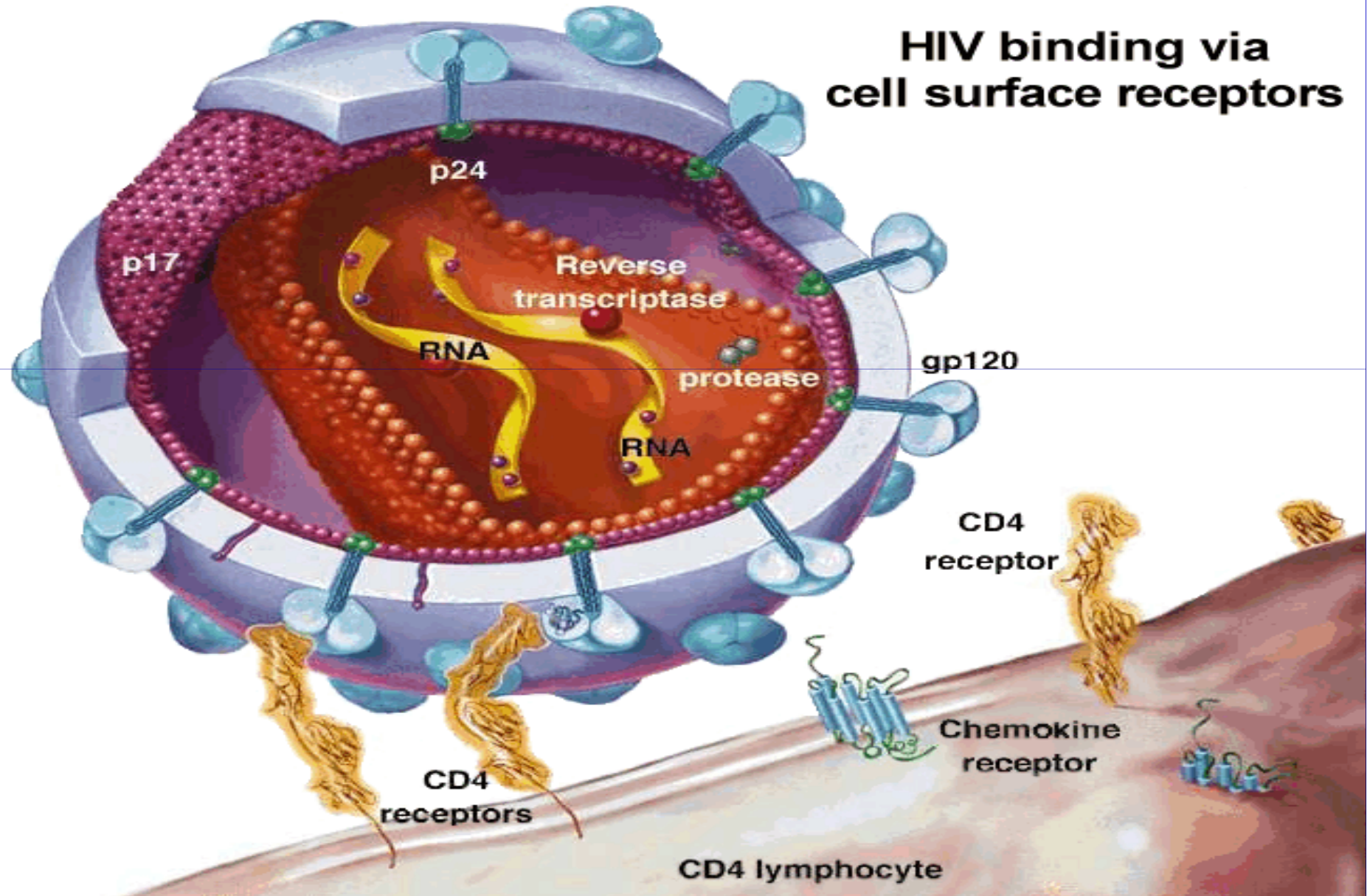


# THE BIOLOGY OF HIV

# HIV particle and genome



# HIV Particle





# Classification of HIV

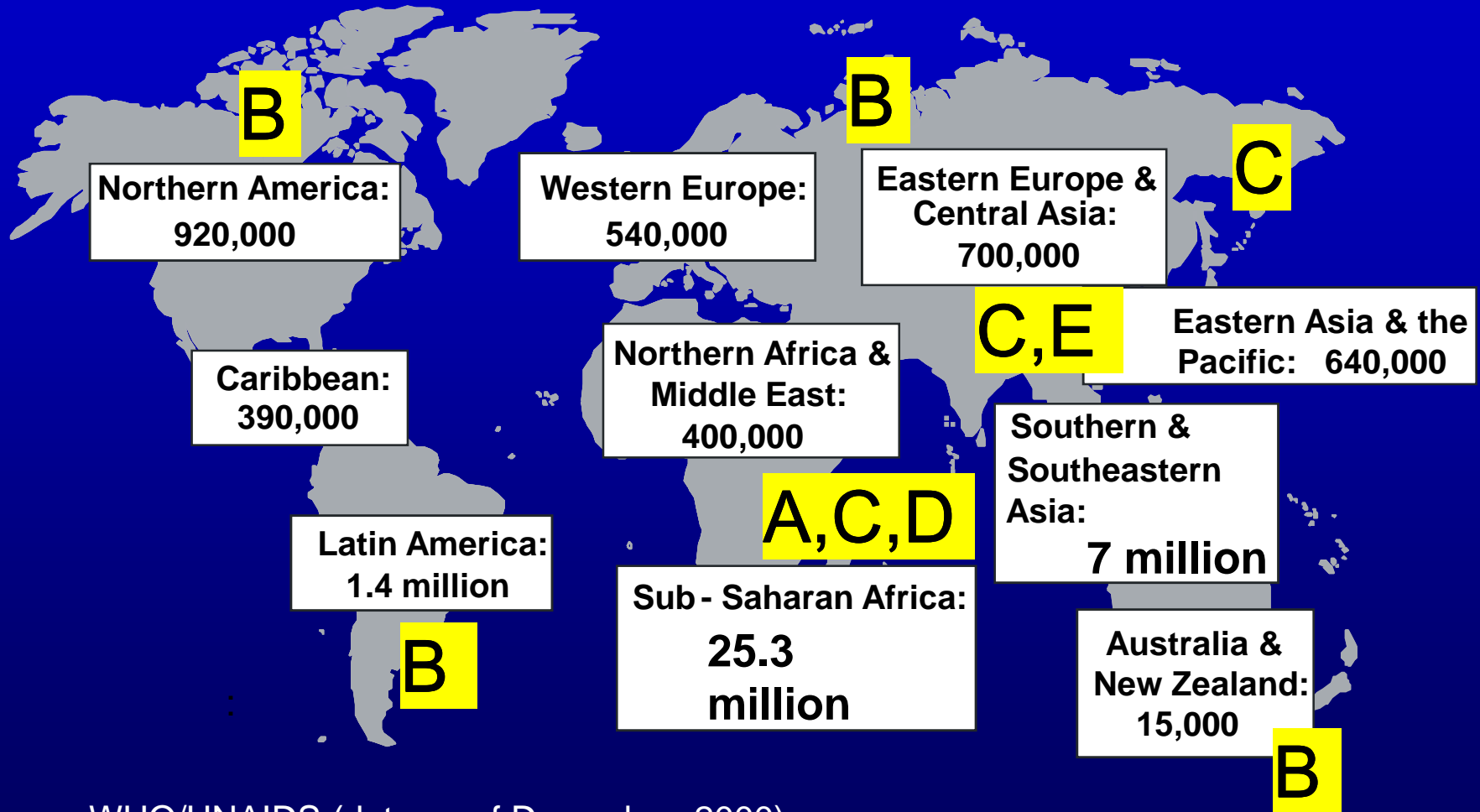
---

- Human Immunodeficiency Viruses include
  - HIV-1
  - HIV-2
- HIV-1 is further classified into
  - Group M (for major)
  - Group N (for new)
  - Group O (for outliers)

# HIV genotypes and subtypes

- HIV -1 can be grouped into
  - Subtypes A-J
  - Recombinants viruses
- HIV- 2 can be grouped into
  - 5 subtypes
  - Recombinant viruses
- Circulating strains of HIV-1 subtypes in Tanzania
  - Subtypes A, D, C and Recombinants

# Worldwide Distribution of HIV-1 Viral Subtypes TO UPDATE



Source: WHO/UNAIDS (data as of December, 2000)

9/18/2008



# Importance of HIV subtypes

---

- Development HIV infection screening assays
  - HIV Screening tests have to detect all HIV subtypes including group O
- Development of candidate HIV vaccines
  - Inclusion of local circulating HIV strains in vaccine candidates
- Epidemiology of HIV epidemic
  - Monitoring of circulating HIV strains over time
- ?HIV transmission

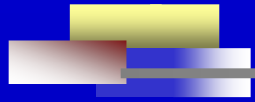




# HIV QUASI SPECIES

---

- HIV has enormous potential for change
  - mutations
  - high rate of replication errors during reverse transcription
- HIV copies in an infected person are not all identical but are rather like a swarm of closely related viruses (quasi-species).



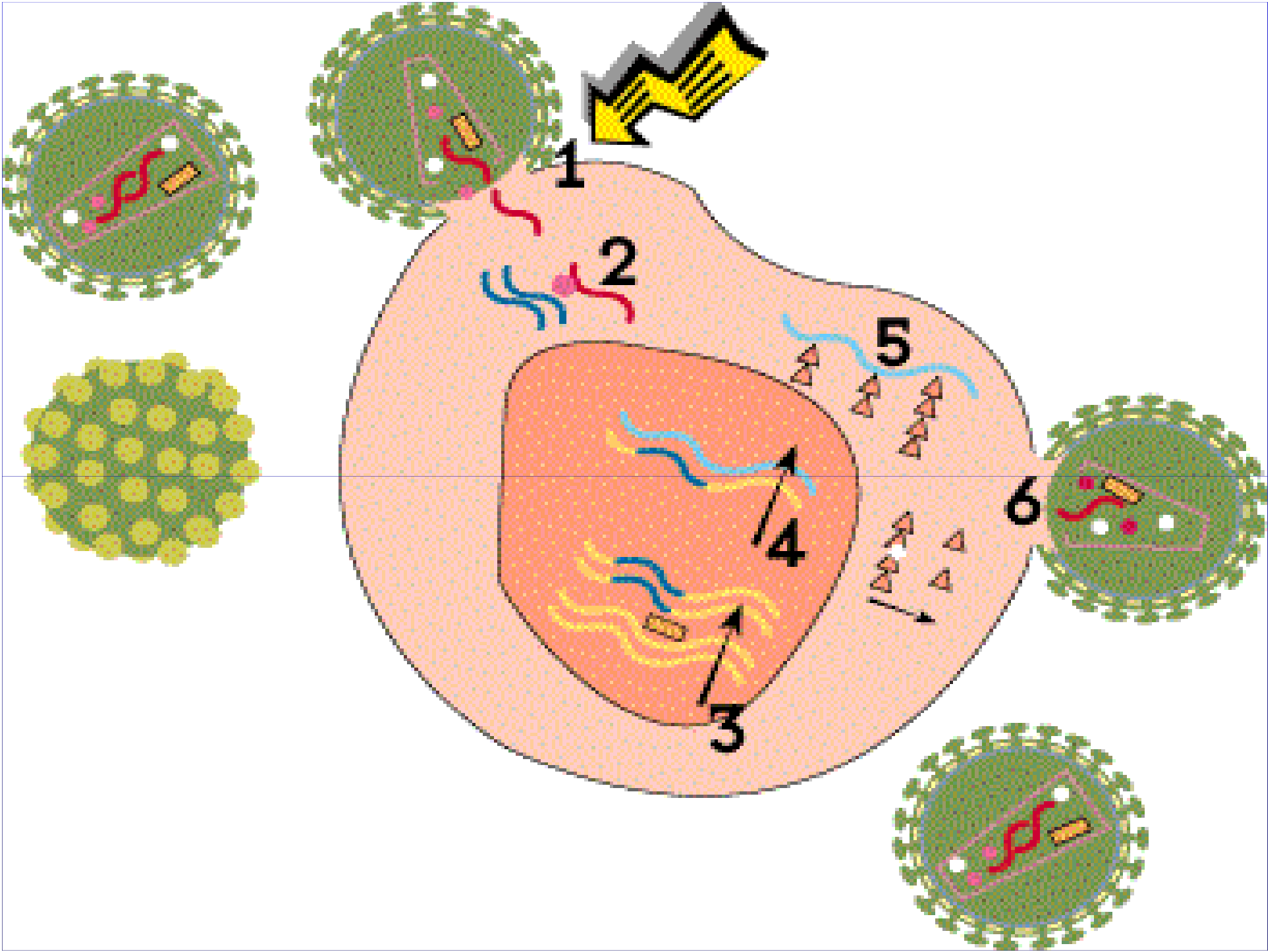
# HIV Life Cycle



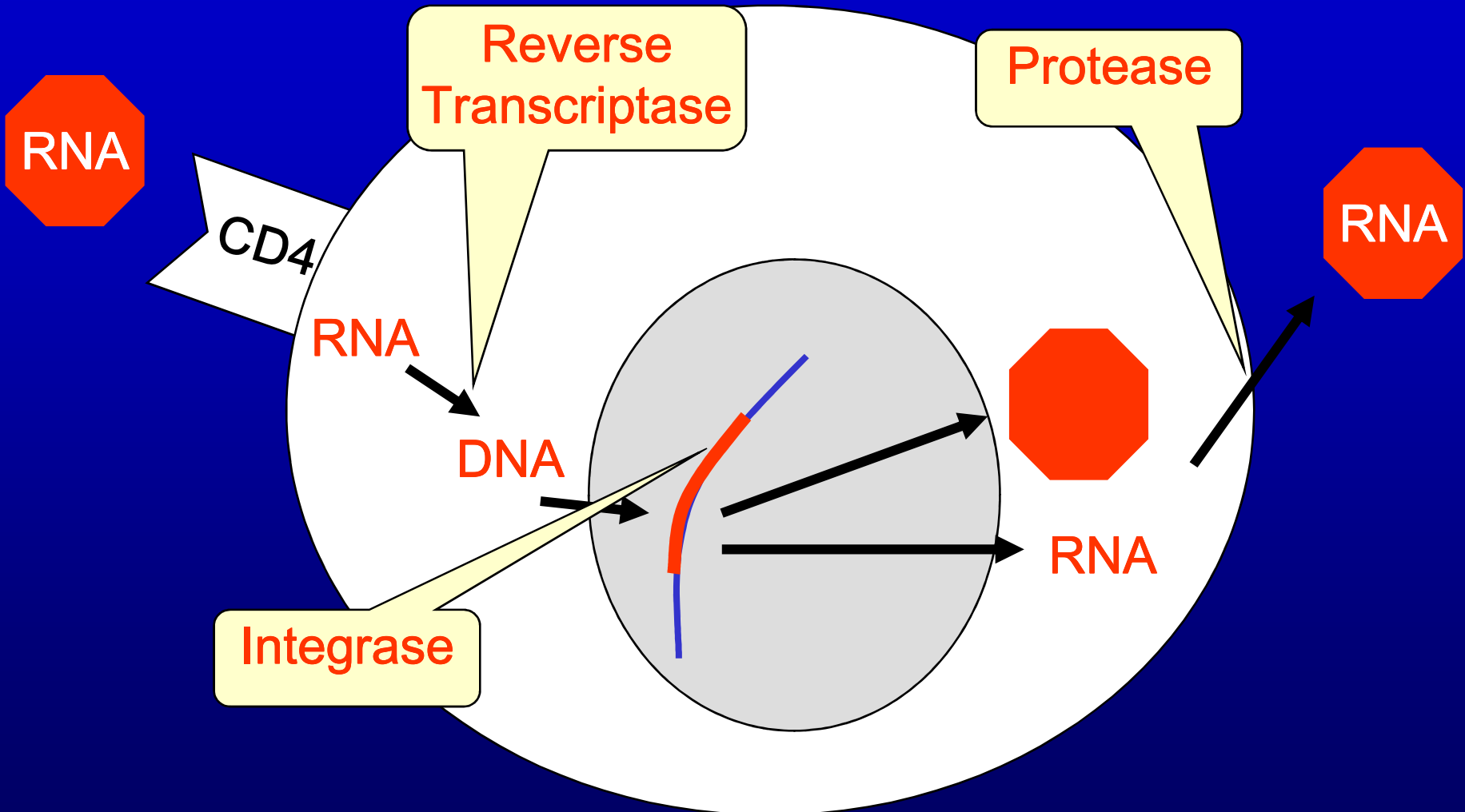
# Life Cycle of HIV 1

---

- Major steps in HIV replication include:
  - Attachment of HIV to susceptible cells
  - Release of HIV genetic material (RNA) into the cell
  - Reverse transcription to produce DNA
  - Integration of pro-viral DNA into host cell DNA
  - Synthesis of viral proteins
  - Assembly and release of viral HIV particles



# HIV Life Cycle



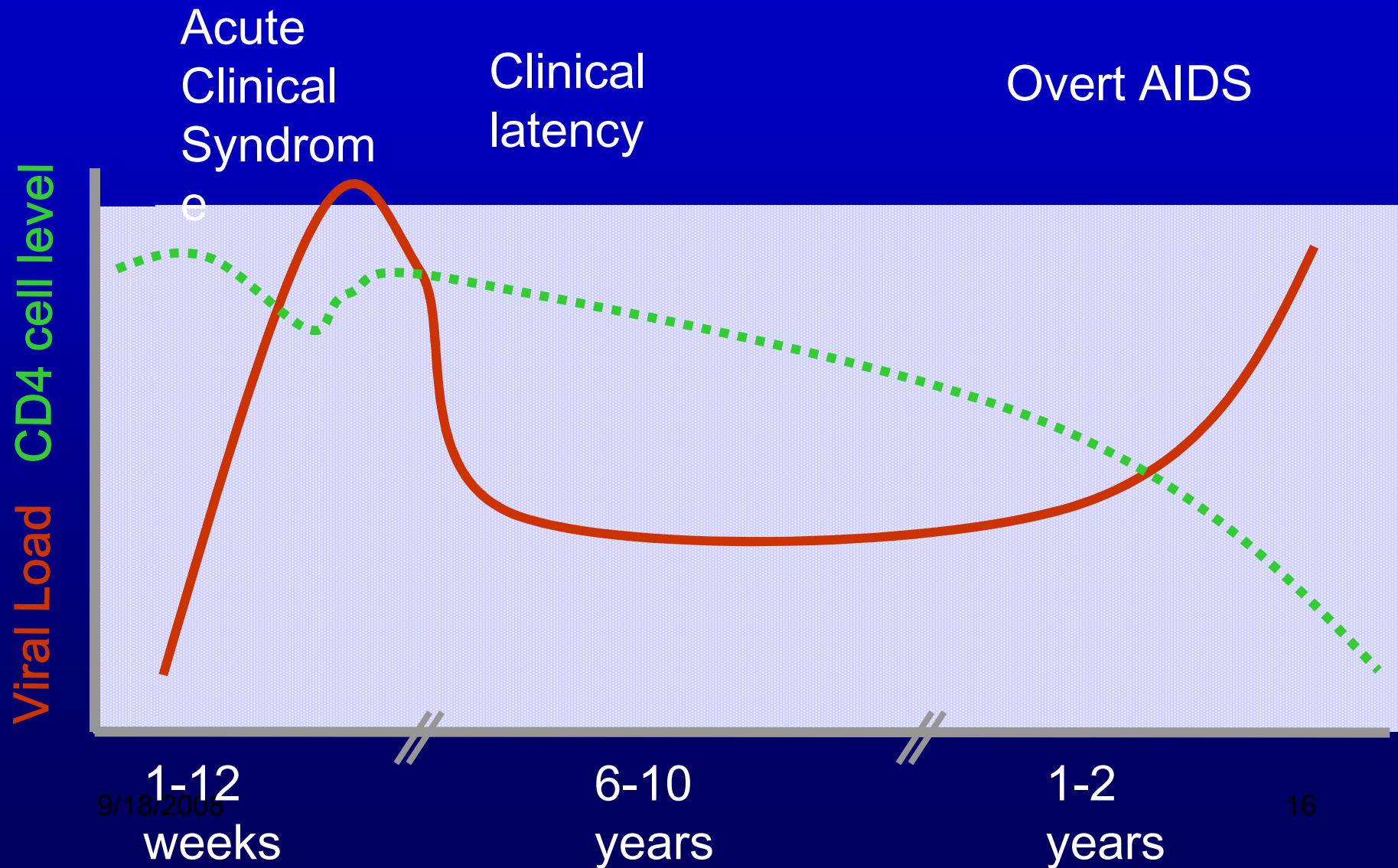


# NATURAL HISTORY OF HIV INFECTION

# Prognostic Markers of HIV Infection

- **Clinical markers**
  - Generalised lymphadenopathy
  - Hairy leukoplakia
  
- **Laboratory makers**
  - **CD4+ T lymphocytes**
    - Absolute cell count for Adults
    - Cell percentages in children
    - An indicator for the status of the immune system (distance to the cliff)
  
  - **HIV Viral Load**
    - An indicator for the amount of viral replication (speed of the train)

# Natural History of HIV-1 Infection

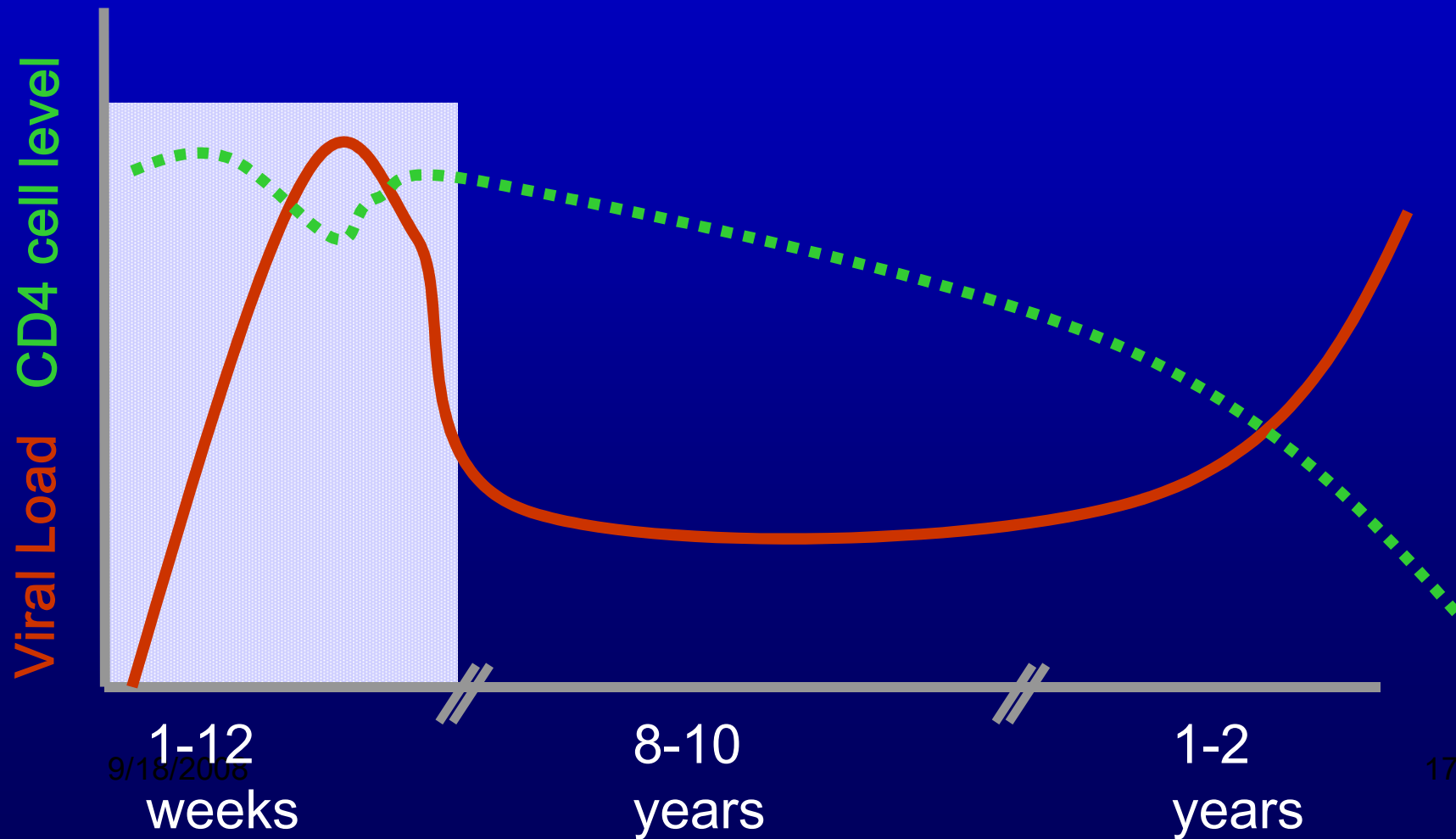


9/18/2006

16



# 'Acute Clinical Syndrome'





# Acute Retroviral Syndrome

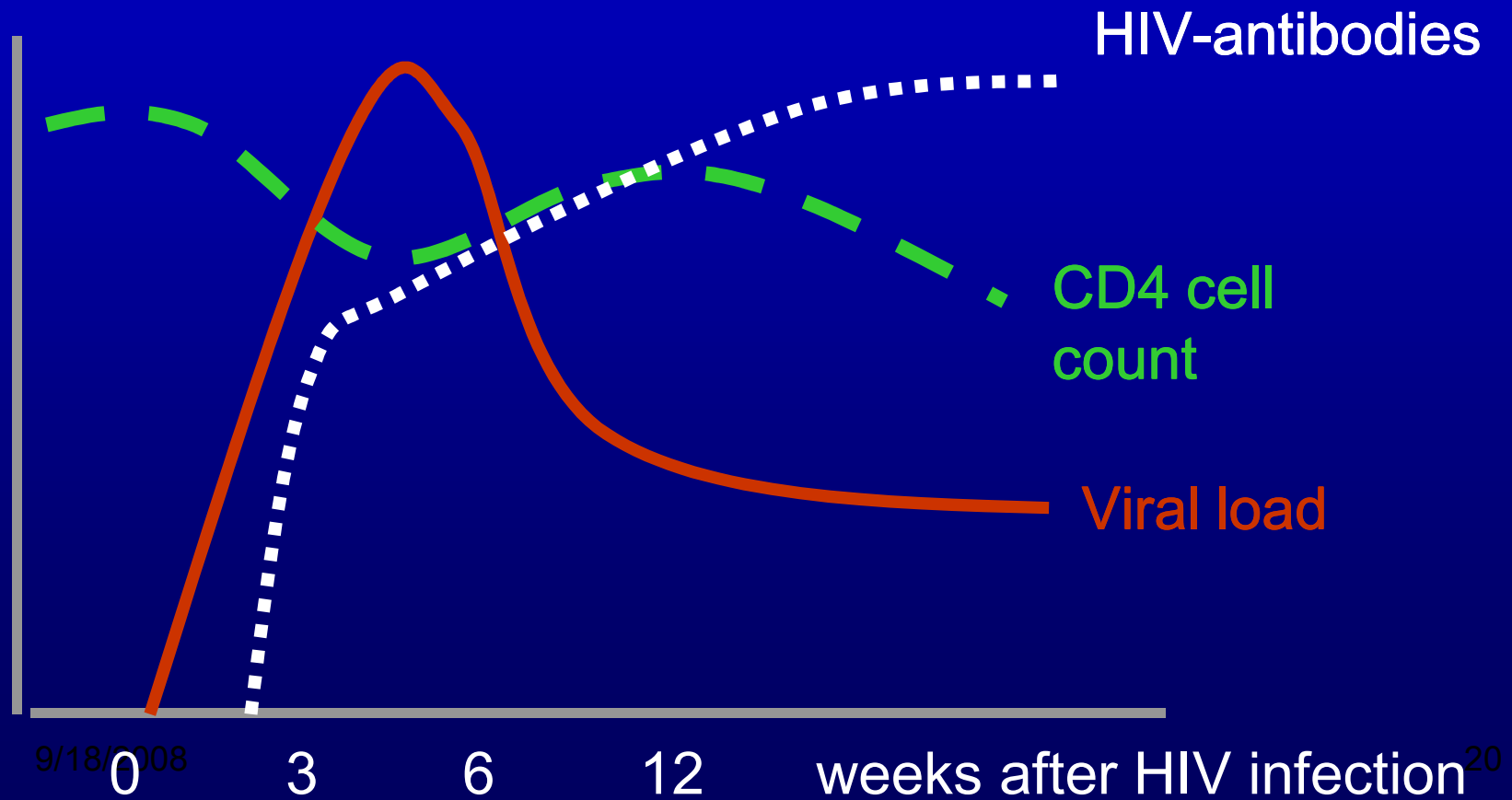
---

- Non-specific 'flu-like' symptoms;
  - Fever
  - Fatigue
  - Pharyngitis
  - Lymphadenopathy
  - Rash

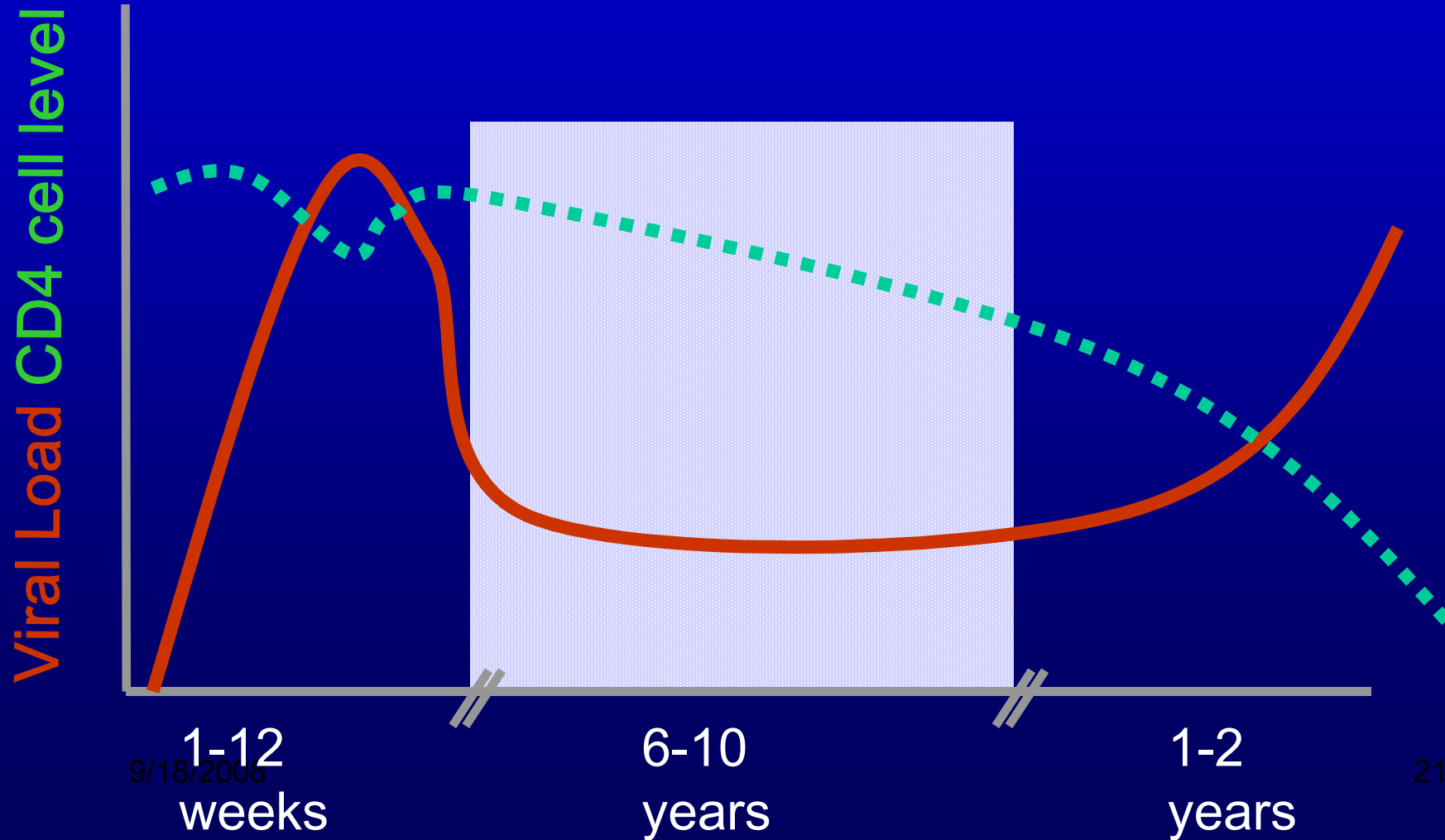
# Pathogenesis of Acute HIV-1 Infection

- Initial infection of CD4 T-cells and macrophages at site of exposure
- Dissemination of infection to lymph nodes
- Burst of viral replication results in intense viremia
- Development of humoral immunity (HIV specific antibodies)
- Response by cellular immunity (HIV-specific CD4 and CD8 cells)

# Acute HIV-1 Infection



# 'Clinical Latency'



9/18/2006

21



# Clinical Latency

---

- At **CD4 cell counts over 500 cells/ $\mu$ l**, many complications overlap with conditions found in the general population (bacterial pneumonia, tuberculosis, minor skin conditions), although they may be more frequent
- At **CD4 counts between 200 and 500 cells/ $\mu$ l**, other conditions, or opportunistic infections, begin to appear (Kaposi's sarcoma, oral or vaginal candidiasis, herpes zoster, etc.).

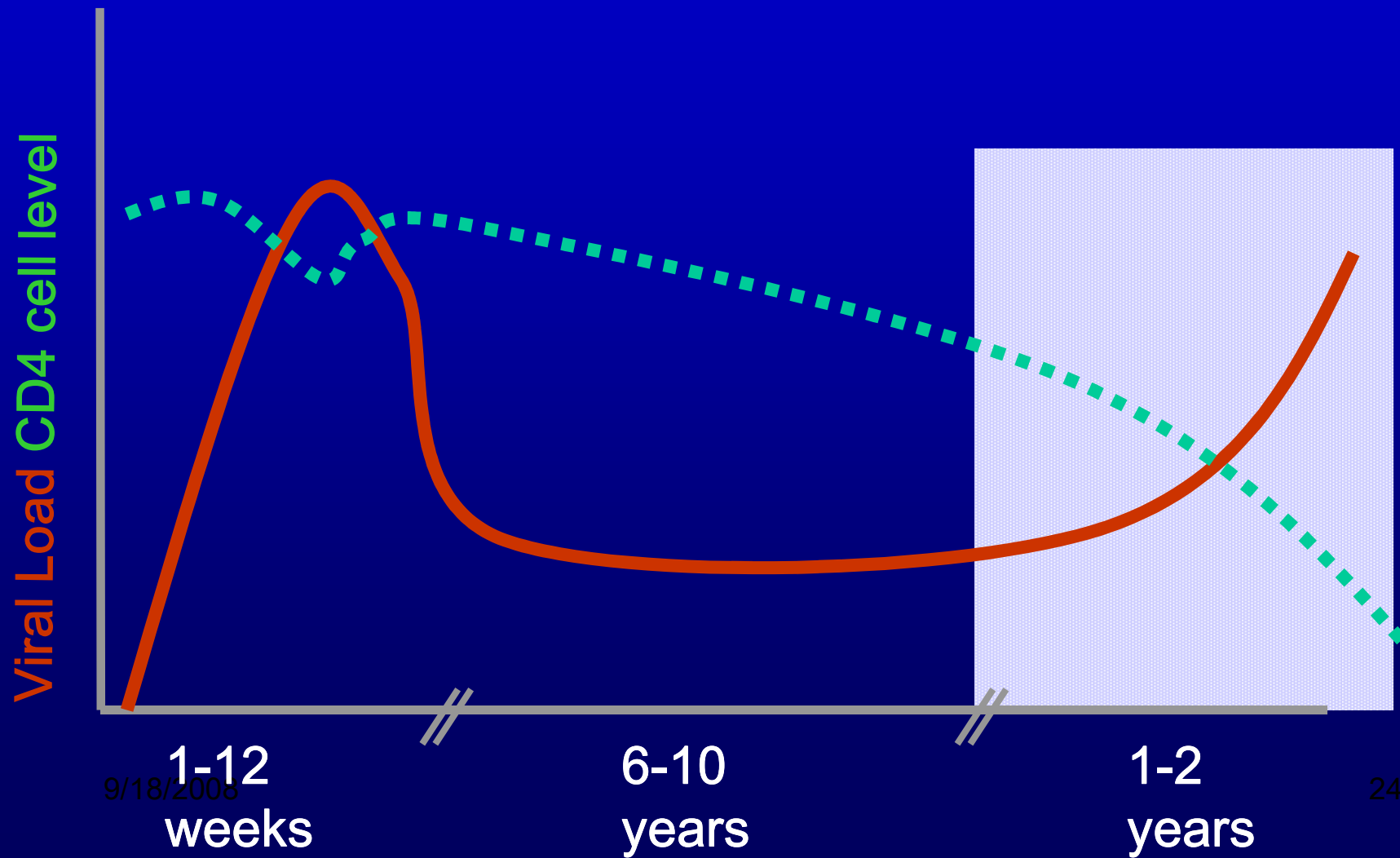


# Chronic HIV-1 Infection

---

- High turnover of CD4 cells
  - Continuous **destruction** and compensatory increased **production** of CD4 Lymphocytes
- Viral load plateaus at viral set point
- Viral reservoir in resting infected cells

# 'Overt AIDS'







# AIDS Manifestations

---

- **CD4 cell count less than 200 cells/ $\mu$ l**
  - Wasting syndrome
  - Pneumocystis carinii
  - Recurrent invasive herpes simplex virus infections
  - Oesophageal candidiasis
  
- **CD4 cell count less than 50 cells/ $\mu$ l**
  - Cryptococcal meningitis
  - Cryptosporidiosis
  - CMV retinitis
  - HIV encephalopathy



# **DISEASE PROGRESSION IN HIV**

# Chronicity of HIV Infection



---

- Inability to eradicate HIV infection
  - CD4 T cell decline
  - Inadequate CTL response
  - Viral reservoir persists
  - Escape of HIV from the immune response
    - Mutational potential of HIV-1

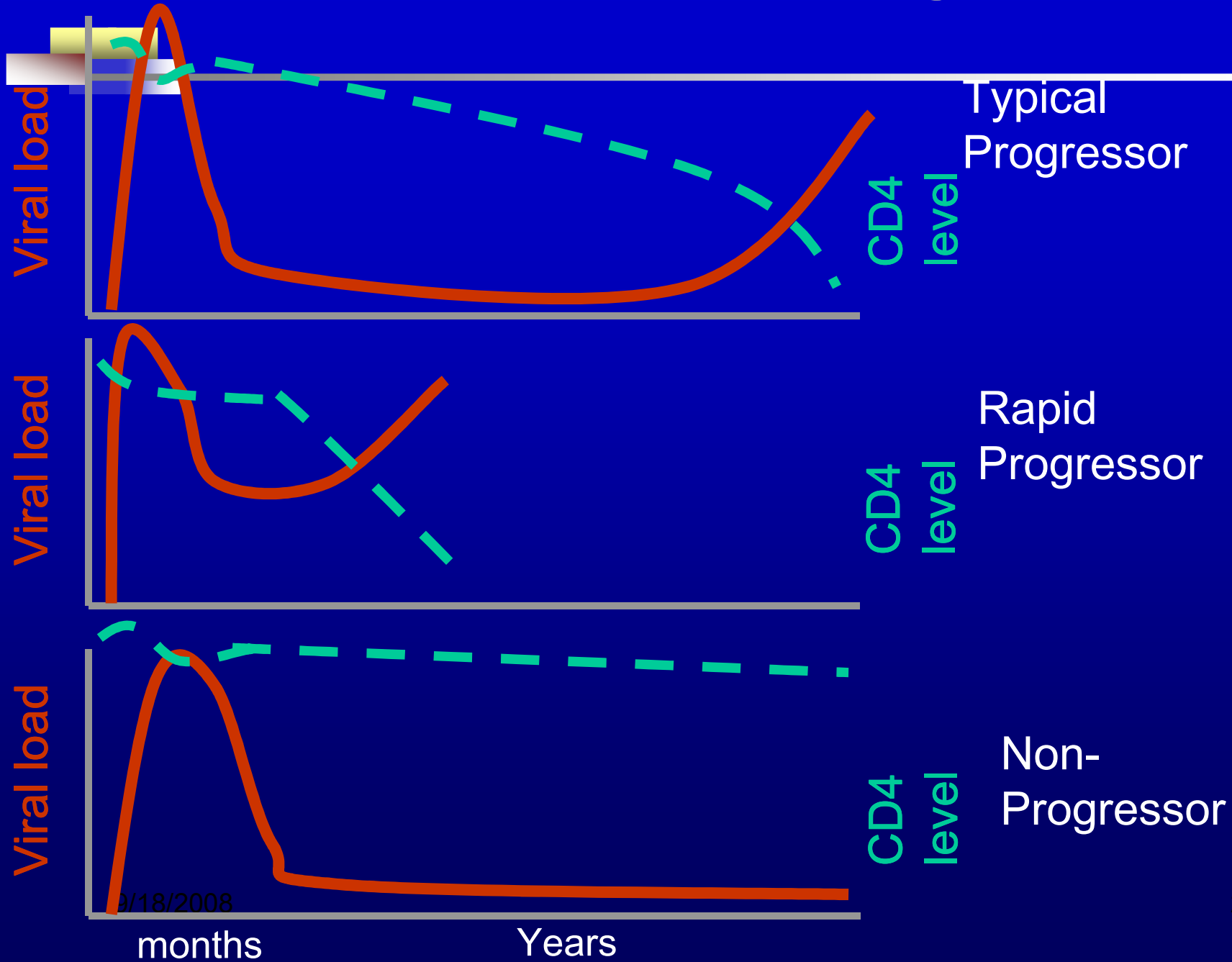


# Rates of HIV disease progression

---

- Based on the clinical picture, rate of CD4 loss and viral load HIV infected individuals tend to show three different spectra of disease progression namely
  - Rapid progressors
  - Typical progressors
  - Long term non progressors

# Rates of HIV disease progression





# HIV Transmission and Prevention

---

- Mode of Transmission
  - Mucosa (genital, oral/rectal, conjunctiva)
  - Blood (transfusion, feto-maternal)
  - Percutaneous (needle stick)
  - Breast milk
- Prevention
  - Avoidance of infected mucosal secretions
  - Safe blood transfusion service
  - Post-exposure prophylaxis
  - Prevention of Mother-to-Child Transmission
  - Avoidance of Breast feeding
- Universal precautions
  - Hand washing
  - Safe disposal of infected material



# Summary

---

- HIV life cycle involves attachment, cell entry, transcription of viral RNA into DNA, integration into human genome and viral assembly and release
- Mutational potential of HIV-1 results in worldwide diversity (quasi species), viral escape from immune response and development of drug resistance
- Viral replication persists throughout infection
- Fundamental pathology is the inability of the host immune system to eradicate the HIV infection resulting in a progressive destruction of the immune system