HIV INFECTION

Snopková S, 4/2020

A lecture outline

- Definition
- Historical chronology
- Epidemiology
- Transmission
- Etiology
- Life cycle of HIV
- Pathogenesis
- Classification of HIV infection
- and natural history
- Clinical manifestation of HIV infection
  - Category A – primary HIV infection
  - Category B
  - Category C – AIDS
- Laboratory tests

DEFINITION

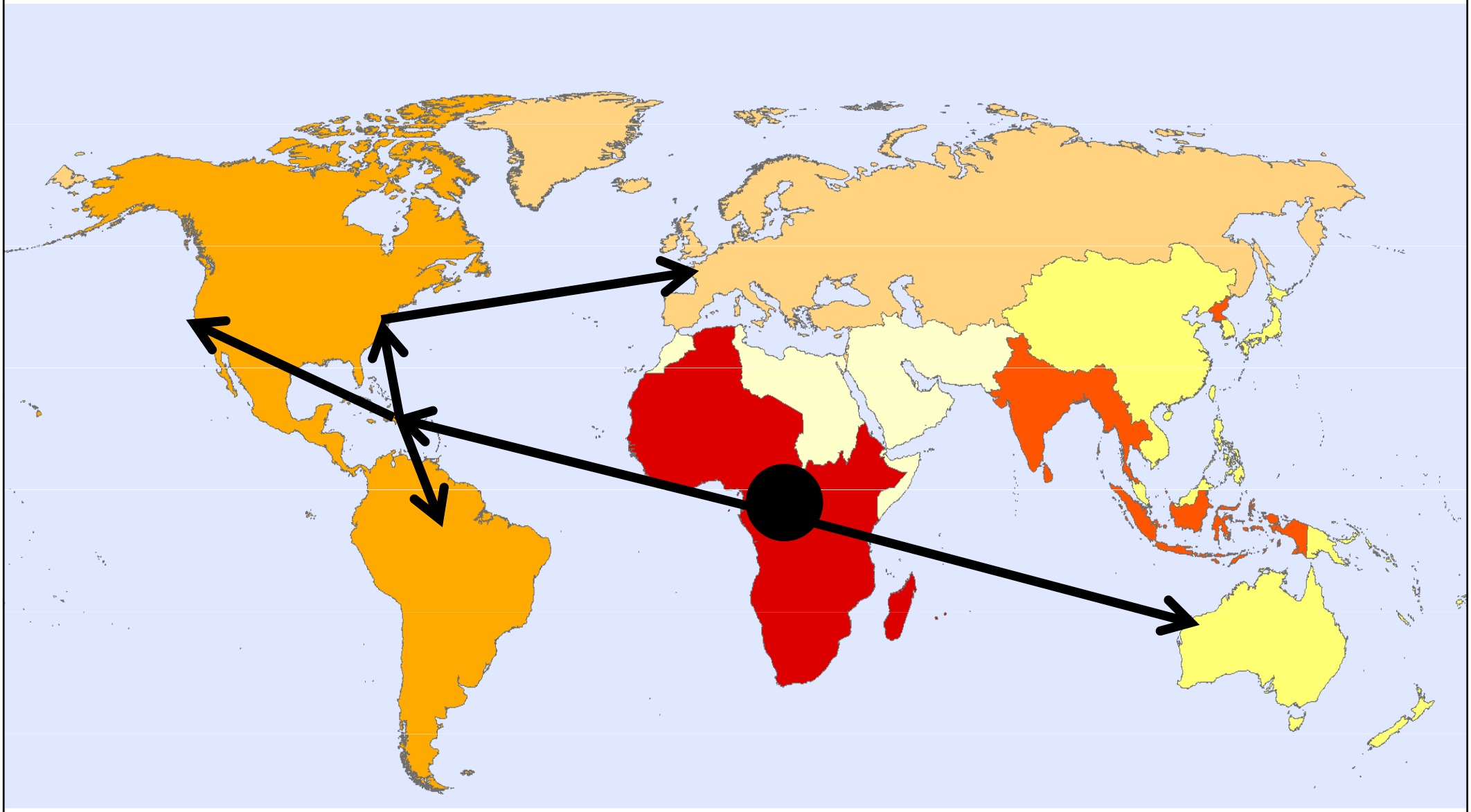
- ***Human Immunodeficiency Virus* (HIV)**
  - Infects human cells and causes gradual loss of immune system function, and these immune alterations predispose to the opportunistic infections, neoplasms, and other conditions (wasting and dementia)
- ***Human Immunodeficiency Virus* infection**
  - is used to describe the cellular and humoral immunodeficiency and the numerous complications that result from the HIV infection
- **Acquired immunodeficiency syndrome (AIDS)**
  - Is the spectrum of disorders resulting from very advanced HIV infection

HISTORICAL CHRONOLOGY

- HIV crossed from chimps to humans in the 1920s in Congo.
  This was probably as a result of chimps carrying the Simian Immunodeficiency Virus (SIV), a virus closely related to HIV, being hunted and eaten by people living in the area.
  It happened in the ,
  people got infected from chimpanzees whose meat they ate

- HIV first began to spread along the historic trade routes of the Congo basin in the 1920s from the forest to the cities
- The area around Kinshasa is full of transport links, such as roads, railways and rivers. The area also had a growing sex trade around the time that HIV began to spread. The high population of migrants and sex trade might explain how HIV spread along these infrastructure routes.
- The first verified case of HIV is from a blood sample taken in 1959 from a man living in what is now Kinshasa in the Democratic Republic of Congo.
- The sample was retrospectively analysed and HIV detected.

Spread of HIV infection



- until the 1970s there were only sporadic unrecognized cases
- since the late 1970s, the infection has spread to all continents

1981

- AIDS was first recognized as a new and distinct clinical entity
- AIDS was first reported in previously healthy men
  - Gottlieb and Friedman reported initial cases of Kaposi‘s sarcoma and *Pneumocystis carinii jiroveci* pneumonia in previously healthy men

1982

- CDC created first definition of AIDS

1983

- a new retrovirus (later called HIV-1) was identified and described as the causative agent of AIDS (formerly HTLV III/LAV)

1985

- first antiretroviral drug was discovered (zidovudine - ZDV, formerly AZT)

1986

- International committee adopted the name *Human immunodeficiency virus* (HIV-1)
- Montagnier discovered HIV-2

HIV-1 subtypes

The most common causes of HIV disease throughout the world is HIV-1, which comprises several subtypes with different geographic distribution

- Geographic distribution
  - A – Central and East Africa, East Europe
  - B – America & Europe
  - C – South Africa & India, Brazil
  - D – Central, East and South Africa
  - E – Tchaj-wan & India
  - F – Romania & Brazil
  - G, H, O – Western Africa

1987

- the first drug for clinical use NRTI – AZT (later ZDV)

1991-1994

- next NRTIs (didanosine, zalcitabine, stavudine, lamivudine…)

1995

- the first protease inhibitor was approved for clinical use

1996 – HAART era

- the introduction of HIV therapy into clinical practice represented a significant step forward in the treatment of HIV infection
- the ability of HAART regiments have transformed HIV infection into a manageable chronic disease in many patients

HAART = cART = OBT = ART

Three-drug combinations are currently recommended
for the initiation of treatment in all patients

HAART – Highly Active AntiRetroviral Therapy
cART - Combination AntiRetroviral Therapy
OBT - Optimalising Basic Treatment
ART - AntiRetroviral Therapy

- Enormous changes in prognosis of HIV/AIDS disease
  - maximally and durably supresses viral load
  - restores immunological function
  - improves quality of life
  - dramatically reduces HIV-related morbidity and mortality

Epidemiology
HIV – a global health crisis

- Since AIDS was recognized as a distinct disease in 1981, the catastrofic nature of this pandemic has been recognized and more fully characterized
- Since the beginning of this pandemic
  - over 78 million individuals worldwide have been infected by HIV-1
  - over 40 million people died
- Number of people

  living with HIV/AIDS is increasing

Summary of the global HIV epidemic (2018)

1.7 million

people newly infected

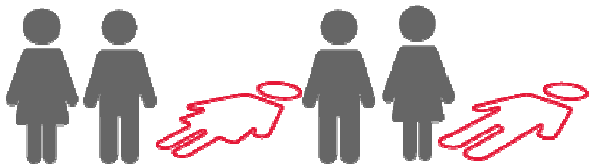
[1.4 million – 2.3 million]

37.9 million

people living with HIV

[32.7 million – 44.0 million]

New HIV infections, or "HIV incidence," refers to the estimated number of people who newly acquired the HIV virus during a year, which is different from the number of people *diagnosed* with HIV during a year. Some people may have HIV but not know it



0.8 million

HIV-related deaths

[0.6 million –1.1 million]

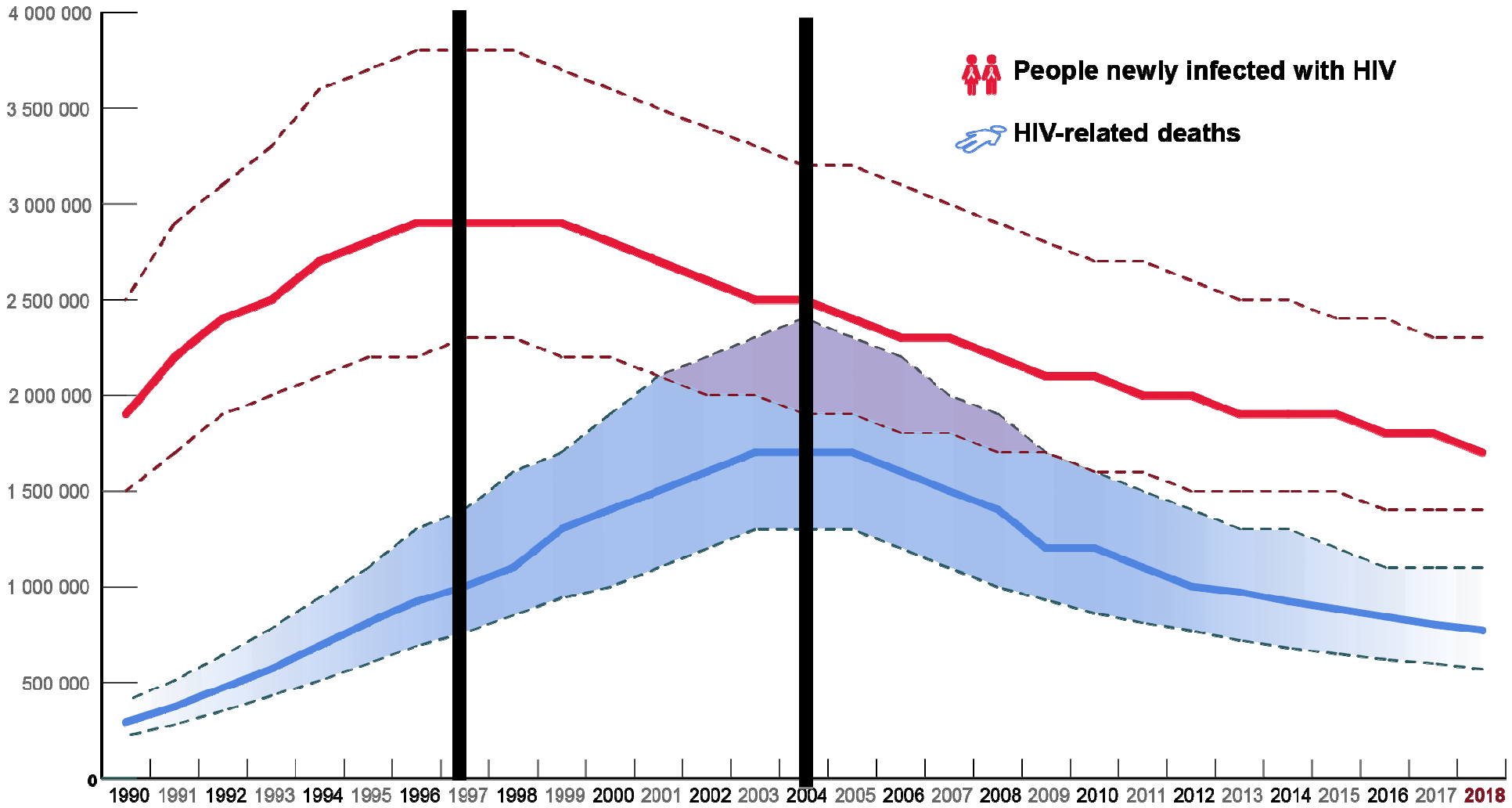
Source: UNAIDS/WHO estimates

World Health Organization

AIDS by the numbers

- ↓ 35% decrease in new HIV infection since 2000
- ↓ 42% decrease in AIDS-related deaths since the peak in 2004
- ↓ 58% decrease in new HIV infections among children since 2000
- ↑ 84% increase in access to antiretroviral therapy since 2010

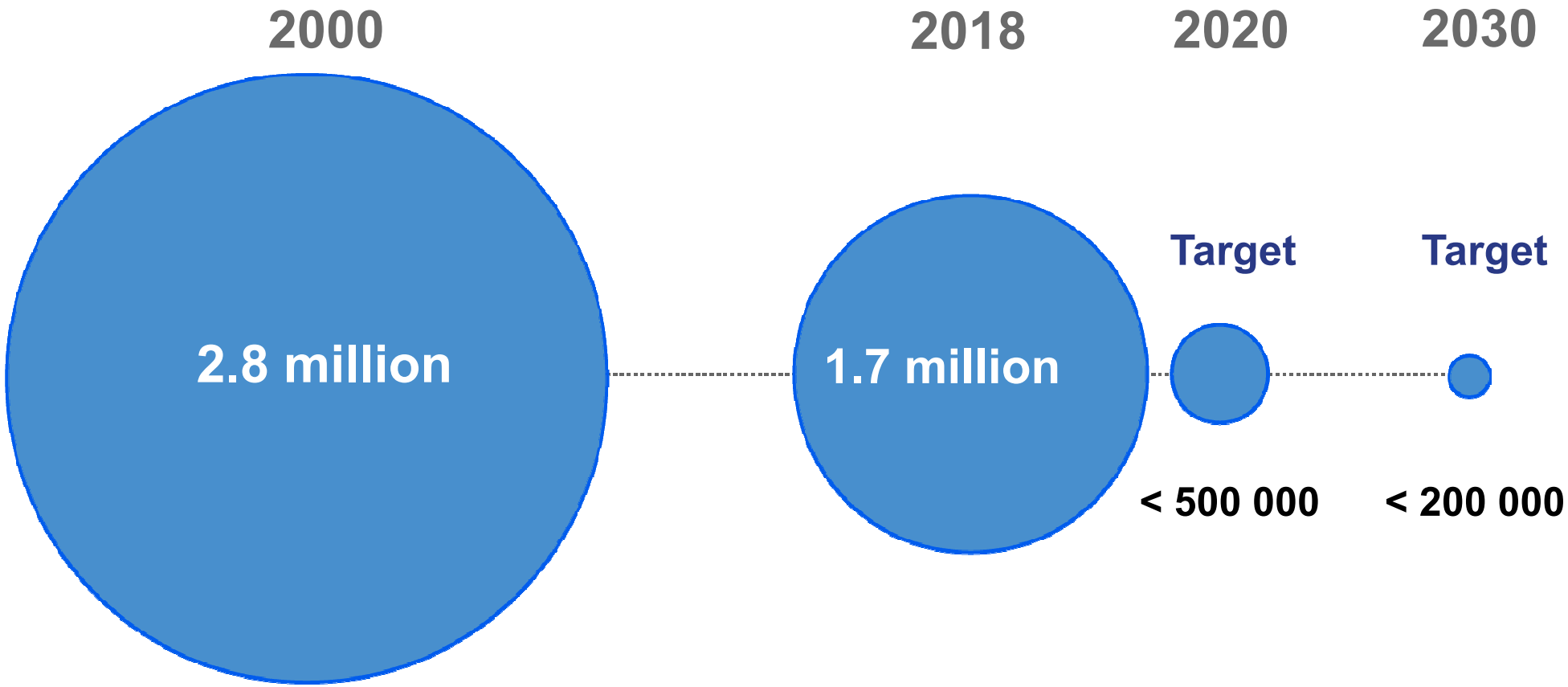
Decline in HIV incidence and mortality over time



- the highest incidence of HIV infection was in 1997
- 3,5 mil people were infected during 1997
- the highest mortality due to HIV infection was in 2004
- 2,0 mil people died due to HIV during 2004

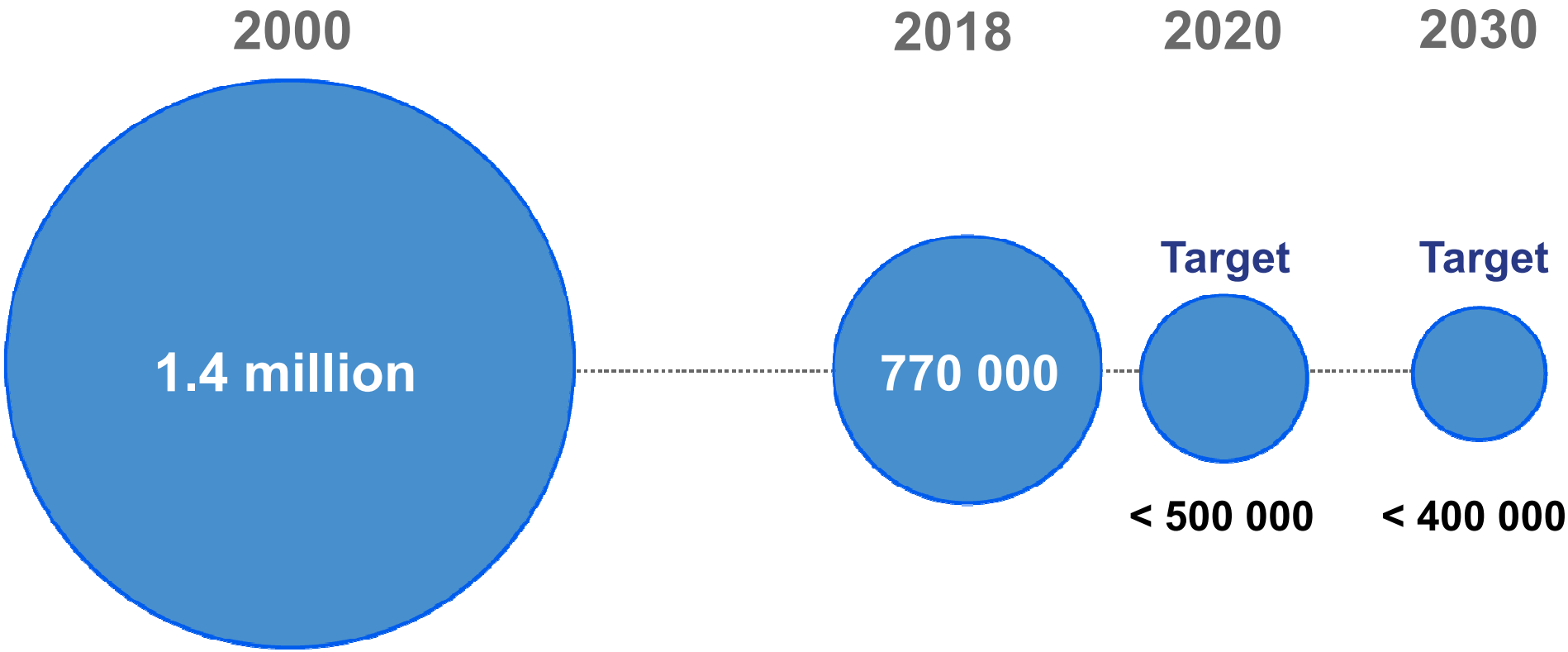
World Health Organization

Global number of people newly infected with HIV



Source: UNAIDS/WHO estimates

Global number of HIV-related deaths



Source: UNAIDS/WHO estimates

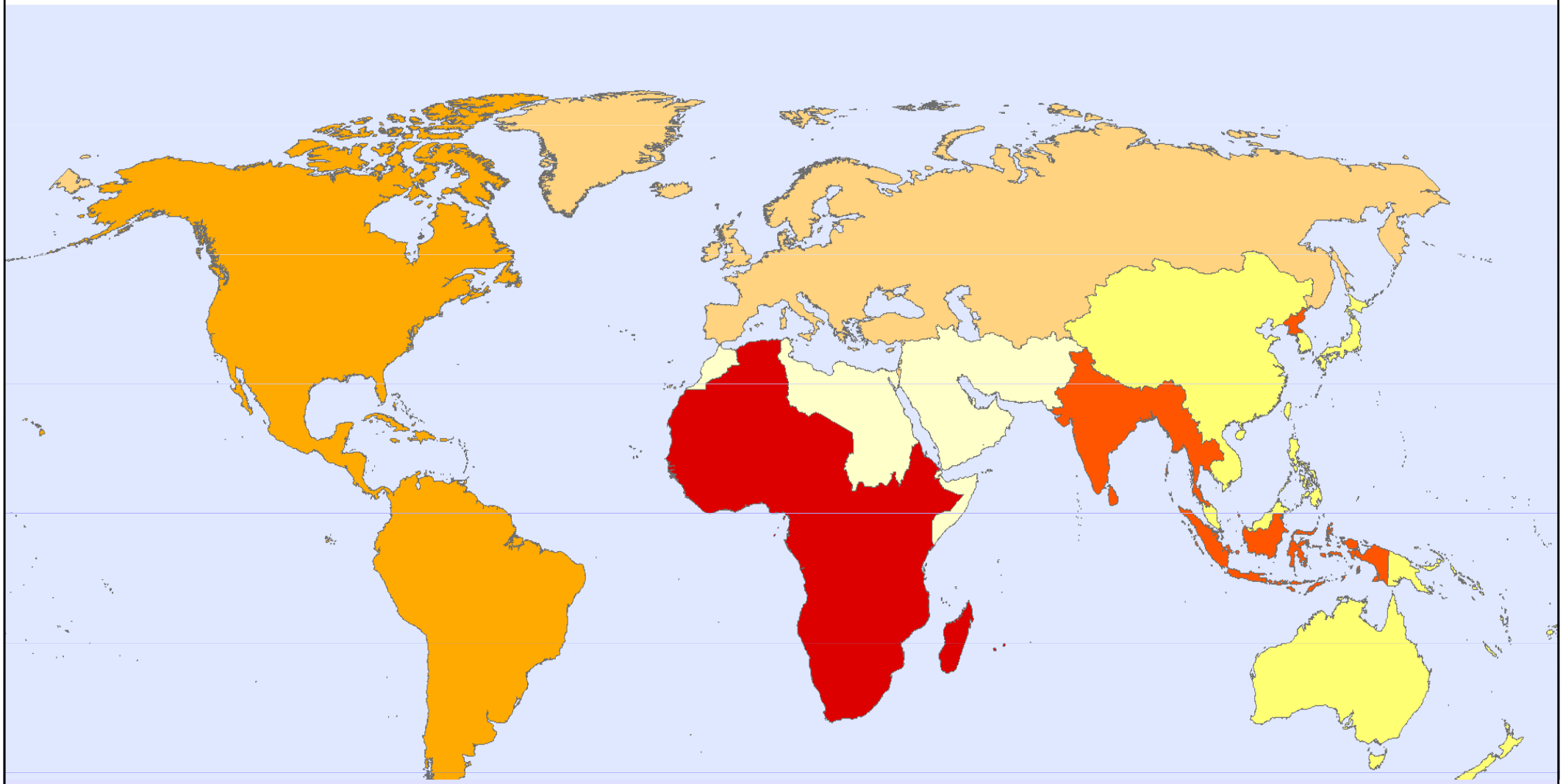
Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
Total	37.9 million [32.7 million – 44.0 million]	1.7 million [1.4 million – 2.3 million]	770 000 [570 000 – 1.1 million]
Adults	36.2 million [31.3 million – 42.0 million]	1.6 million [1.2 million – 2.1 million]	670 000 [500 000 – 920 000]
Women	18.8 million [16.4 million – 21.7 million]	–	–
Men	17.4 million [14.8 million – 20.5 million]	–	–
Children (<15 years)	1.7 million [1.3 million – 2.2 million]	160 000 [110 000 – 260 000]	100 000 [64 000 – 160 000]

Source: UNAIDS/WHO estimates

World Health Organization

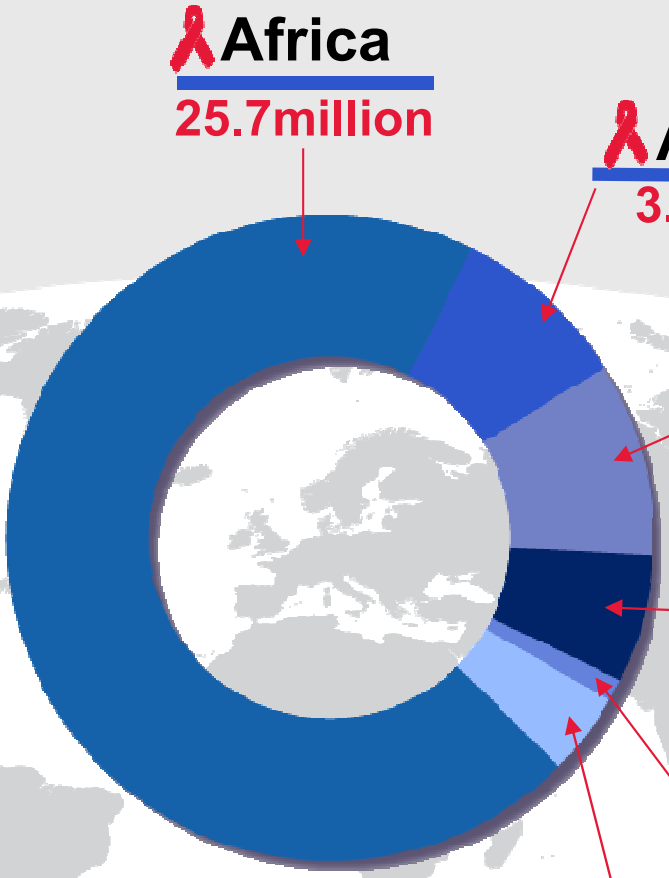
The highest incidences of infection



The vast majority of people with HIV are in low- and middle-income countries.

- 20.6 million people with HIV (57%) in eastern and southern Africa,
- 5.0 million (13%) in western and central Africa
- 5.9 million (16%) in Asia and the Pacific
- 2.2 million (6%) in Western and Central Europe and North America

People living with HIV by WHO region (2018)



37.9 million people living with HIV globally

Africa
25.7million

America
3.5 million

South-East Asia
3.8 million

Europ
2.6 million

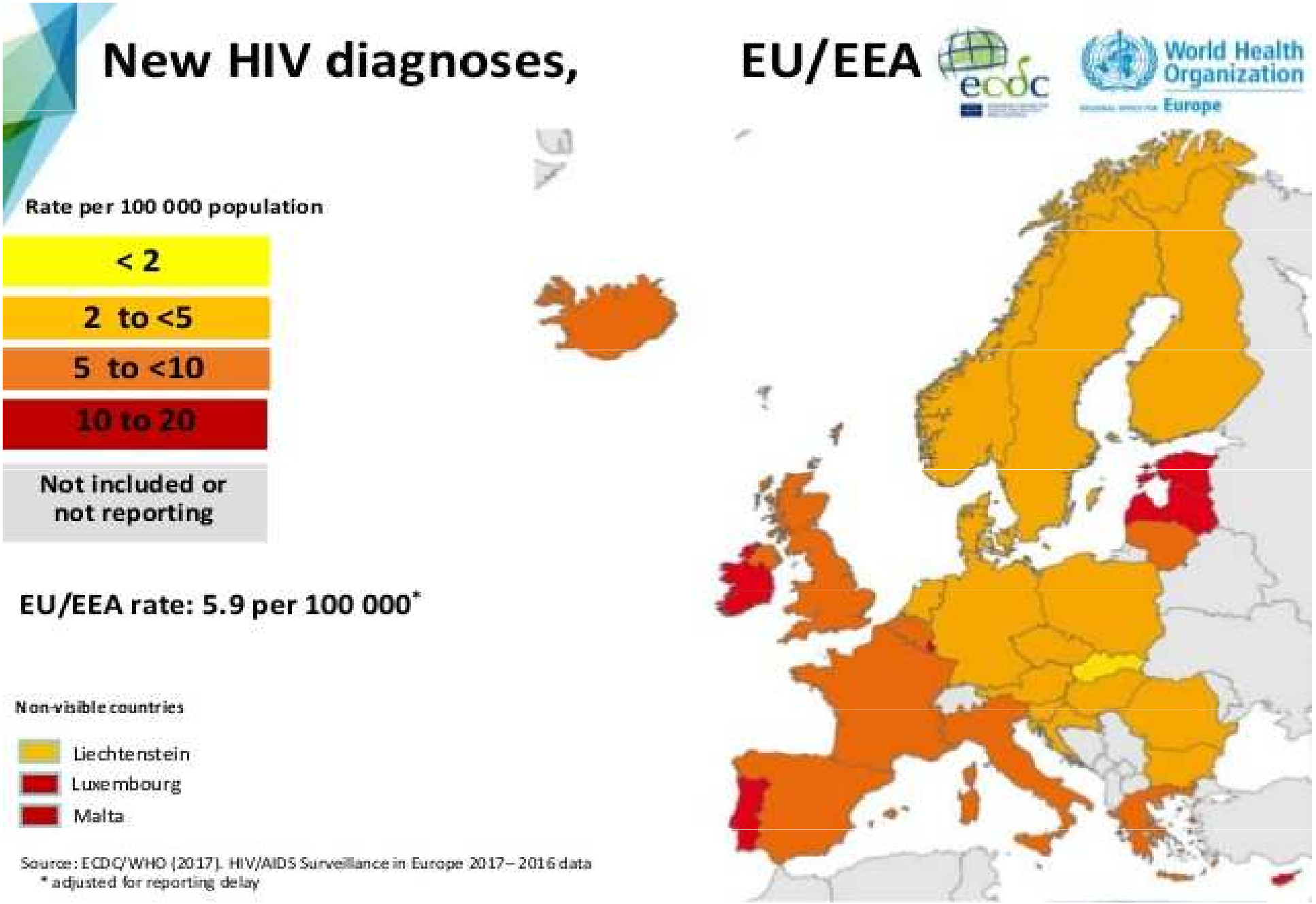
Eastern Mediterranean
400 000

Western Pacific
1.9 million

Source: UNAIDS/WHO estimates

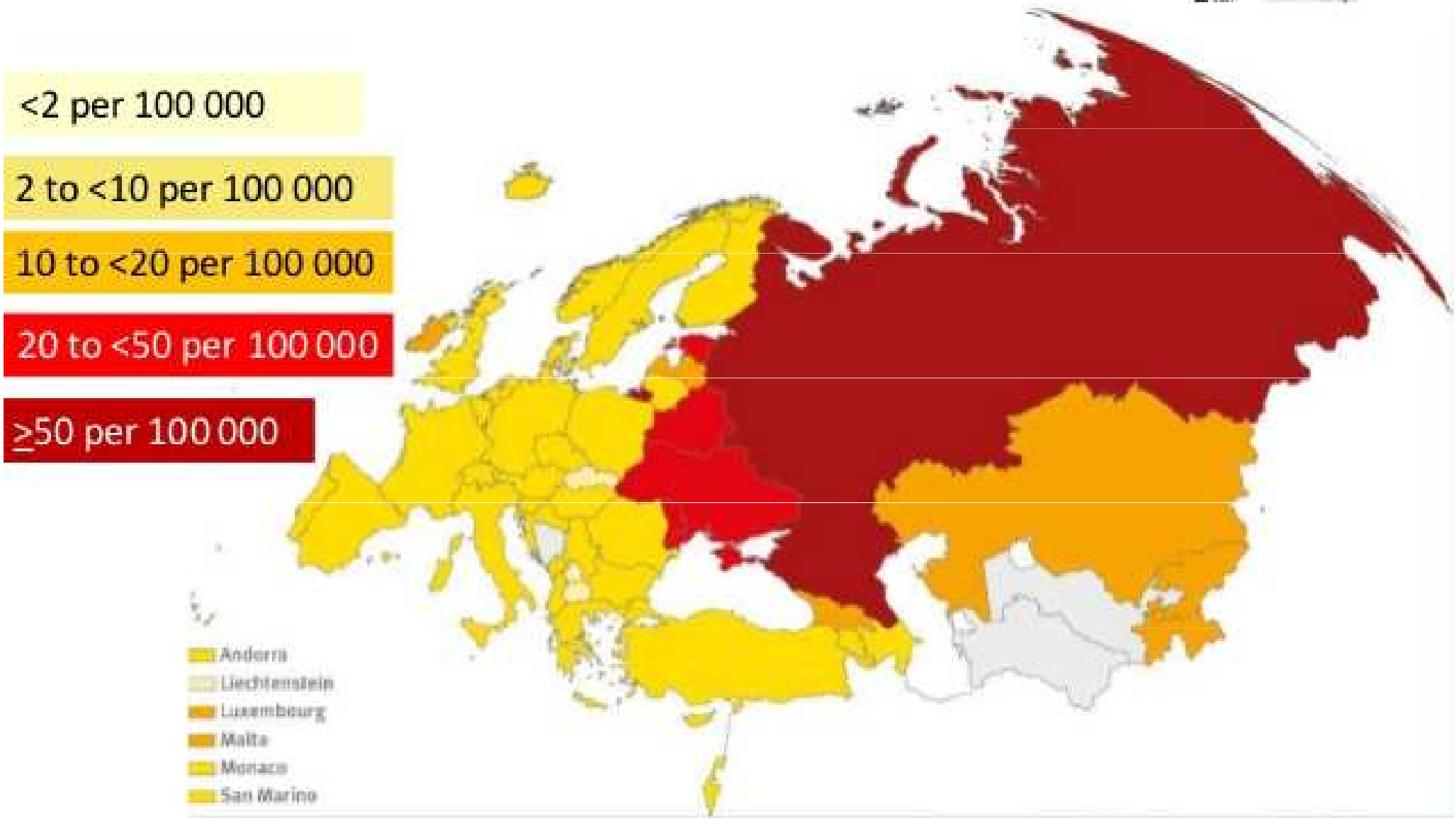
World Health Organization

New HIV diagnoses, EU/EEA



Source: ECDC/WHO (2017). HIV/AIDS Surveillance in Europe 2017–2016 data
* adjusted for reporting delay

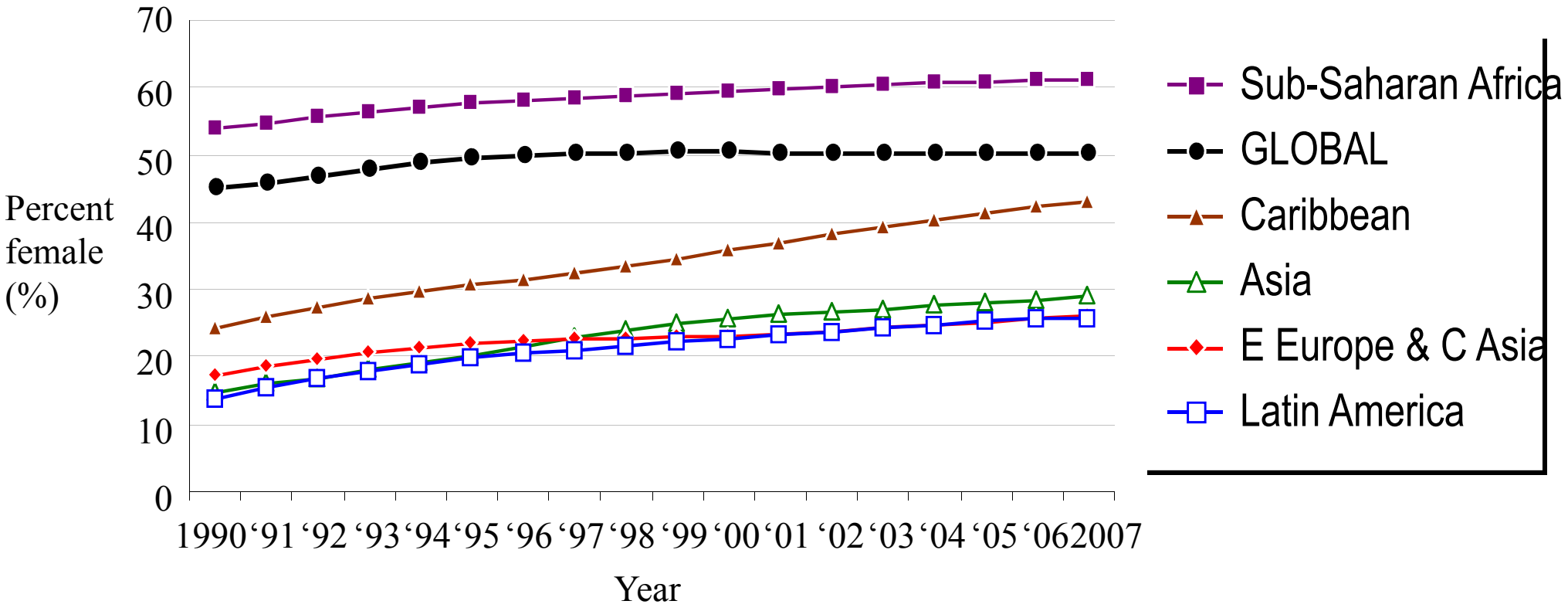
New HIV diagnoses in Europe,



> 1 mil HIV+ people live in Russia

> 64% of all new HIV/year diagnoses in Europe were in Russia

Percentage of adults (15+) living with HIV who are female

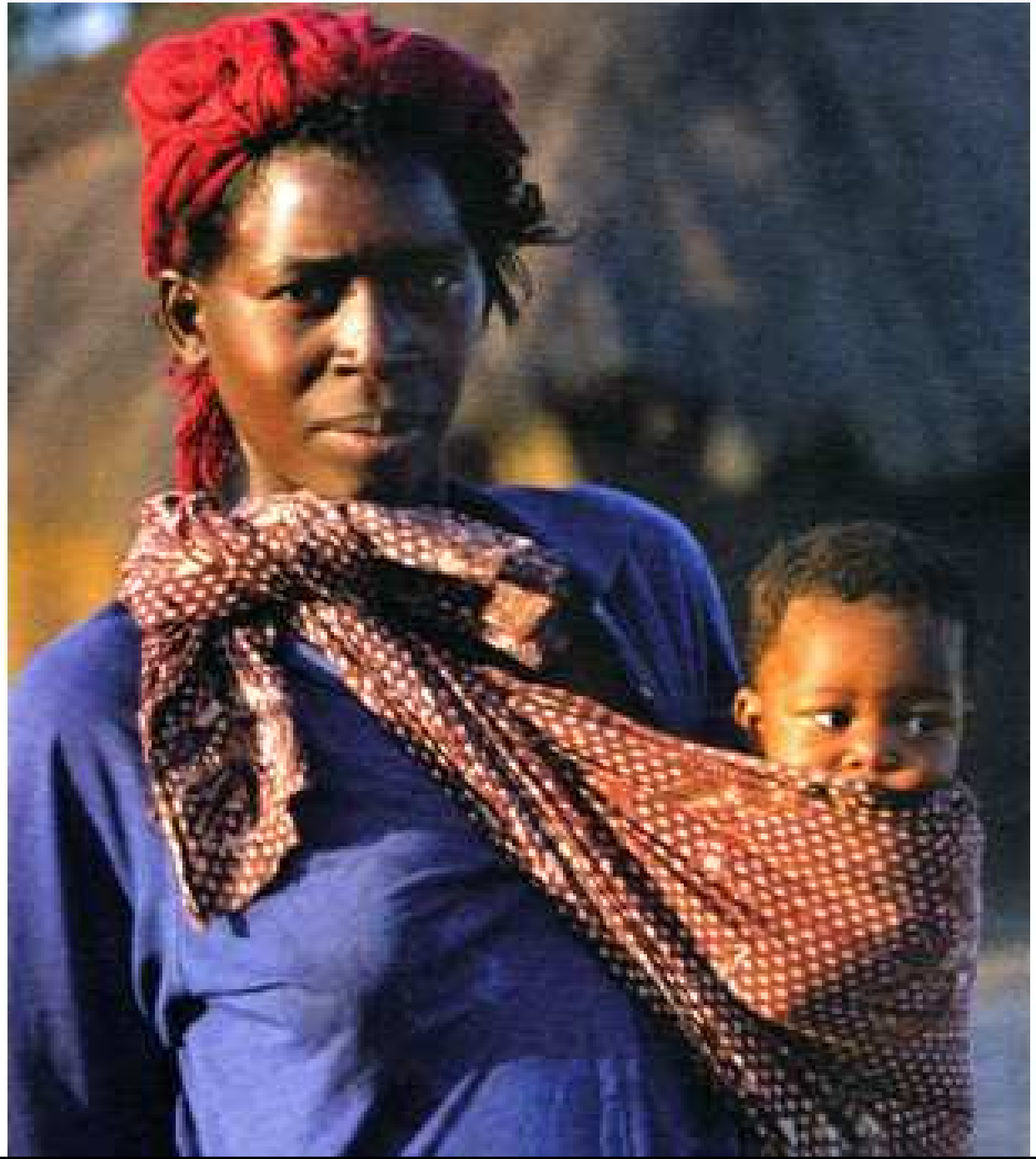


HIV+ female

- **In total > 52%**
- **In Sub-Saharan Africa > 62%**

⇒

more HIV+ children



TRANSMISSION

HIV has been isolated from bodily fluids

With high/titer viremia

- **blood**
- **semen**
- **cervicovaginal secretion**

These bodily fluits have been implicated in the transmission of HIV

With low/titer viremia

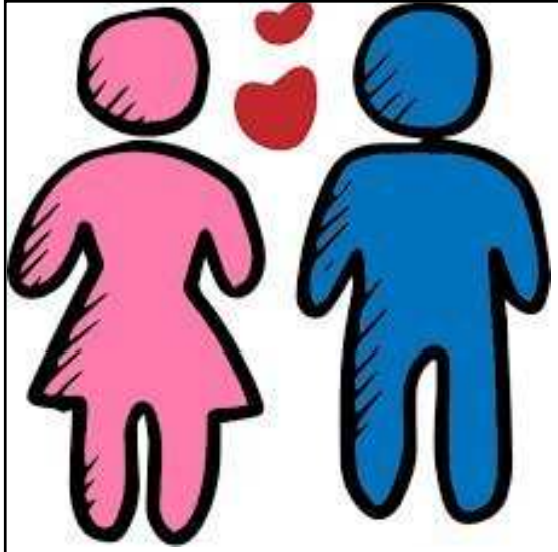
- **saliva**
- **tears**
- **urine**
- **CSF**

These bodily fluits have not been implicated in the transmission of HIV

Modes of HIV transmission

HIV is transmitted through three primary routes:

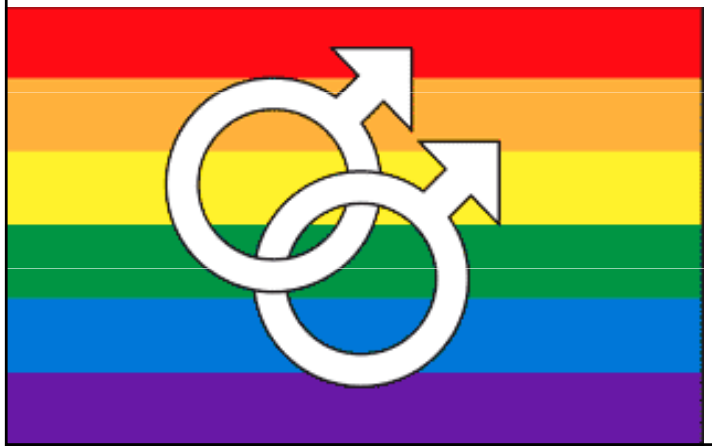
1. **sexual**
2. **parenteral**
3. **vertical**



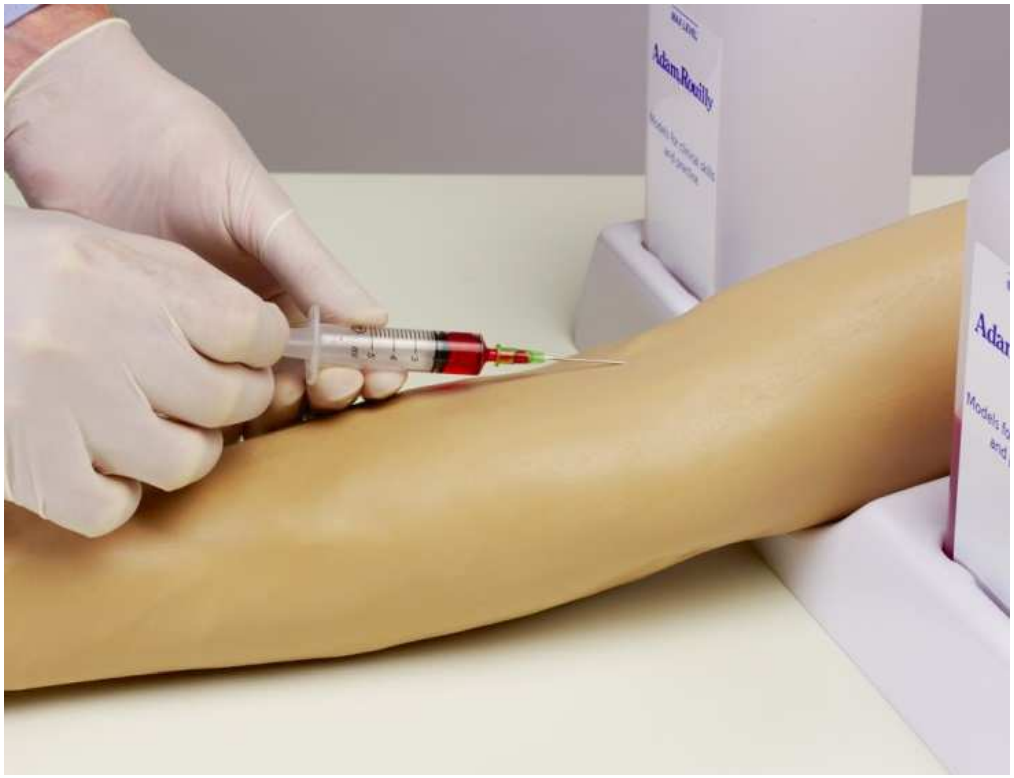
1. Sexual rout

Sexual contact with an infected person is the predominant mode of transmission wordwide (> 95 % of HIV infection)

- **Heterosexual intercourse**
  - The dominant mode (90%) wordwide
- **Homosexual intercourse (MSM)**
  - Men who have sex with man
  - Homosexual and bisexual men
  - The main mode in North America, Europe and Australia



2. Parenteral rout (exposure)



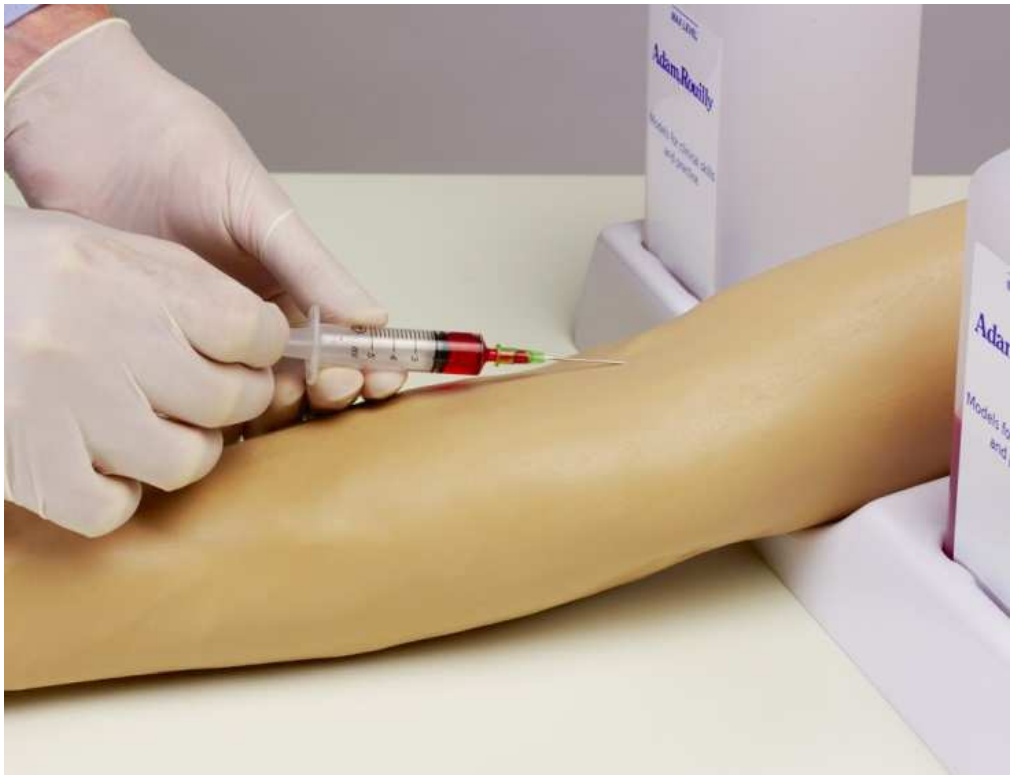
1. **Blood transfusion and blood products can be infected by HIV**

- recipients are in risk acquiring of HIV
- hemophiliacs, plasma, clotting factors, whole blood, blood cellular components, recipients of tissue, organ transplants, semen

Transfusion of infected blood or blood components

- as a risk factor for acquiring HIV has dramatically decreases in incidence
- secondary to the availability of a screening of all blood products since 1987

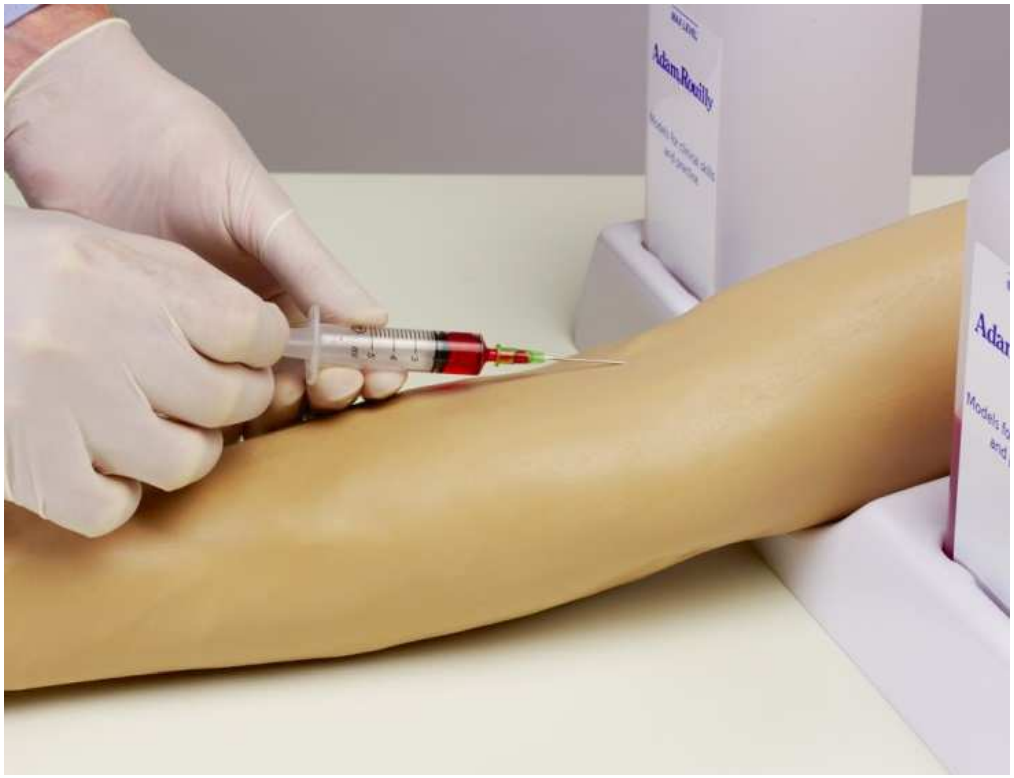
2. Parenteral rout (exposure)



2. Contaminated injection and medical equipments

- Drug users, sportman
- Nosocomila
- Health and laboratory workers…

2. Parenteral rout (exposure)



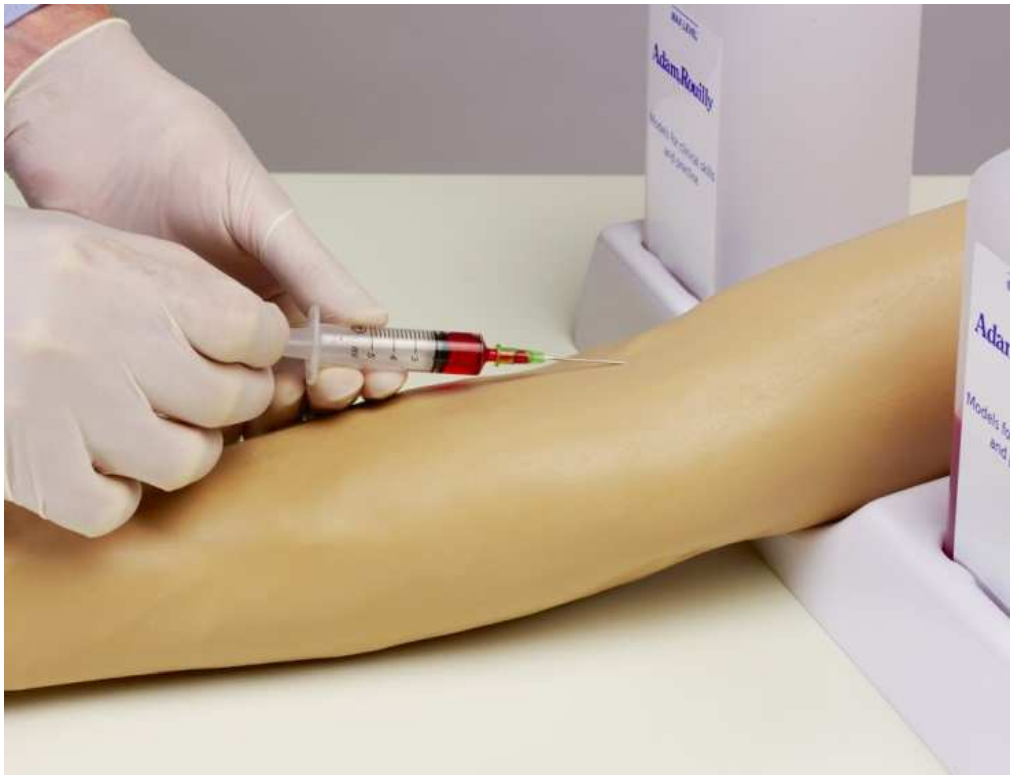
The probability transmission of HIV infection **after skin puncture** with infected materials depends on multiple factors

- High titer viremia of the patients
- Amount of blood on the needle
- Advanced HIV infection…

Without antiretroviral therapy

is estimated to be **0.3 – 0.5%**

2. Parenteral rout (exposure)

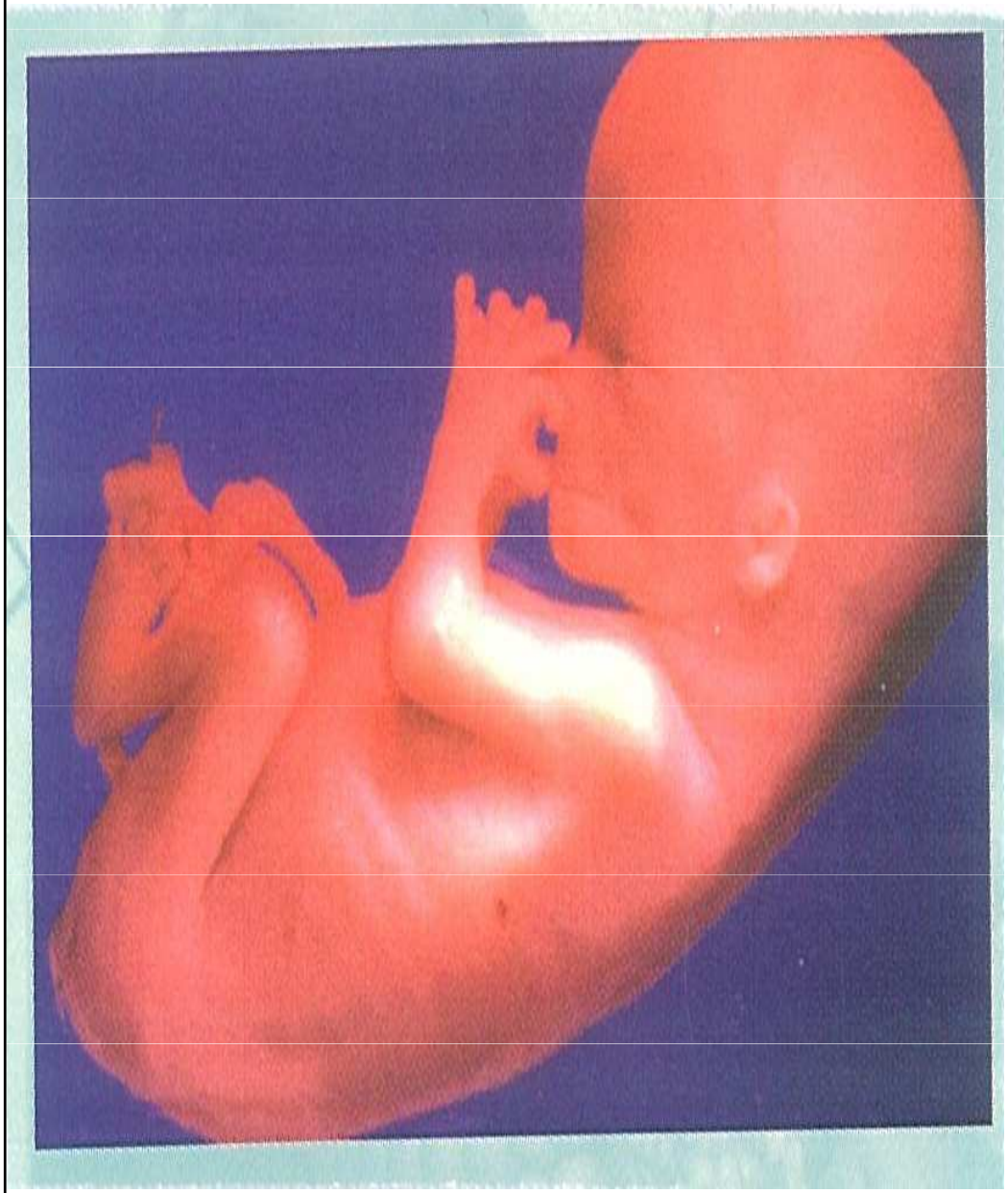


Postexposure prophylasis (PEP)

In case of skin puncture with infected materials

- Prompt administration of a combination regiment of ART drugs (PEP)
- Significantly decreases the likelihood of HIV infection following needle-stick injuries

3. Vertical rout (mother-to-child)



Perinatal transmission may occur

1. **During pregnancy** (in utero)
2. **During delivery** (at birth, intrapartum)
3. **During breastfeeding**

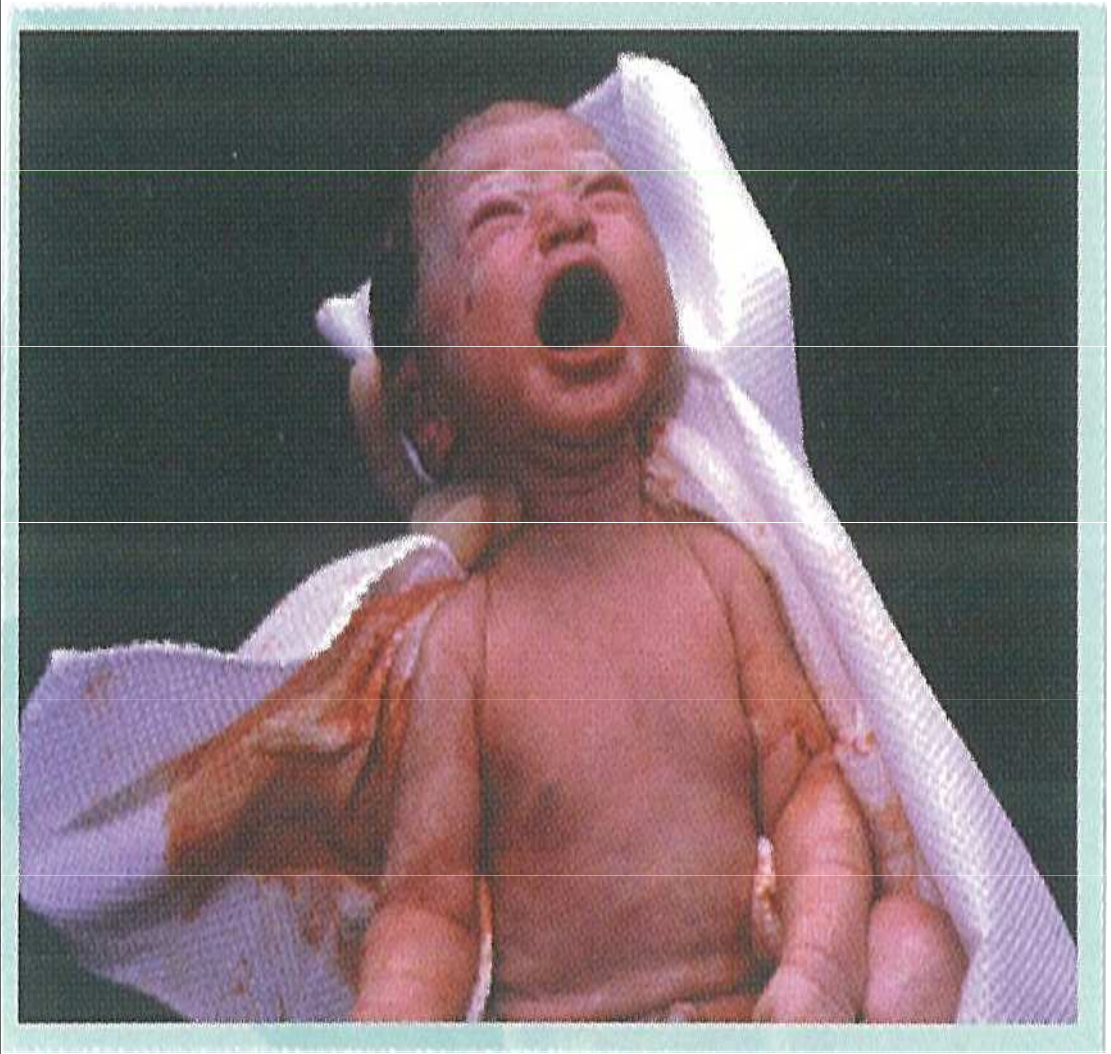
Perinatal transmission rates range

- from 22 to 46% (without ART)

In Europe and North America

- from 15 to 25% before ART

3. Vertical rout (mother-to-child)



Maternal ART has been shown to decrease vertical transmission dramatically

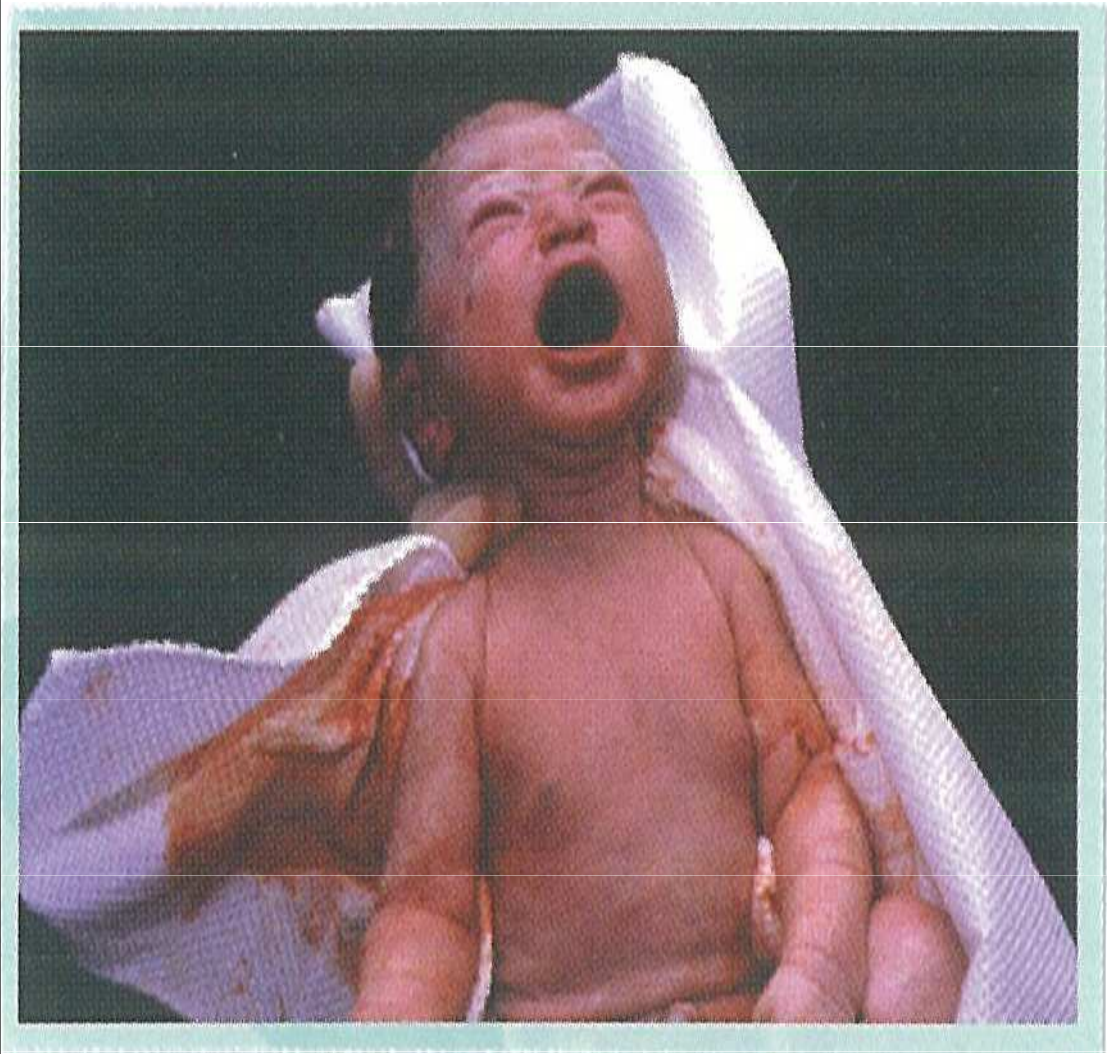
- in Europe and North American countries

  < 1,5% of all newborns

In 2018

- 92% of pregnant women with HIV received ART to prevent transmitting HIV to their babies during pregnancy and childbirth and to protect their own health.
- This is compared to 49% in 2010.

3. Vertical rout (mother-to-child)

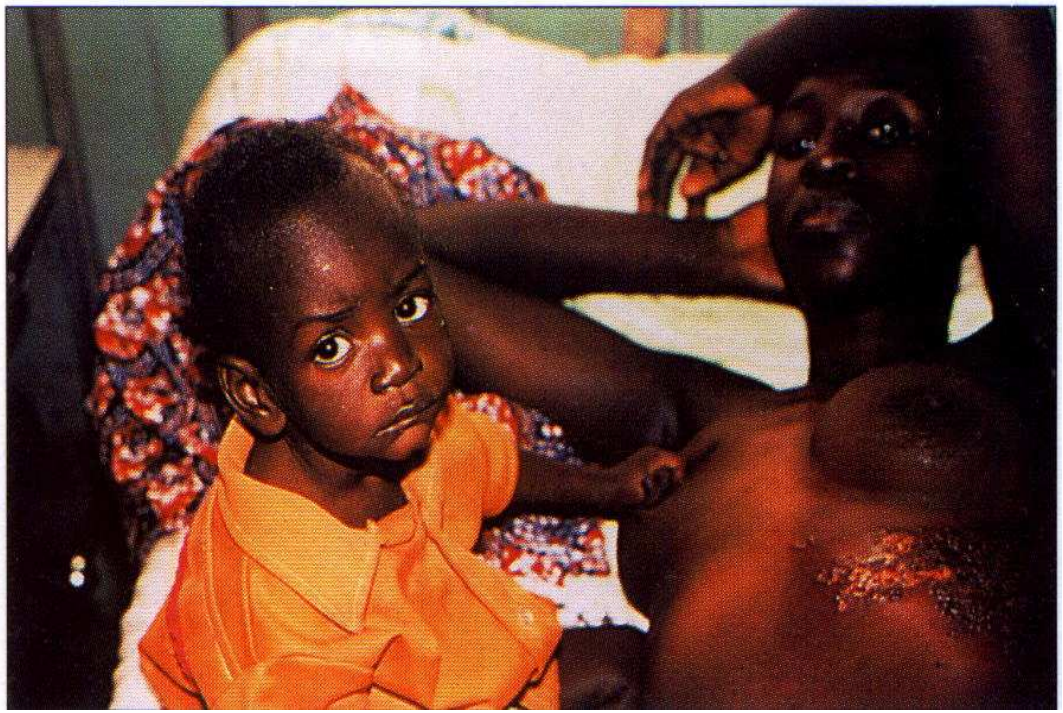


Decreasing

mother-to-child transmission

- Use of ART by the mother and use of AZT by the infant after delivery
- Cesarean section
- Avoidance of breastfeeding

3. Vertical rout (mother-to-child)



Breastfeeding is very important for HIV transmission. Risk breastfeeding is about 10%.

Factors thought to increase risk of mother-to-child transmission

- High maternal viral load and no ART
- Prolonged membrane rupture
- Natural delivery
- Prematurity of newborn
- Low birth weight of newborn
- breasrfeeding

No transmission

- **Household contacts not sexually involved with infected persons are not risk for acquiring HIV**
- **Family members who shared bathrooms and eating utensils with HIV+ patients did not become infected**
- **Mosquitoes do not transmit HIV**
- **No cases of transmission from human bites have been reported.**

Saliva contains neutralizing factors.

ETIOLOGY

HIV

- **belongs to the family of human retroviruses and the subfamily of lentiviruses**

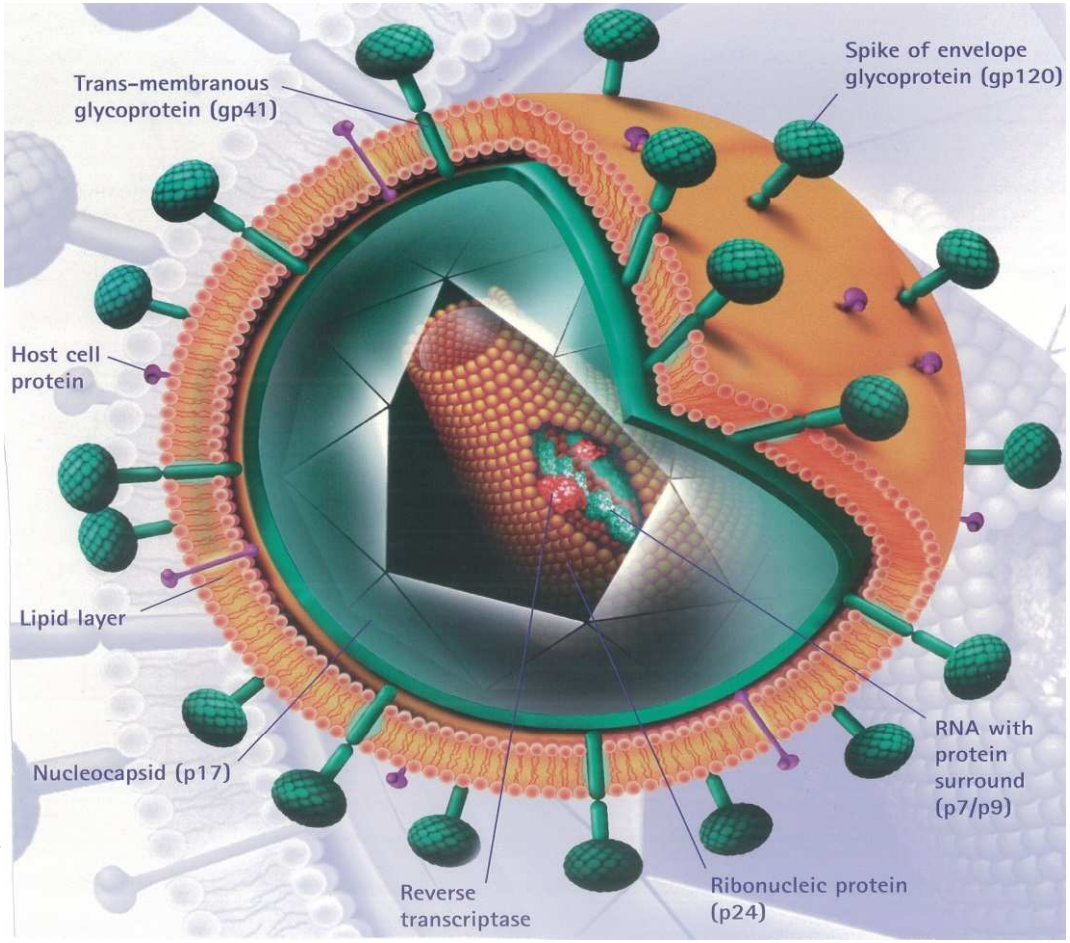
HIV = causativ agent

Family: *Retroviridae*

Genus: *Lentivirus*

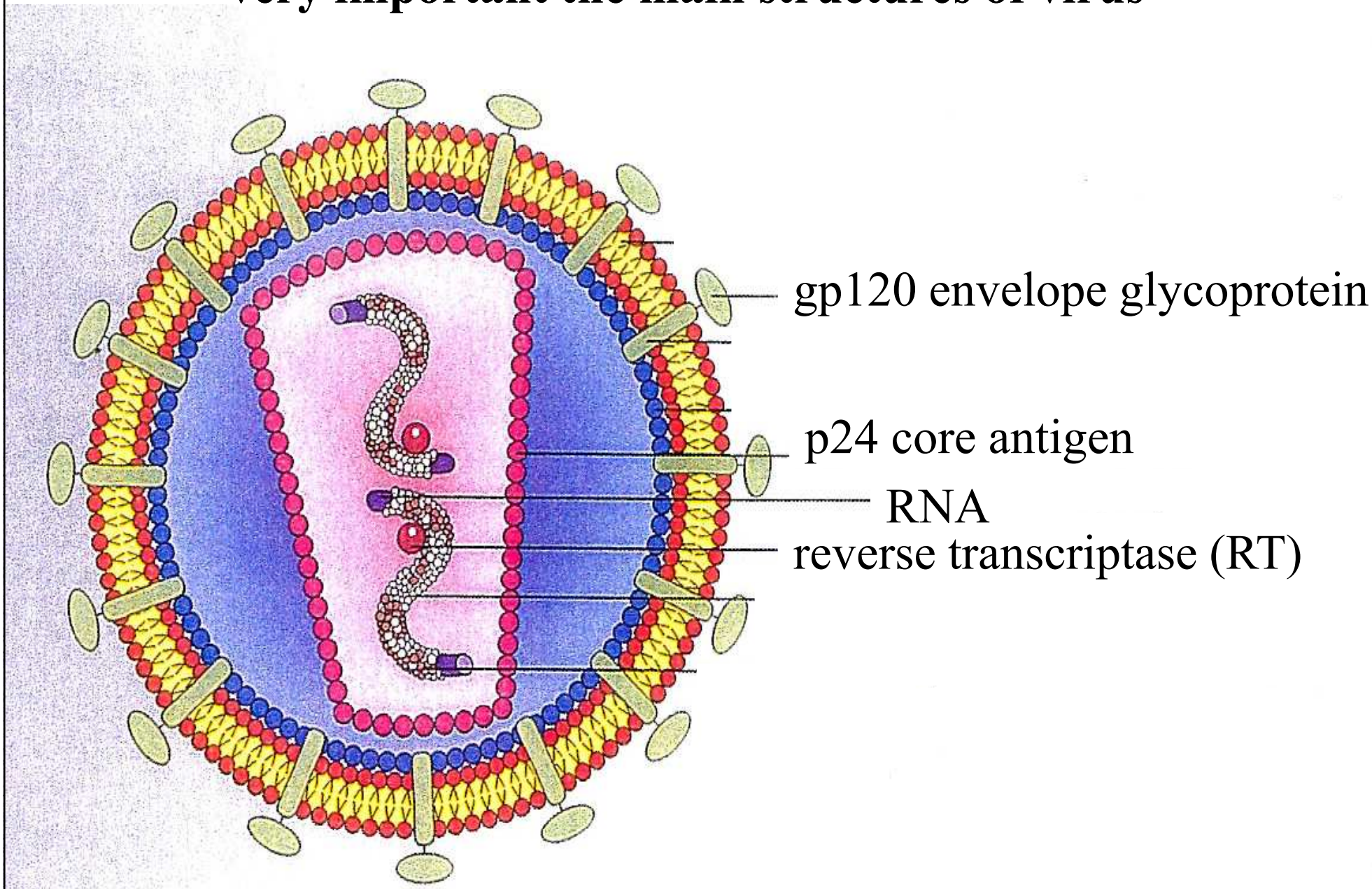
HIV-1, HIV-2

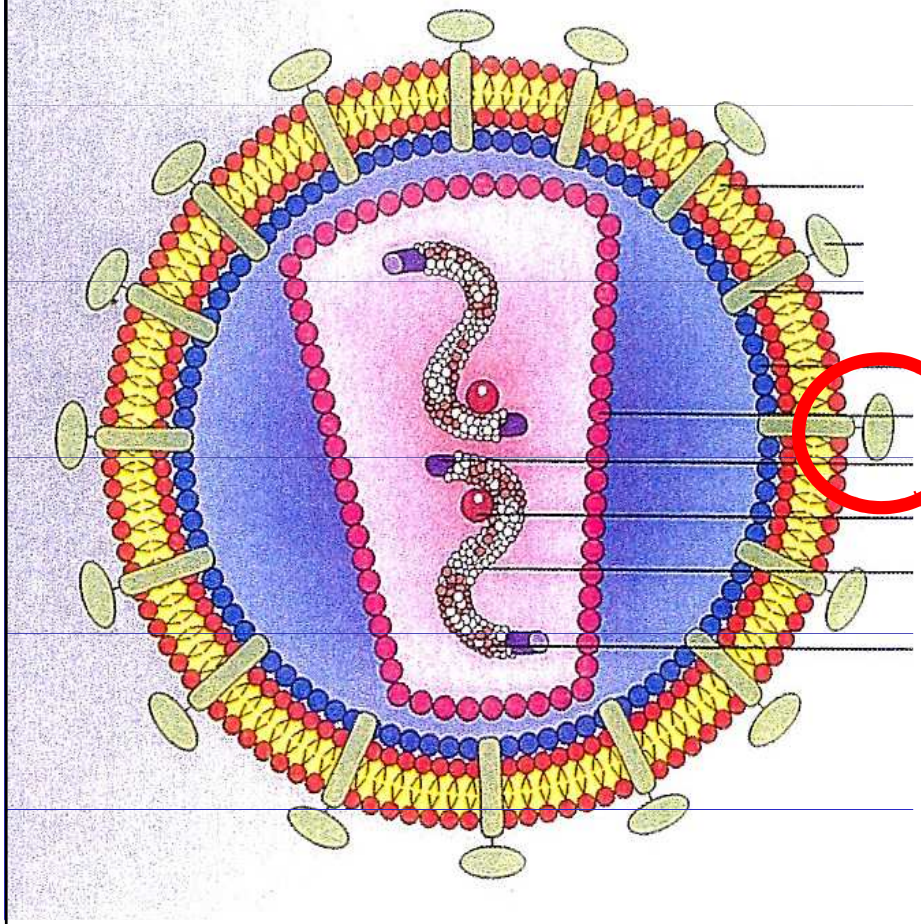
SIV…



Virion structure

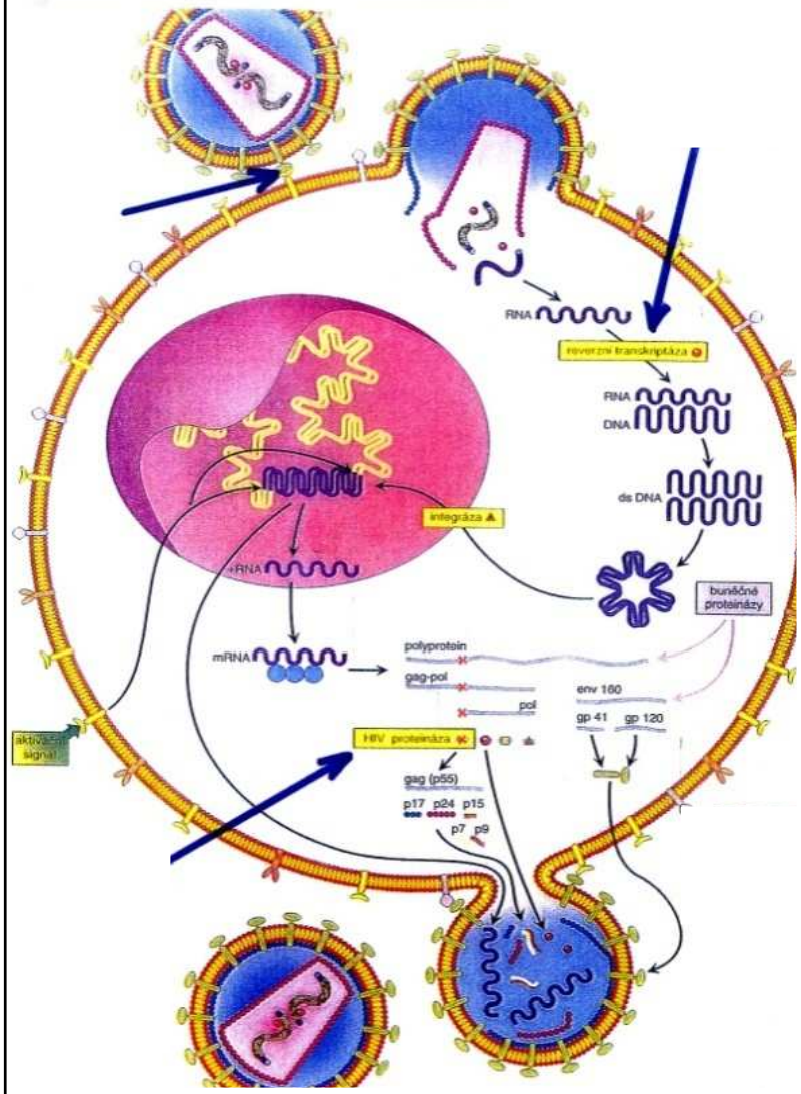
– very important the main structures of virus





Free virus
and possibly virus-infected cells
enter the blood
during initial infection

The HIV envelope
glycoprotein 120
have a high affinity
for the CD4 molecule (receptors)
on the surface of CD4 cells
(helper cells, Th lymphocytes)

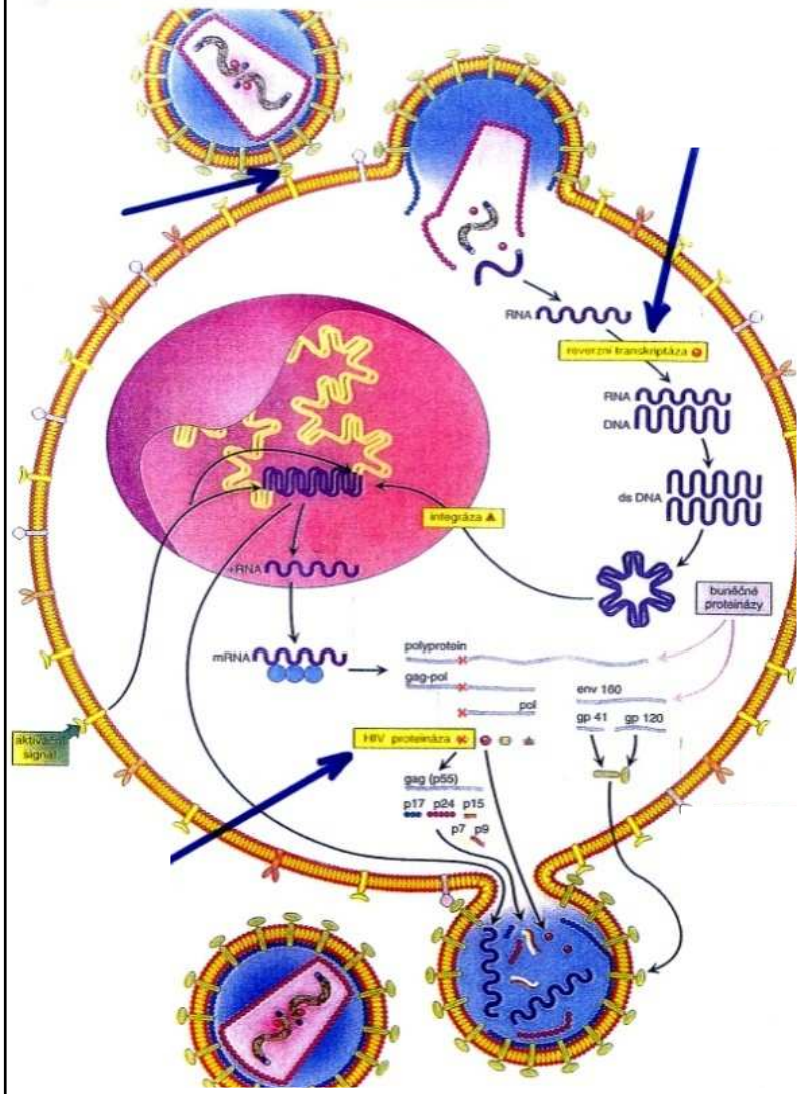


Life cycle of HIV

1. **Adsorption to CD4+ cell cereptor (and coreceptors)**

2. **After HIV binds to CD4 receptor, the viral and cellular membranes fuse and the HIV nucleoprotein complex enters the cytoplasm**

3. **Uncoating follows – into the host cells**



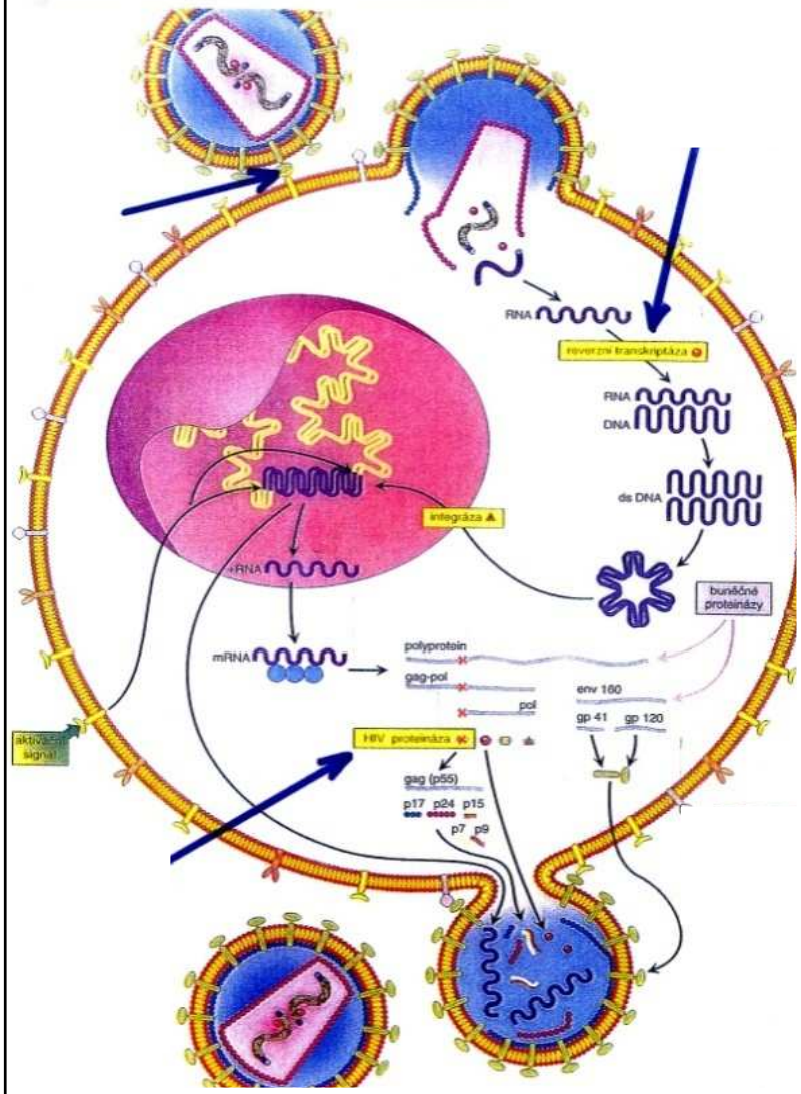
4. **Using its retroviral reverse transcriptase, the HIV initiates viral DNA synthesis, using its own RNA as a template**

5. **The double-stranded viral DNA enters into the nucleus of host cell**

6. **Integration of the DNA into host chromosome is catalyzed by integrase (another retroviral enzyme)**

7. **When a CD4 cell with integrated provirus (DNA) is activated, retroviral synthesis is begun, directed by the cell´s infected DNA**

8. **Synthesis of viral proteins is started**

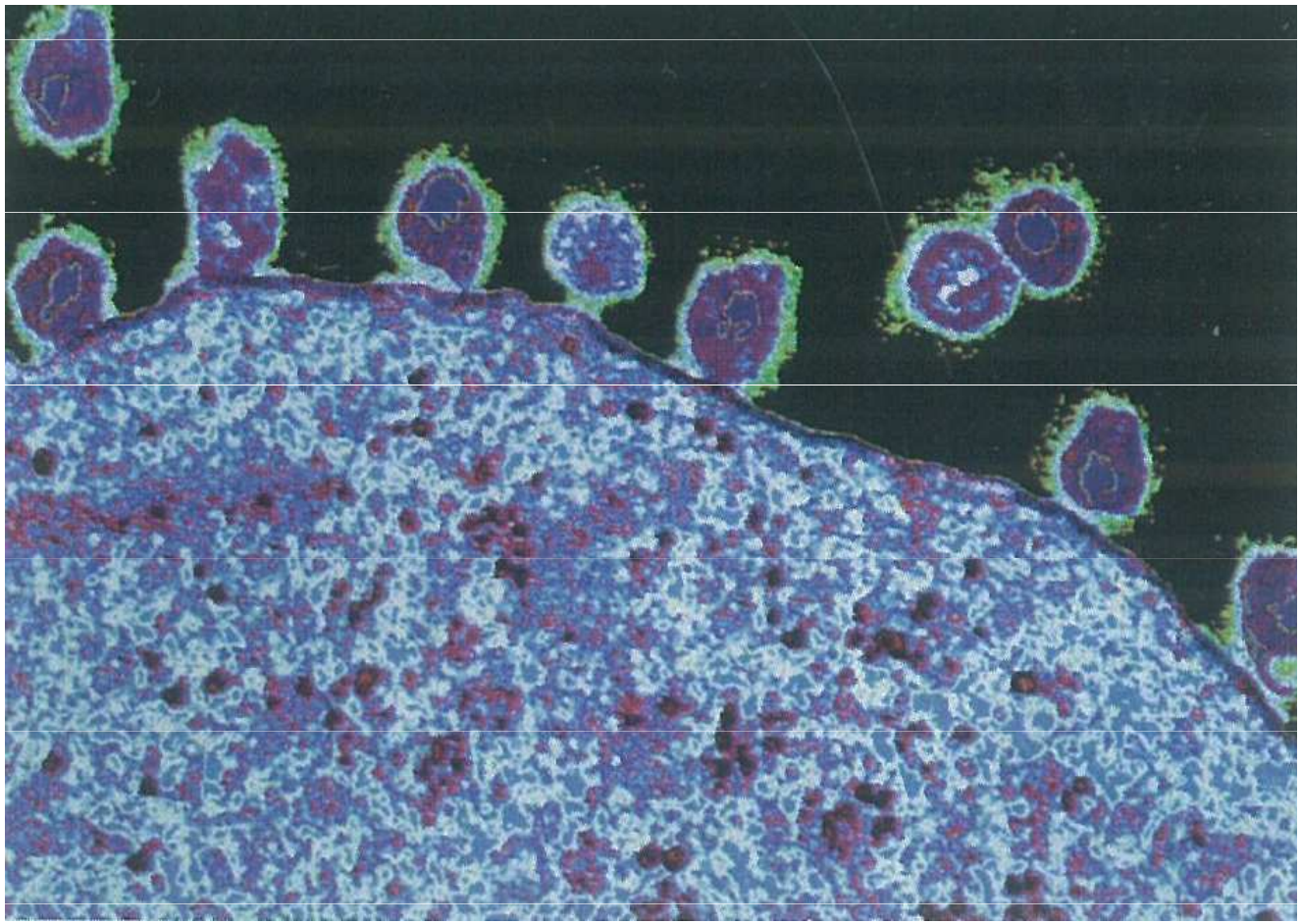


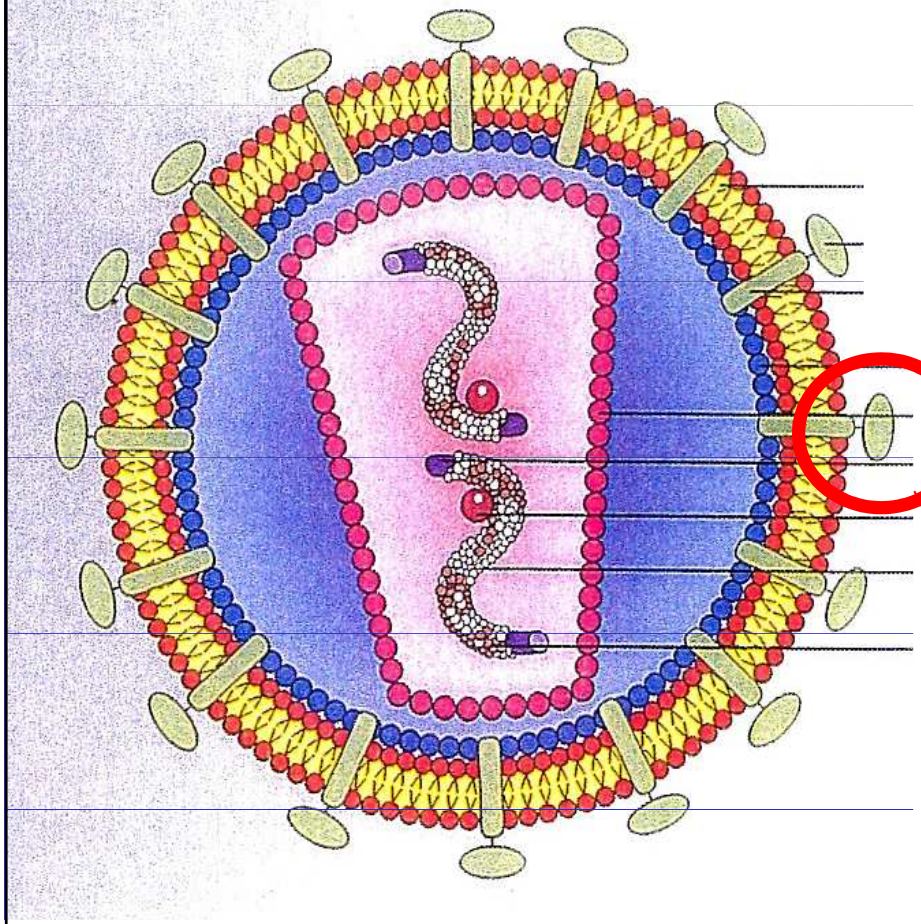
9. Mature viral cores are produced through action on viral protease (another retroviral enzyme)

10. New viral particles are produced by budding at the cell plasma membrane

11. The complete virus is extruded into the bloodstream

Electron micrograft of HIV budding from a CD4+ cell,
The complete virus is extruded into the bloodstream





PATHOGENESIS

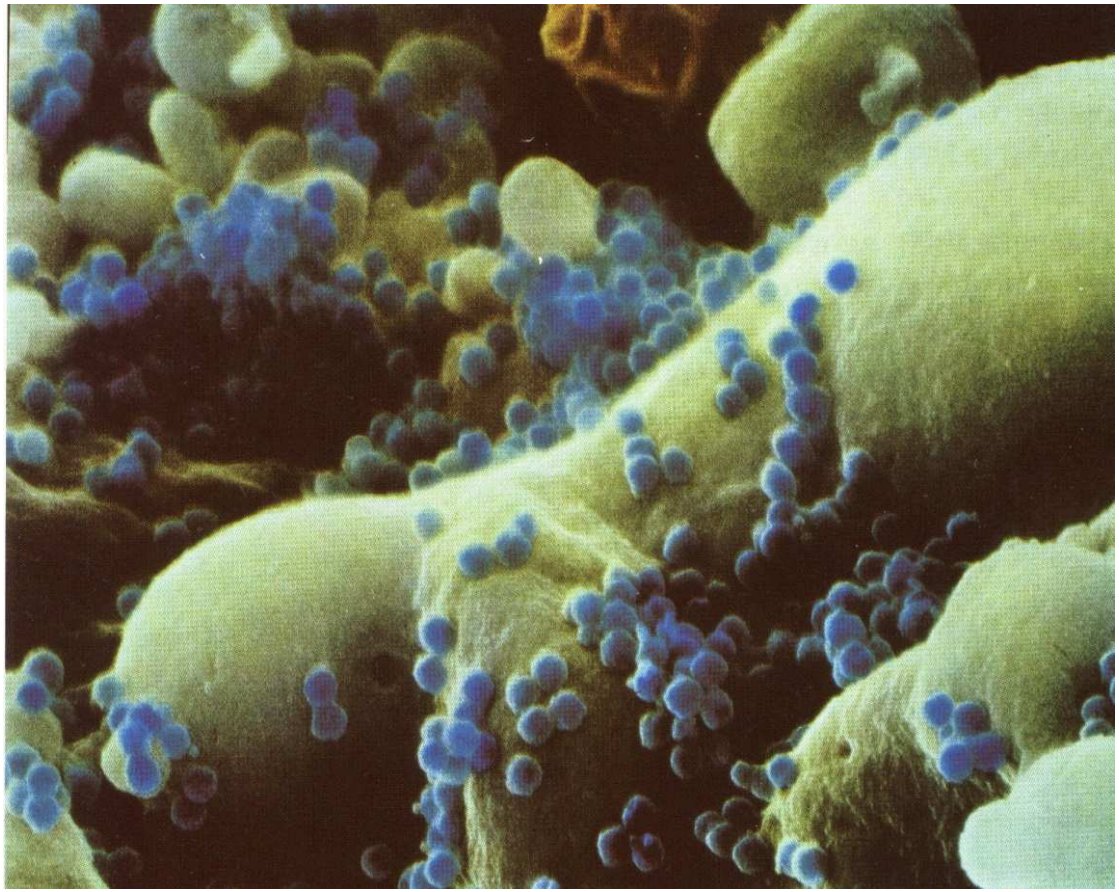
Free virus
and possibly virus-infected cells
enter the blood during initial infection

- The HIV envelope glycoprotein 120 have a high affinity for the CD4 molecule (receptor) on the surface of CD4 cells (helper cells, Th lymphocytes)

- Productive viral replication is lytic to infected T cells

- Loss of number of CD4 cells is basis of advanced infection

CD4+ lymphocytes and HIV



A decrease in function

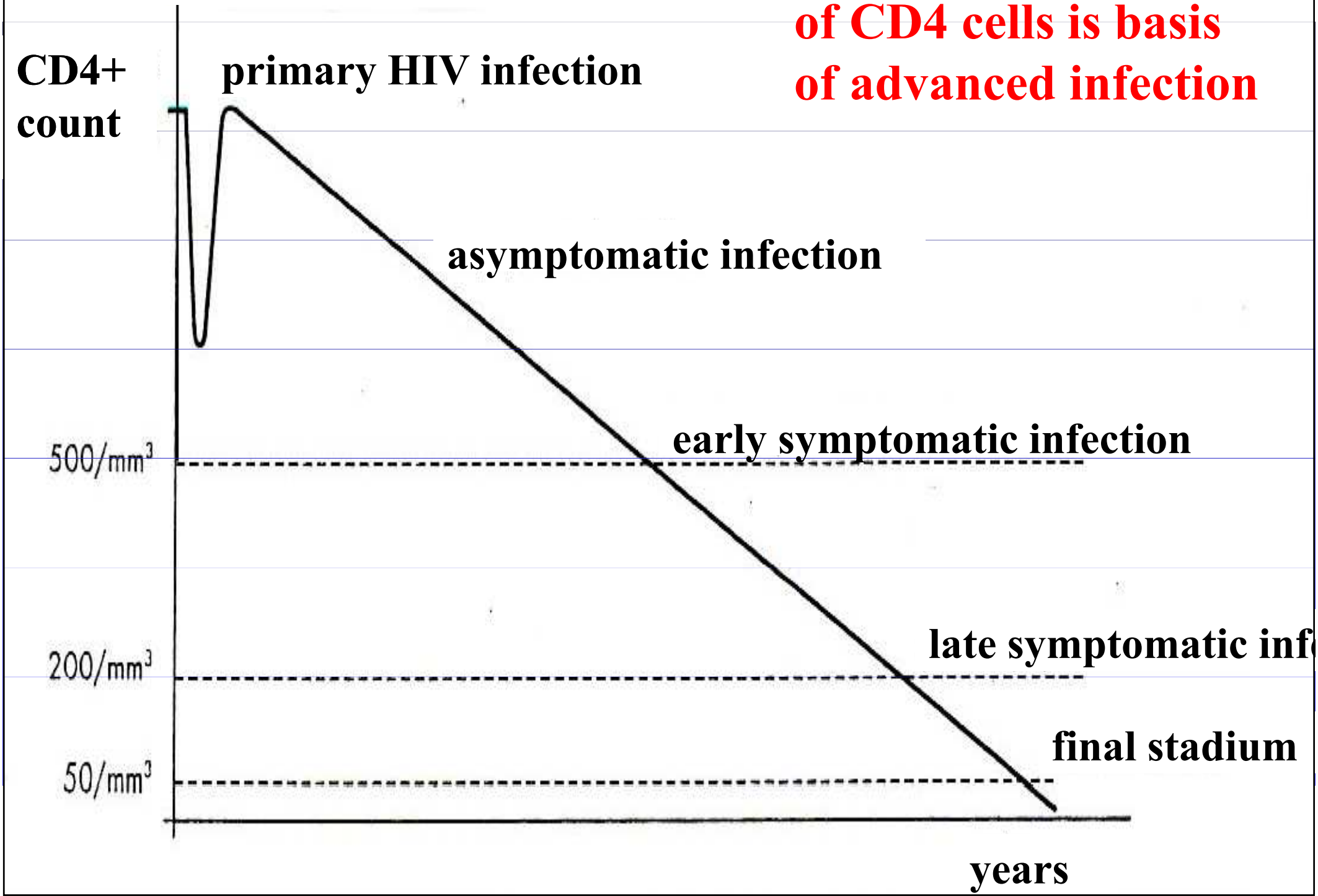
as well as number

of CD4 cells

is central

to the immune dysfunction

CD4+ lymphocytes depletion – gradual loss of number of CD4 cells is basis of advanced infection



HIV infects

- monocytes, macrophages, B cells
- dendritic cells, Langerhans cells in GI
- bone marrow cells, myocardial cells…

Infection by HIV into many cells may contribute greatly to various clinical syndromes of HIV infection and AIDS

Other host cells

- also are infected by HIV
- these cells do not appear to be lysed by the virus
- cells that do not express CD4 receptor can also be infected by HIV (mechanisms are unknown)

Classification of HIV infection

In 1993 the CDC issued a revised classification system for HIV

CDC – Centers for Disease Control
and Prevention, Atlanta, USA

Criteria for HIV infection for adult person include:

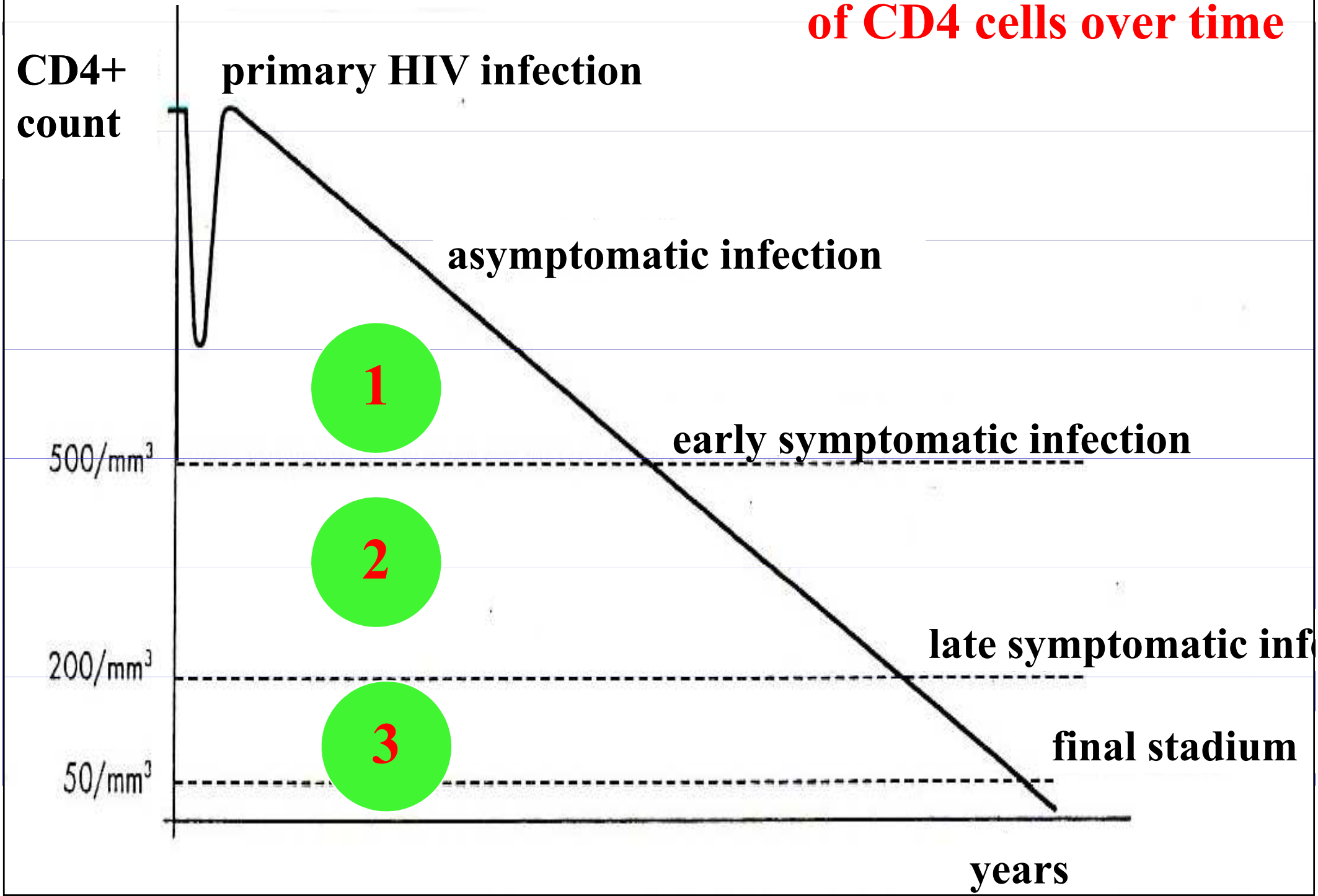
- laboratory categories
- clinical categories

Laboratory categories

- The three categories corresponding to CD4+ lymphocyte counts
- The percentage of CD4+ lymphocyte also can be use
- Normal values are a mean of 800 to 1050 cells per µl (mm^3)

Laboratory category	CD4+ T-cell count	%
1	≥ 500/mm^3	≥ 29 %
2	200 - 499/mm^3	14-28%
3	< 200/mm^3	<14%

CD4+ lymphocytes depletion – gradual loss of number of CD4 cells over time



Clinical categories

– corresponding to clinical condition

A
- acute primary HIV
- asymptomatic infection
- persistent generalized lymphadenopathy (PGL)

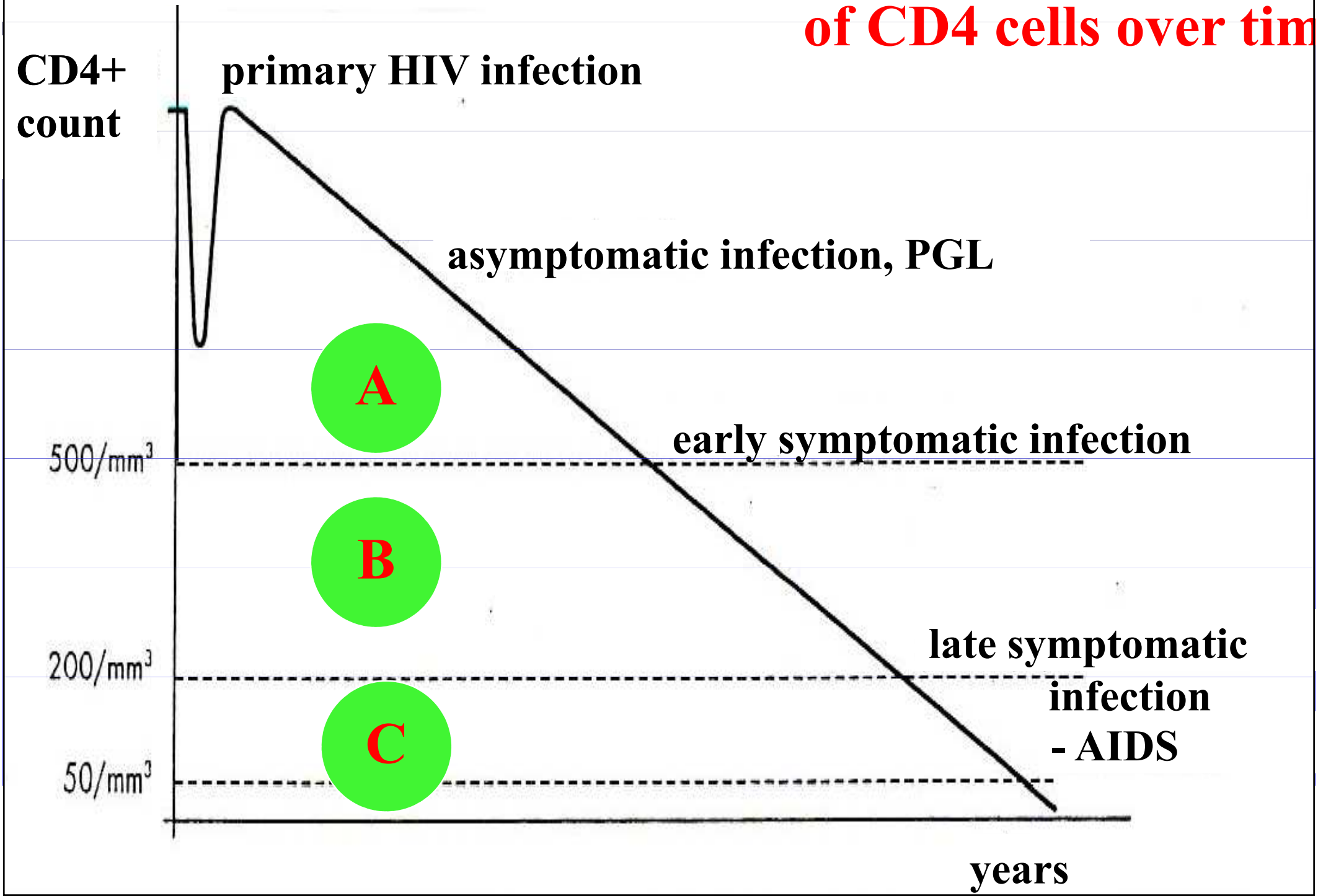
is not typically associated with OI

Risk for OI begins

B
- symptomatic infection (not A or C condition)

C
- AIDS indicator condition

CD4+ lymphocytes depletion – gradual loss of numb of CD4 cells over tim

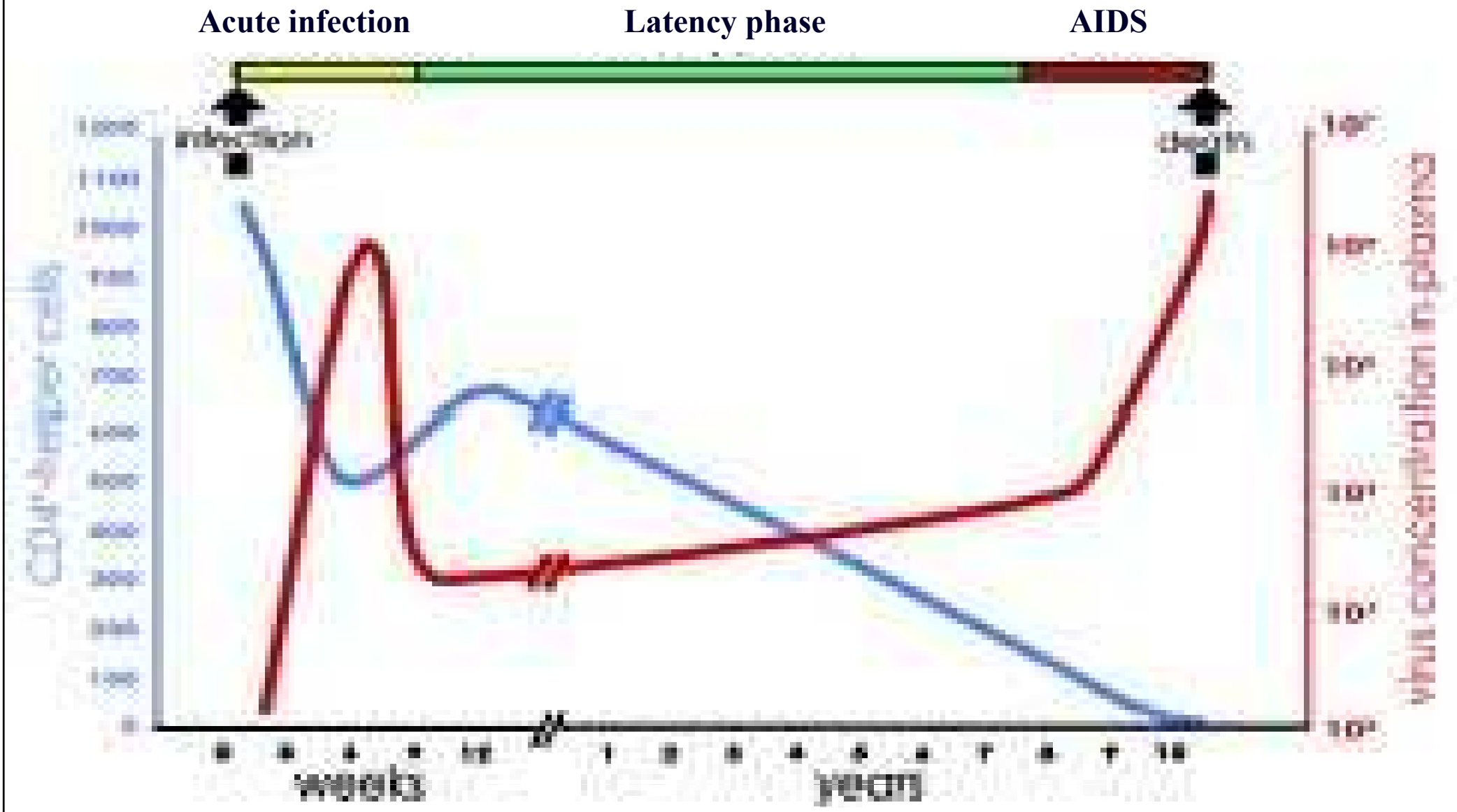


These variants of laboratory and clinical categories are possible.

Laboratory categories		Clinical categories		
CD4+ T-cell categories		A asymptomatitic, acute(primary) HIV or PGL	B symptomatic, not A or C conditions	C AIDS -indicator conditions
1	≥500/mm^3	A1	B1	C1
2	200-499/mm^3	A2	B2	C2
3	<200/mm^3	A3	B3	C3

Natural course of HIV infection (without treatment)

- **Gradual loss of number of CD4 cells over time**
- **Gradual increase of number of viral copies (increase of viral load)**



CD4 = immunological mark; VL = virological mark

Category A

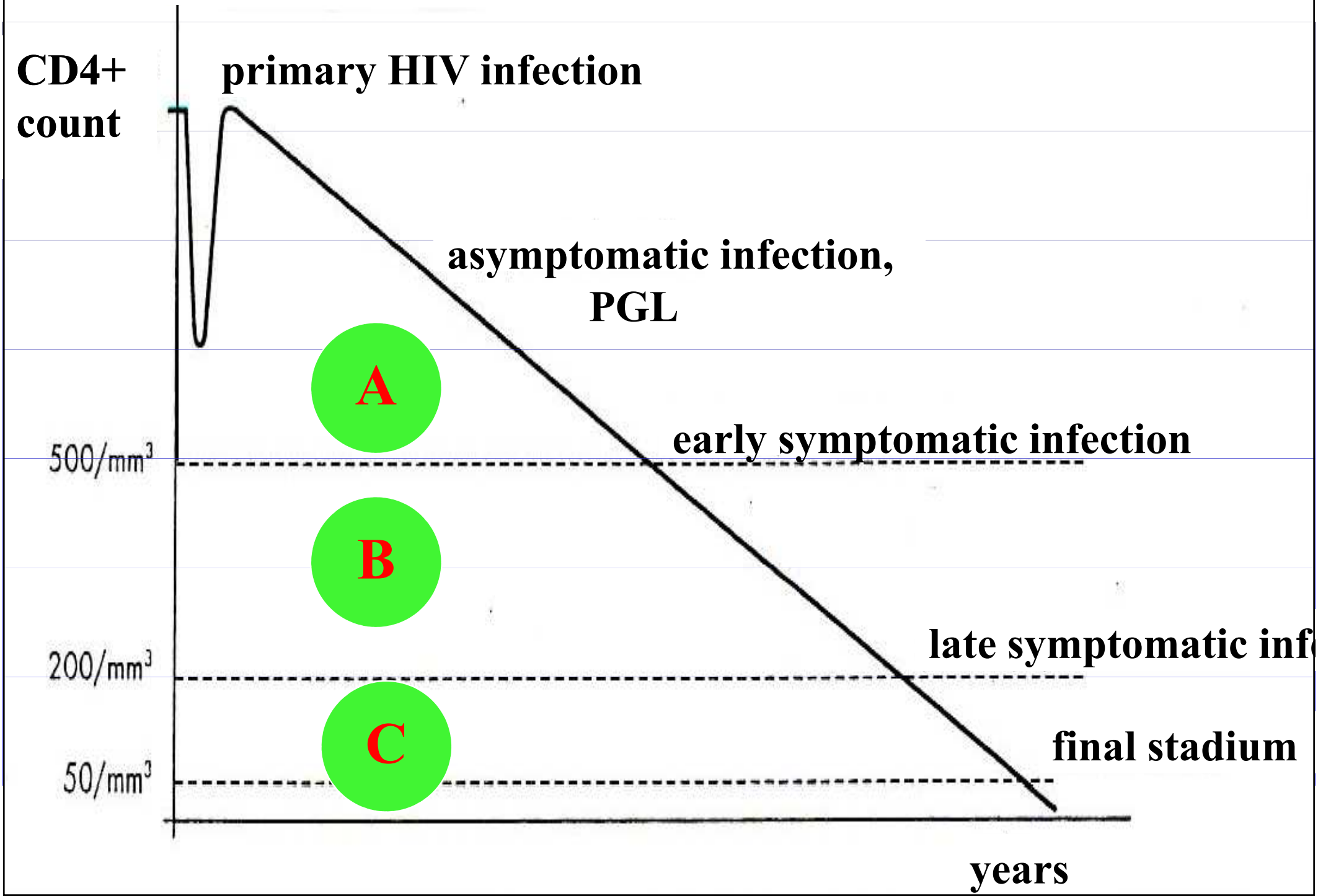
- Consists of one or more of the following conditions in an adolescent or adult with documented HIV infection

- Conditions listed in categories B and C must not have occured

Includes:

- Acute (primary) HIV infection
- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy (PGL)

CD4+ lymphocytes depletion



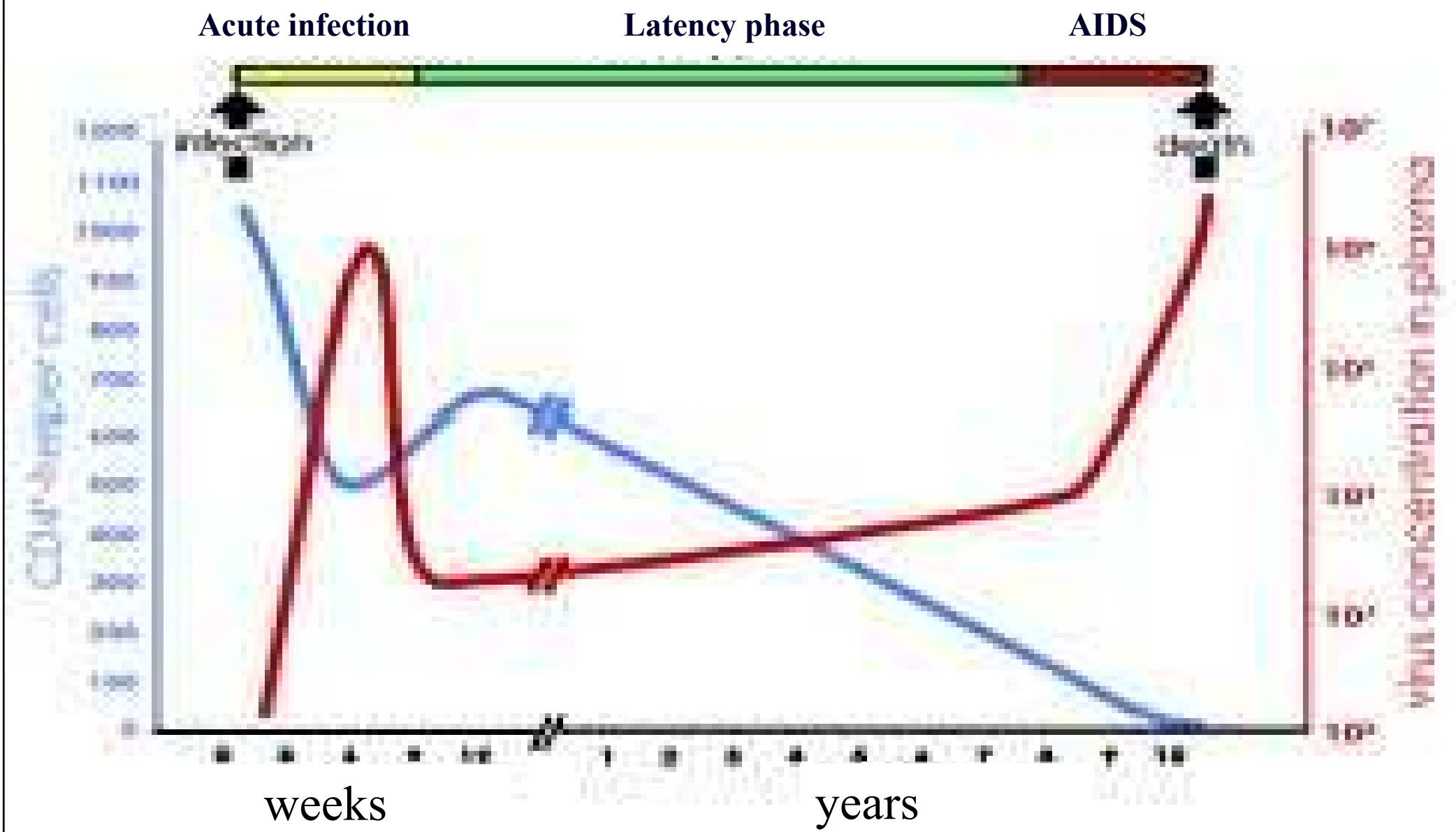
Acute primary HIV infection
(mononucleosis-like syndrome, acute retroviral syndrom)

Occures:

- up to 70% of HIV-infected persons
- between 2 and 8 weeks after initial infection
- acute symptoms last 3 days to 3 weeks
- a variety of nonspecific signs and symptoms have been associated with the acute retroviral syndrome

Natural course of HIV infection (without treatment)

- Gradual loss of number of CD4 cells over time
- Gradual increase of number of viral copies (increase of viral load)



Natural course of HIV infection (without treatment)

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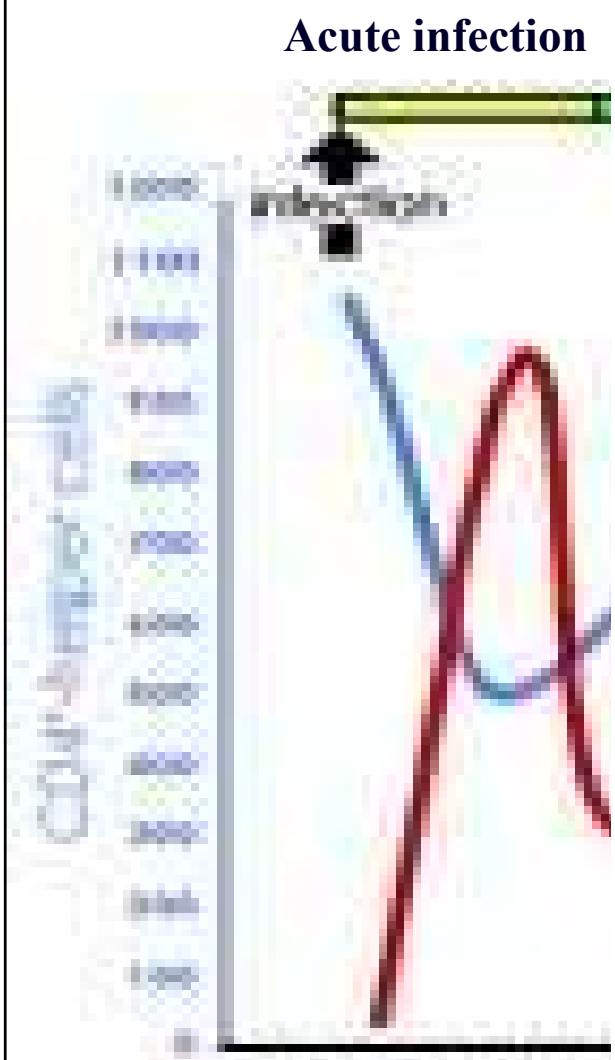


- Usually 2 to 8 weeks after infection
- Production of **antibodies** to HIV is started (time of seroconversion)
- Significant but
  transient fall in CD4 cells count
- **Wide dissemination of virus**
- Symptoms include
  a glandular fever-like illness with fatigue,
  fever lymphadenopathy
  and seroconversion rash…

- **Most individuals have no symptoms**

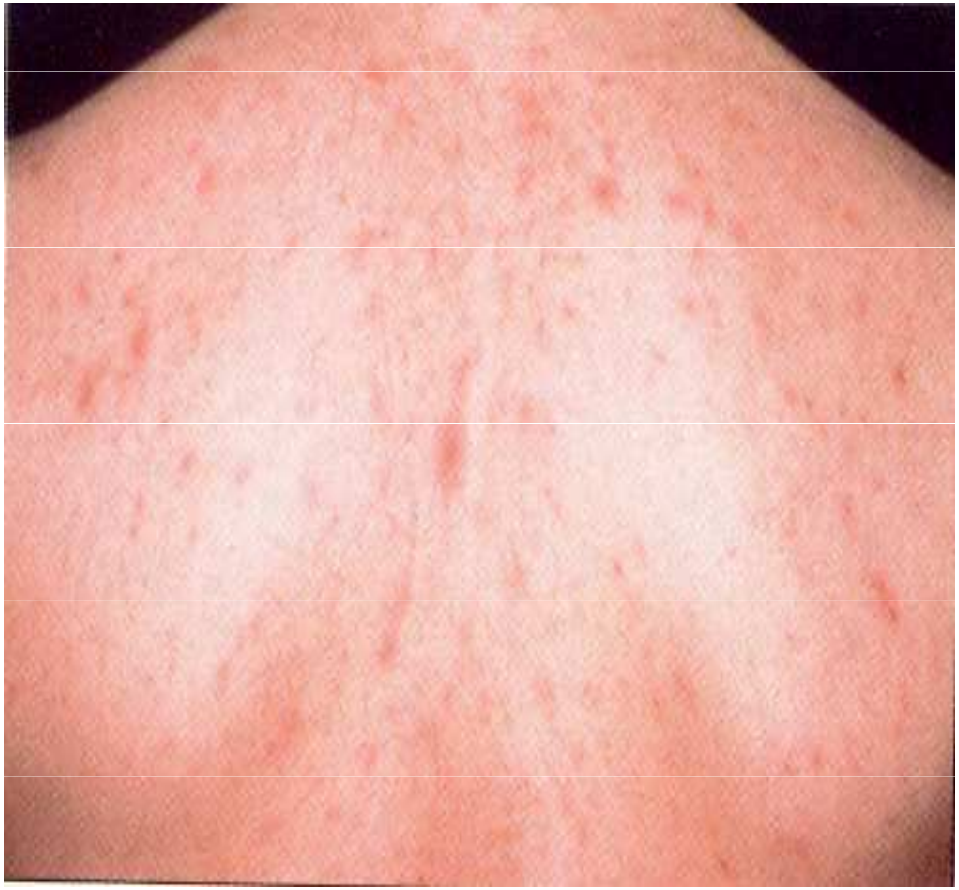
Signs and symptoms of primary HIV infection

A variety of nonspecific signs and symptoms have been associated with the acute retroviral syndrome

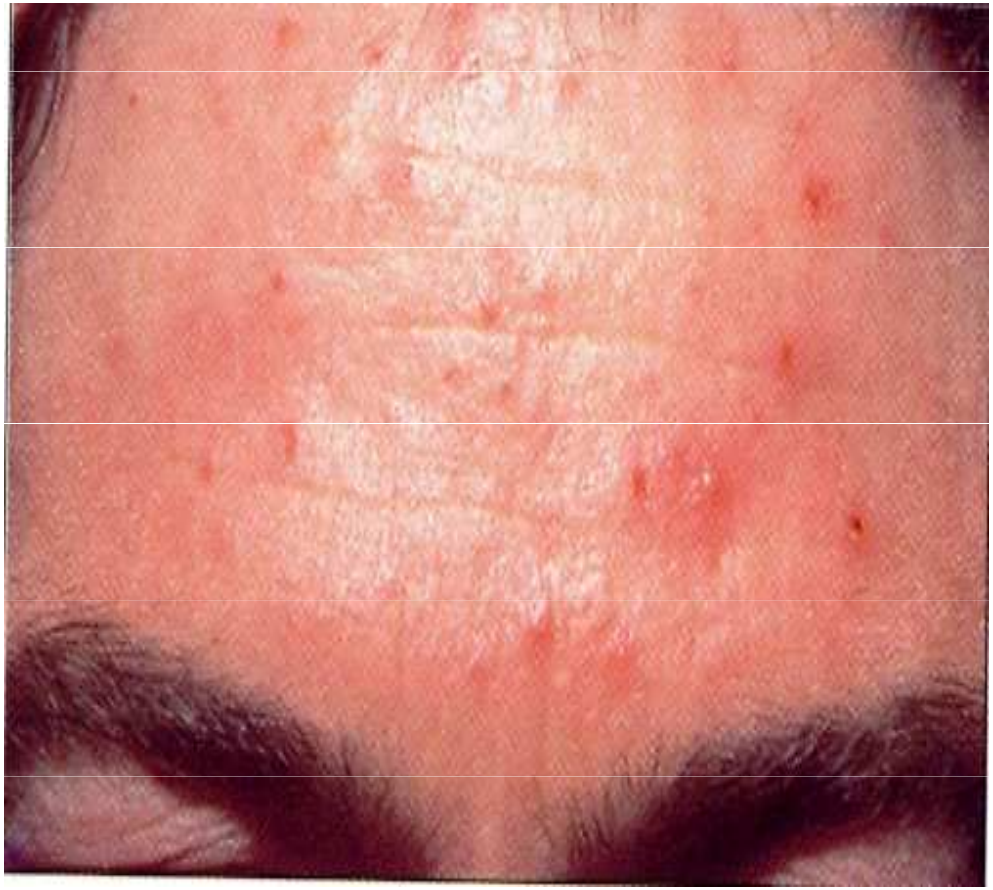
- Fever 77%
- Lethargy/ fatigue 66%
- Rash 56%
- Myalgia 55%
- Headache 51%
- Pharyngitis 44%
- Cervical adenopathy 39%
- Arthralgia 31%
- Oral ulcer 29%
- Pain on swallowing 28%
- Axillary adenopathy 24%

Acute primary HIV infection

Rash on the back



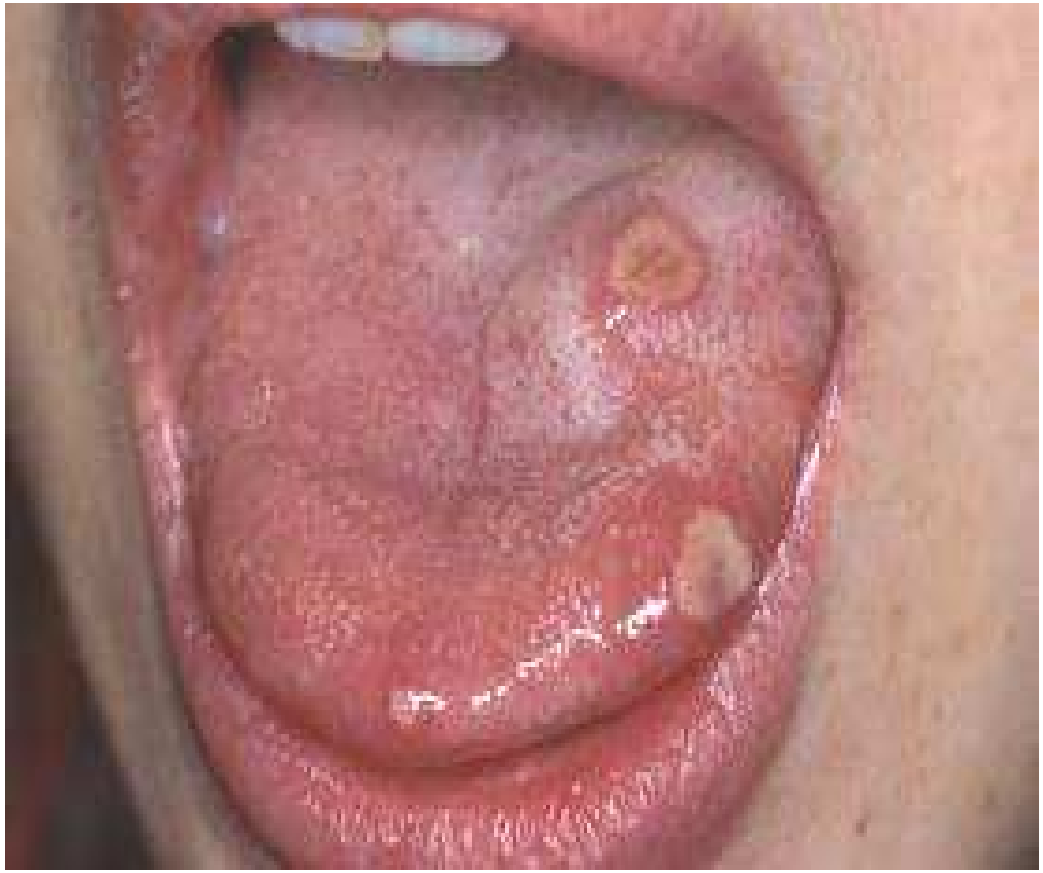
Seborrhoeic dermatitis



Acute primary HIV infection

Herpetic gingivitis – oral ulcer (trush)

Herpetic gingivitis



- Weight loss 24%
- Nausea 24%
- Diarrhea 23%
- Night sweats 22%
- Cough 22%
- Anorexia 22%
- Abdominal pain 19%
- Oral candidiasis 17%
- Vomiting 12%
- Photophobia 12%
- Meningitis 12%
- Genital ulcer 7%
- Tonsillitis 7%
- Depression 7%
- Dizziness 6%

Laboratory – in primary HIV infection

- **Lymphopenia**
- **Transient decrease of CD4+ lymphocyte count**
- **p24 – HIV core antigen**

  - may be detected in serum and CSF
    within 2 weeks of exposure to HIV
    and may persist for weeks or months
- **anti-HIV**

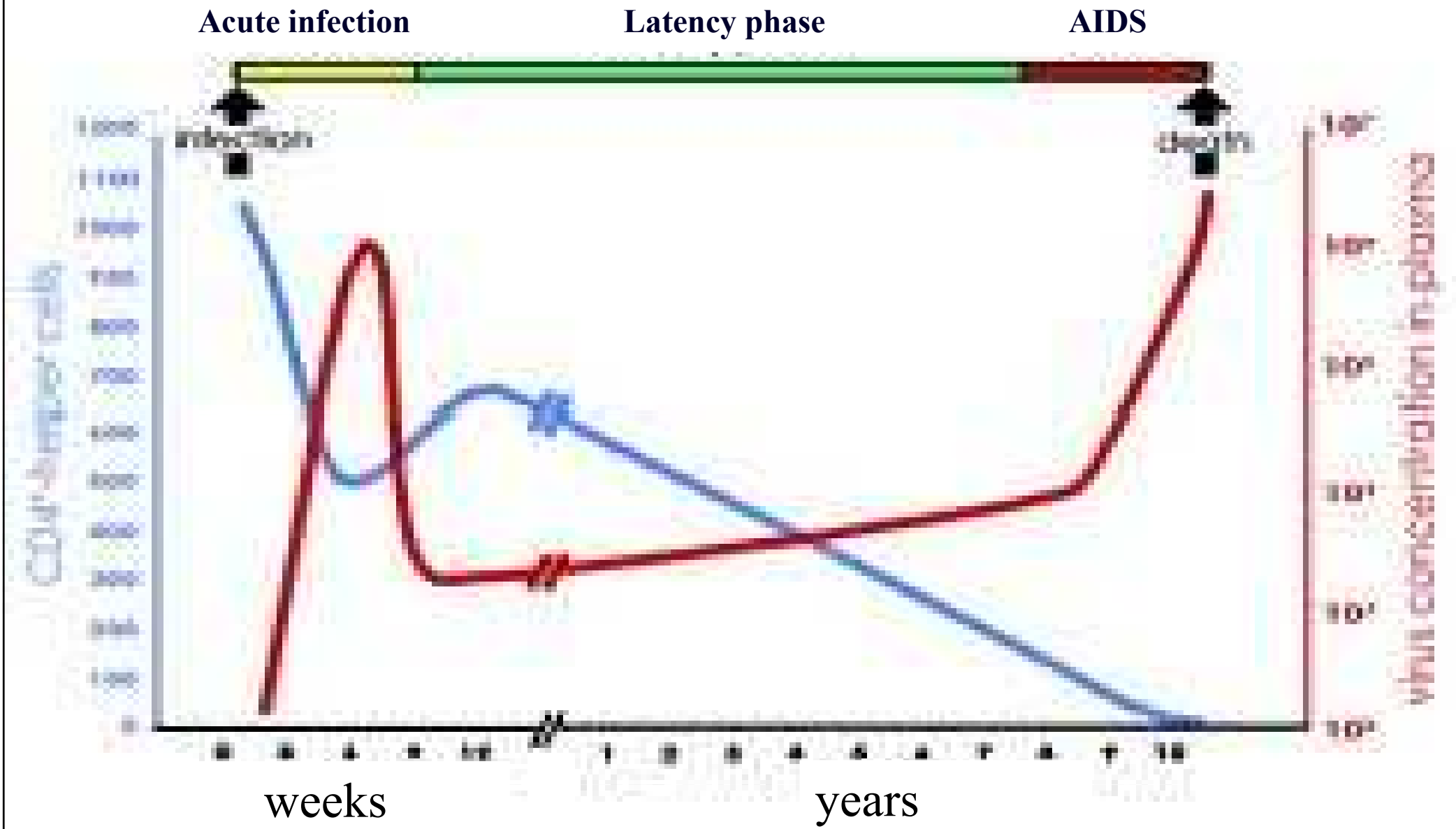
  antibodies to HIV usually are detected within 2 months after HIV exposurre not within primary HIV infection

Asymptomatic HIV infection

- the vast majority of individuals infected with HIV are asymptomatic
- this asymptomatic state
  may be prolonged
- this period of latency is, in fact,
  a time of intense viral replication
  and immune response

Natural course of HIV infection (without treatment)

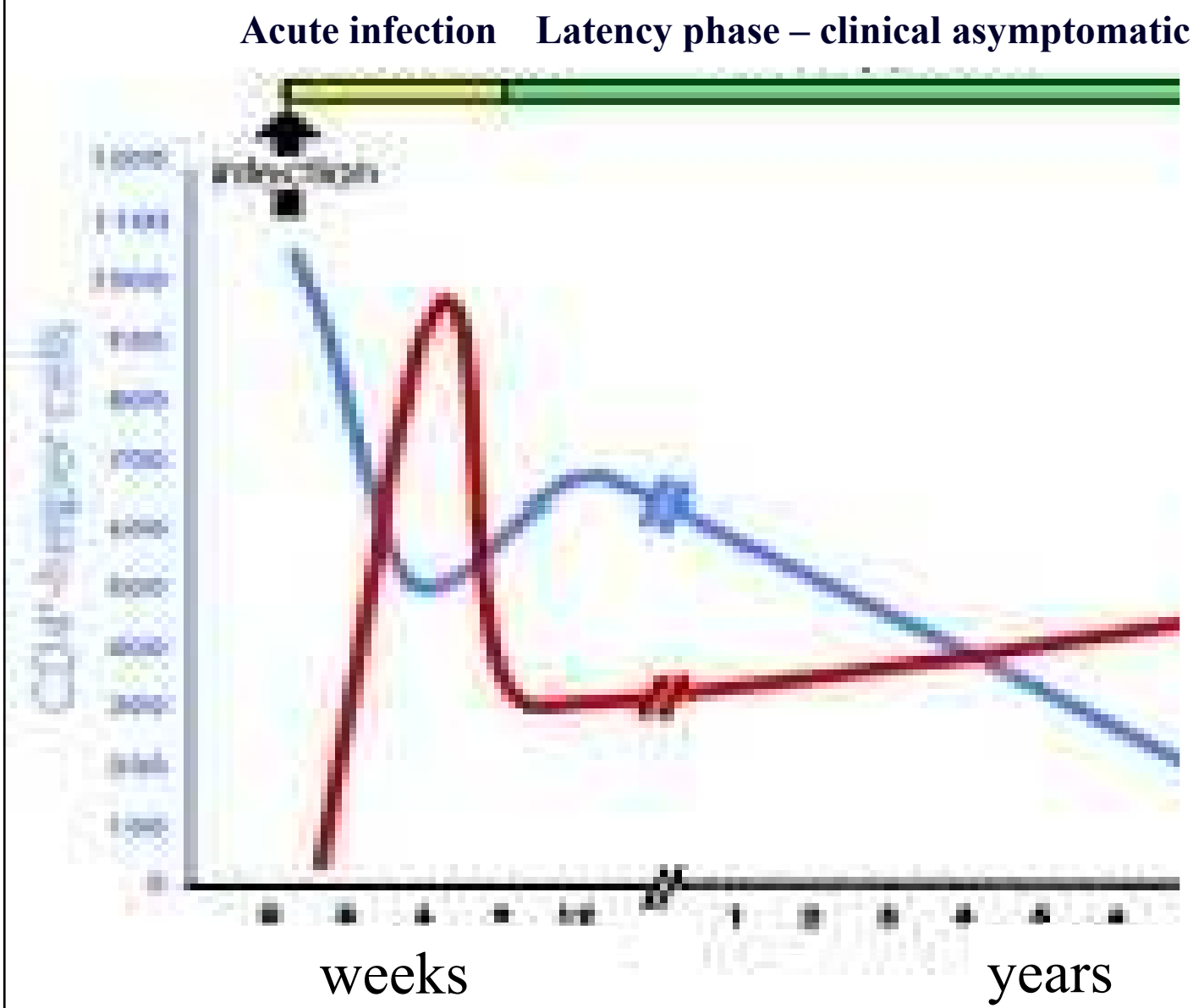
- Gradual loss of number of CD4 cells over time
- Gradual increase of number of viral copies (increase of viral load)



Viral load (VL) = the number of copies of RNA HIV-1 per 1 ml of plasma

Natural course of HIV infection (without treatment)

- Gradual loss of number of CD4 cells over time
- Gradual increase of number of viral copies (increase of viral load)



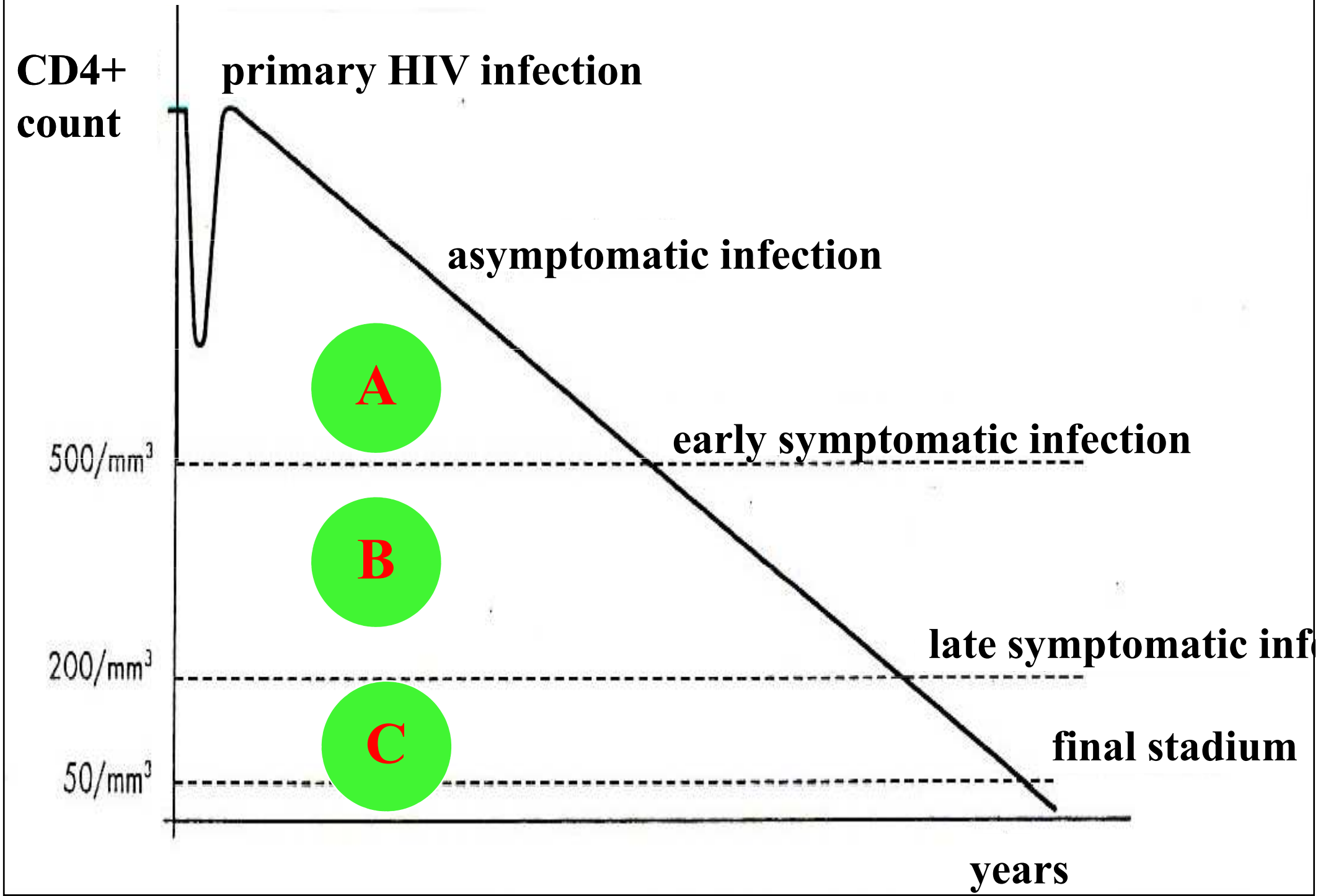
- May last for approxim. 10 years
- This not a period of virological and immunological latency
- **CD4 cell counts** gradually **fall** over time
- Immune systém Weakens as **viral load increases**

Predictors of HIV-disease progression

clinical	immunological	virological
• oral candidiasis • involution of PGL • constitutional symptoms (fever, night sweats, weight loss…)	• ↓ CD4+ cell count • ↑ β-2-microglobulin • ↑ neopterin	• ↑ viral load • ↑ p24 antigen

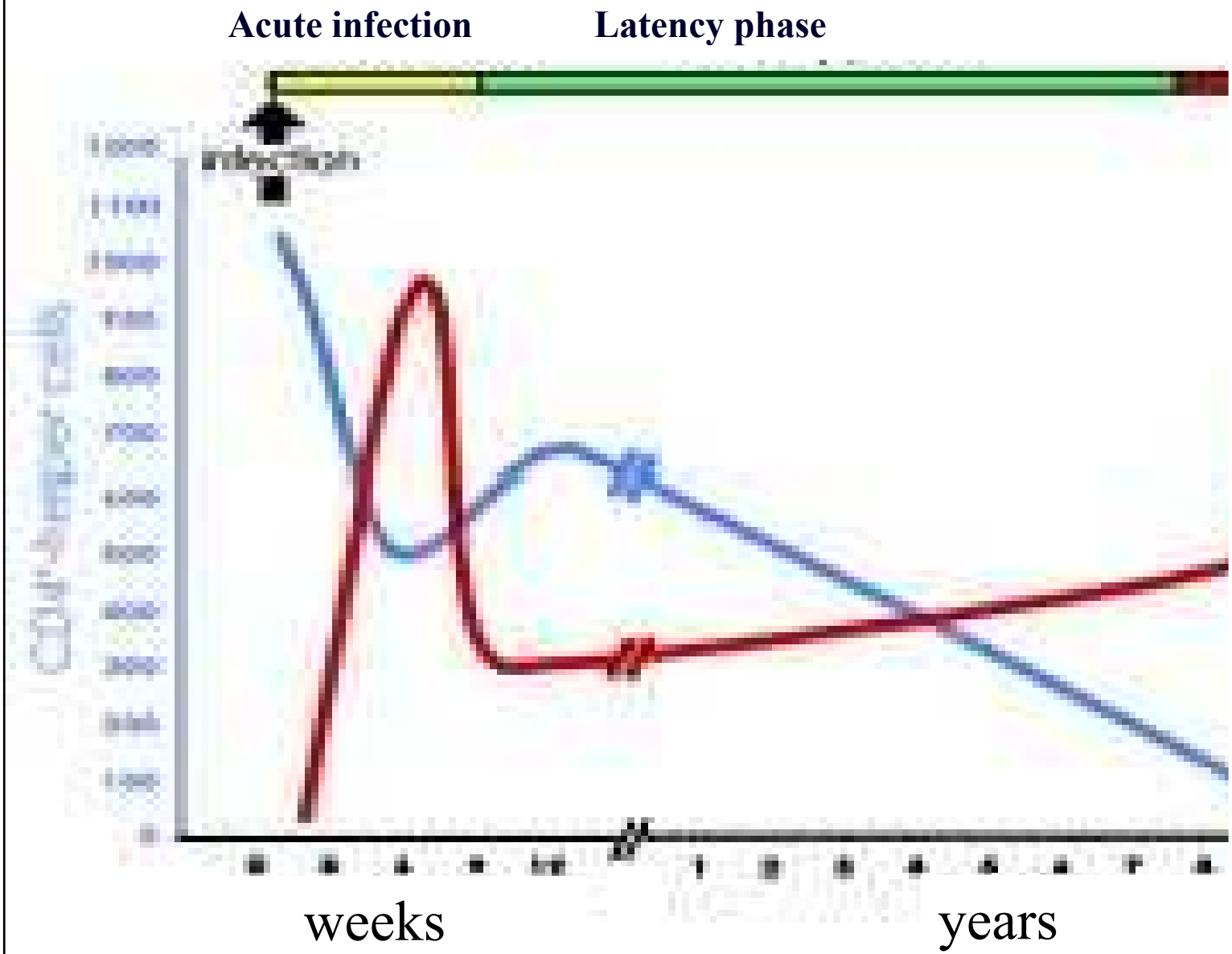
CLINICAL CATEGORY B

CD4+ lymphocytes depletion



Natural course of HIV infection (without treatment)

- **Gradual loss of number of CD4 cells over time**
- **Gradual increase of number of viral copies (increase of viral load)**



- **CD4 cell counts fall**
- **Viral load increases**

- Immune system weakens

- Clinical symptoms begin to appear

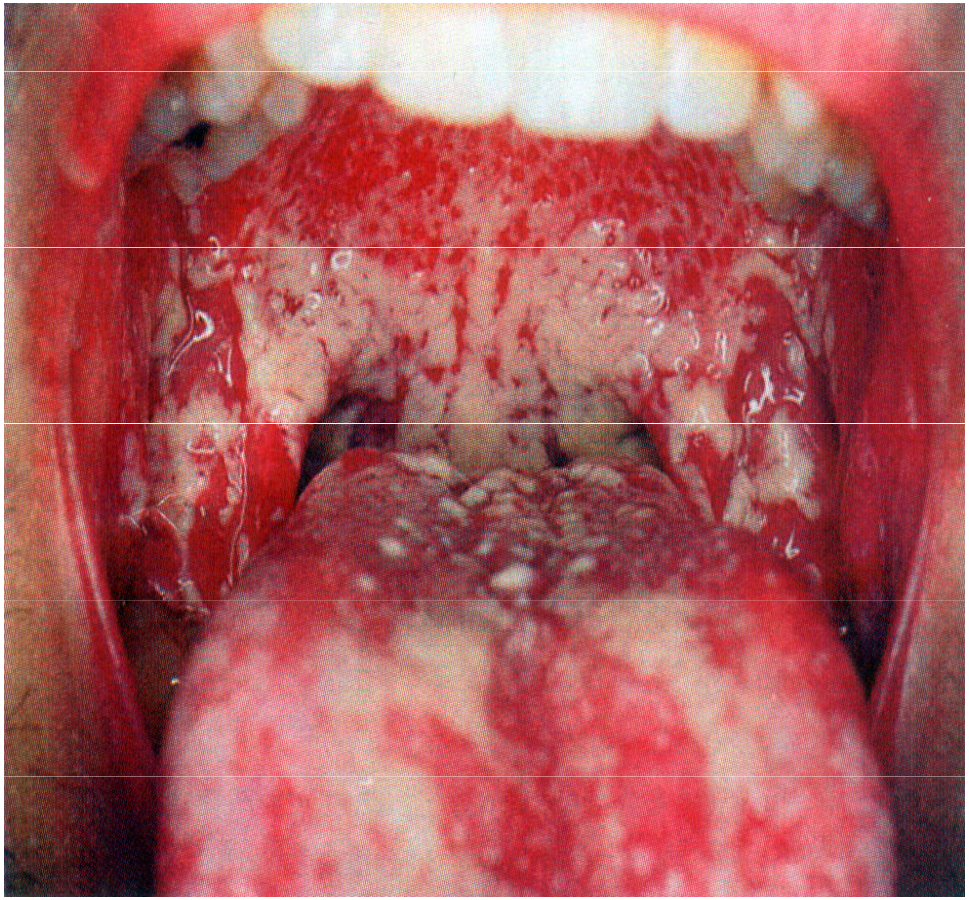
Category B
= symptomatic HIV infection

- Consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical category C
- Examples of conditions in clinical category B include:

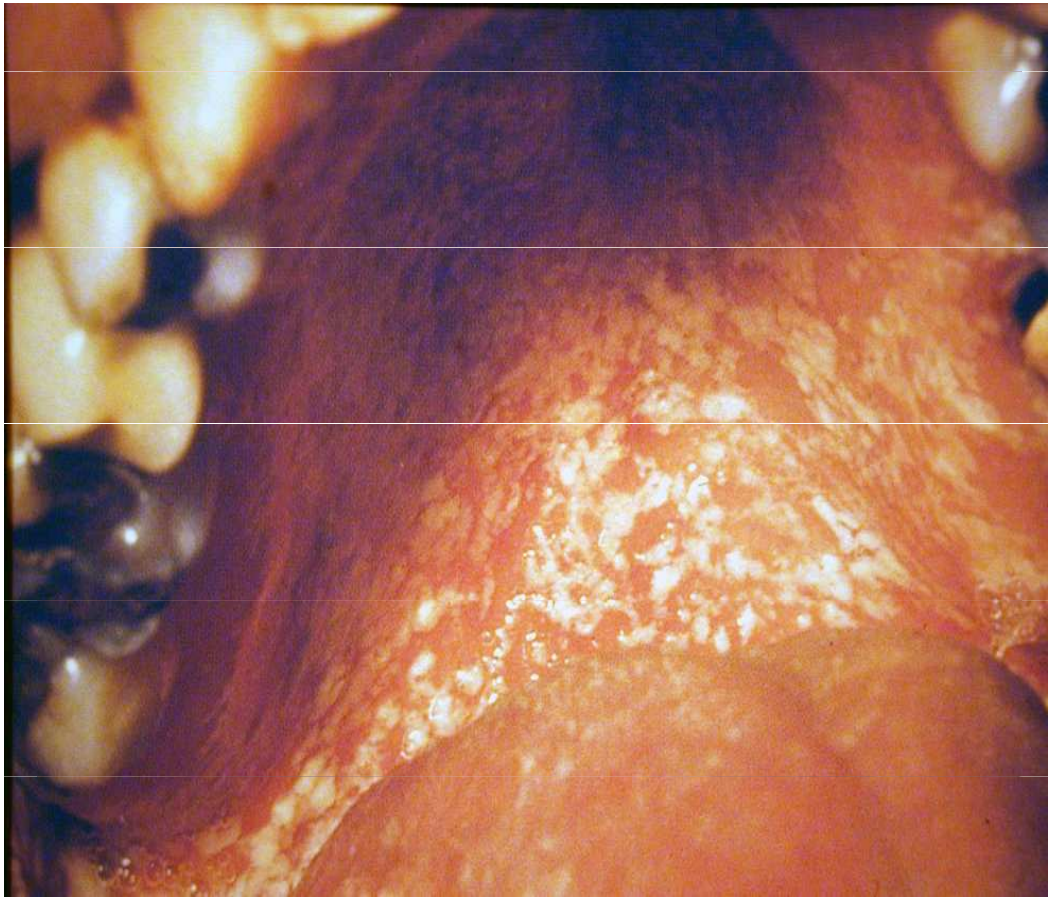
- Fever of >38.5 C > 1 month
- Diarrhea > 1 month

Clinical category B

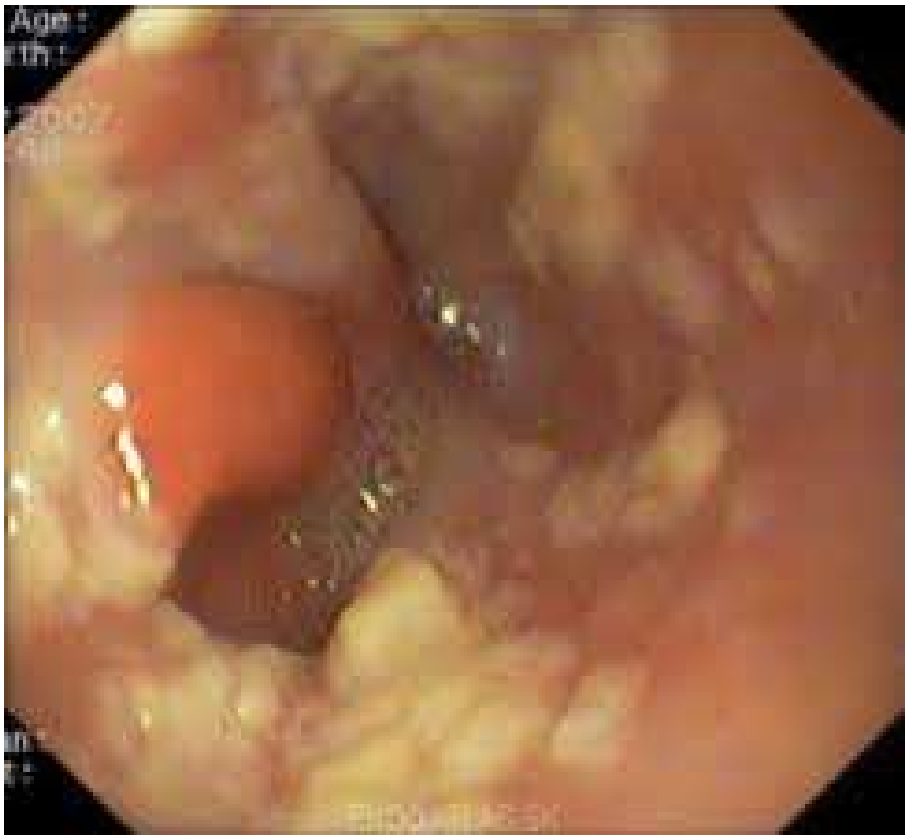
Oropharyngeal candidosis on the bucal mucosa, on the tongue…

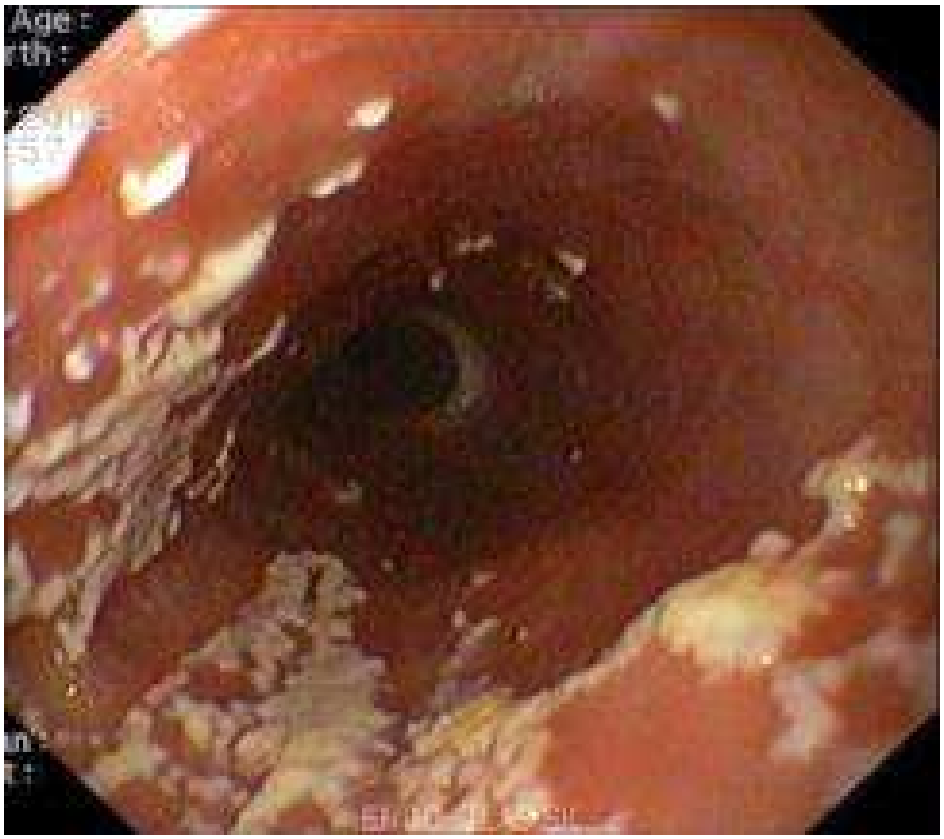


Oropharyngeal candidosis on the palatum



Esophageal candidosis



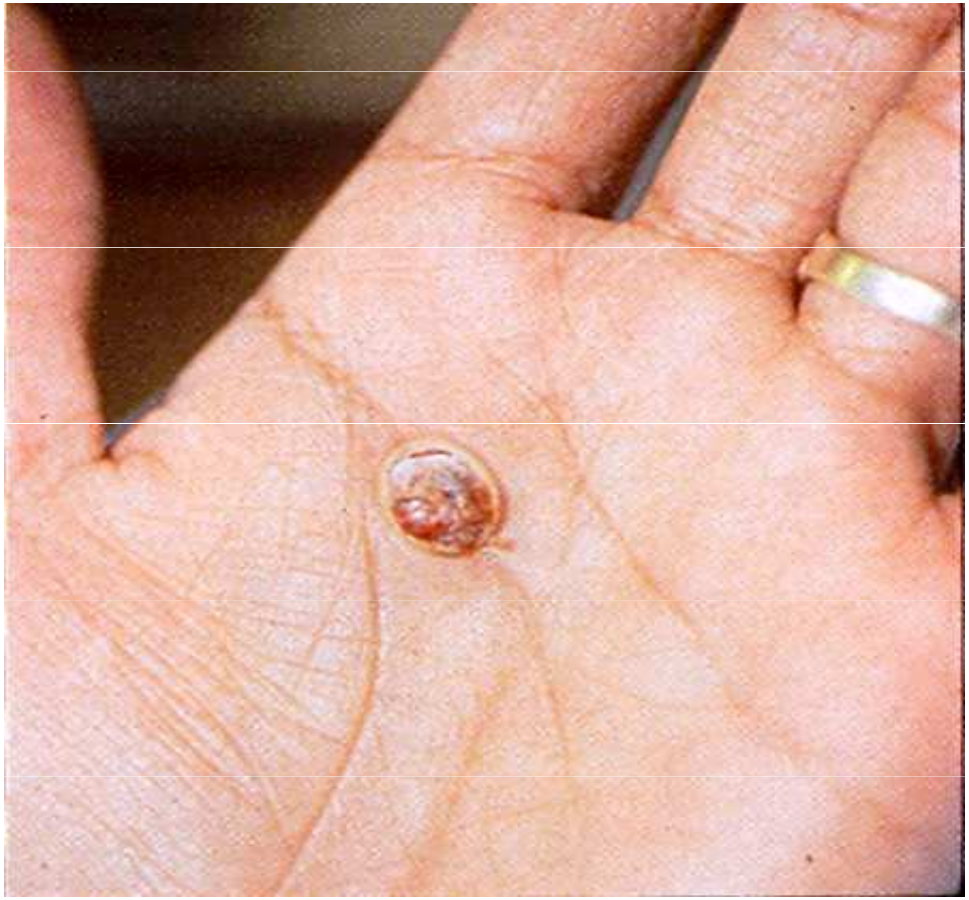


Endoscopic picture

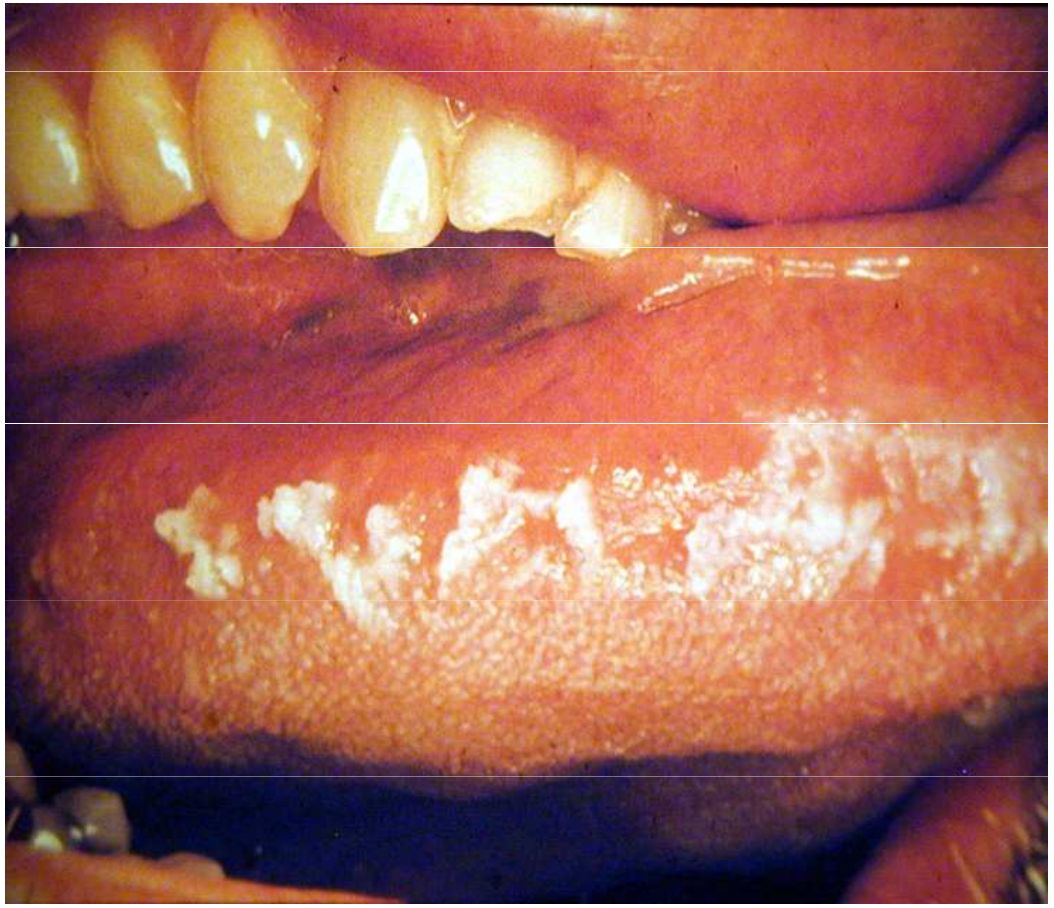
- **Vulvovaginal candidosis**
- **Lymphoid interstitial pneumonitis (LIP)**
- **Cervical dysplasia or carcinoma in situ**
- **Pelvic inflammatory disease (PID)**
- **Listeriosis**
- **Bacillary angiomatosis**
- **Trombocytopenia**
- **Peripheral neuropathy**

Clinical category B

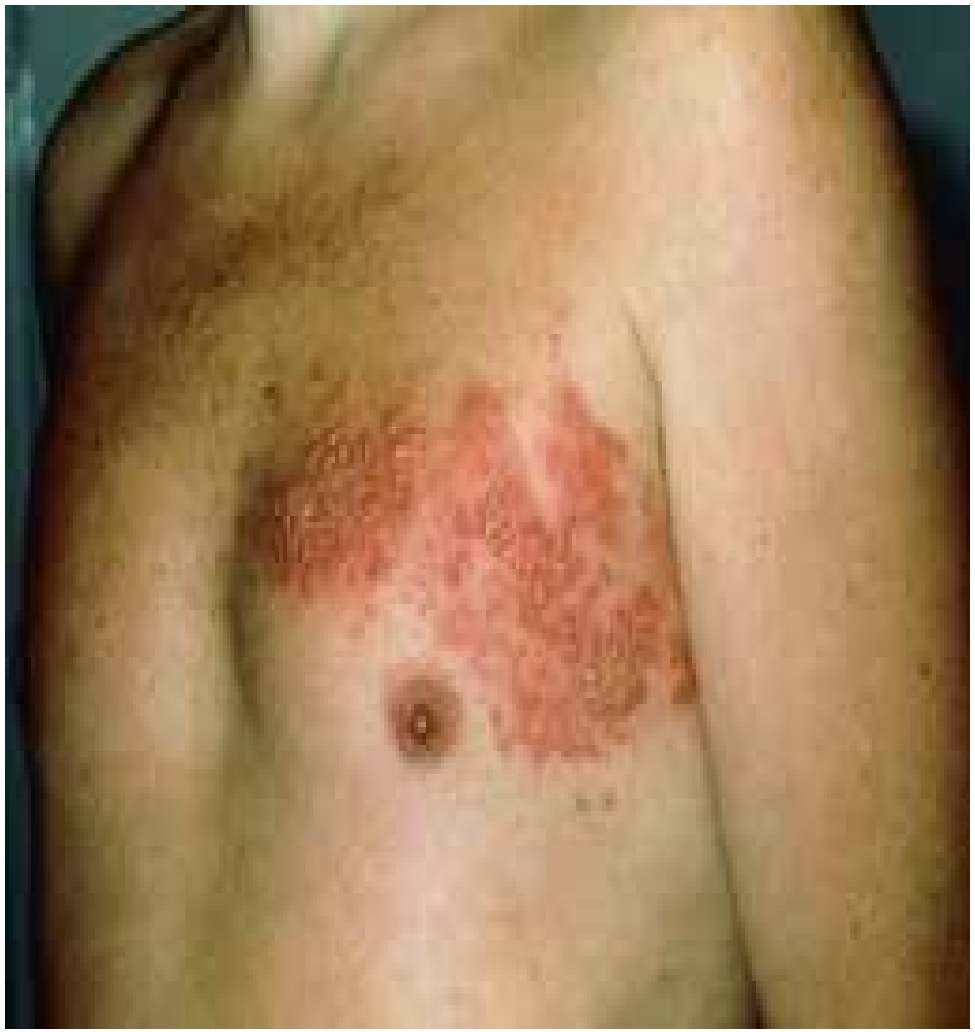
Bacillary angiomatosis (*Bartonella henselae, Bartonella quintana)*

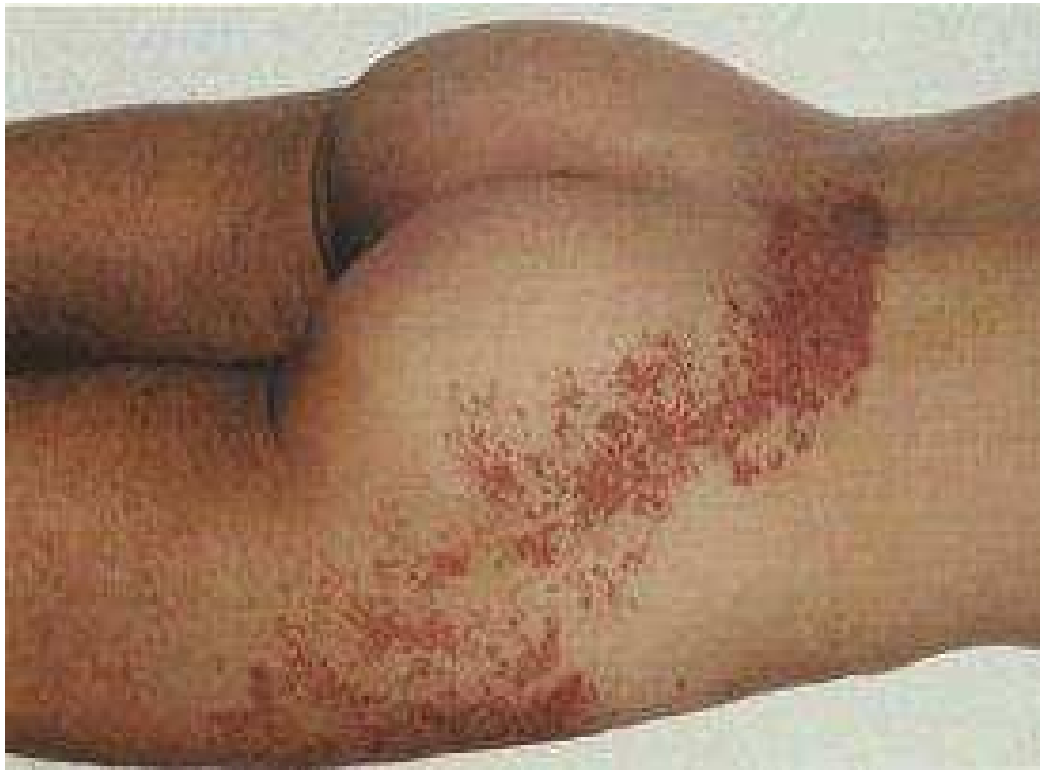


Oralhairy leucoplacia (cobblestonetongue)



Herpes zoster recurrent or multidermatomal





Clinical caterory C - AIDS

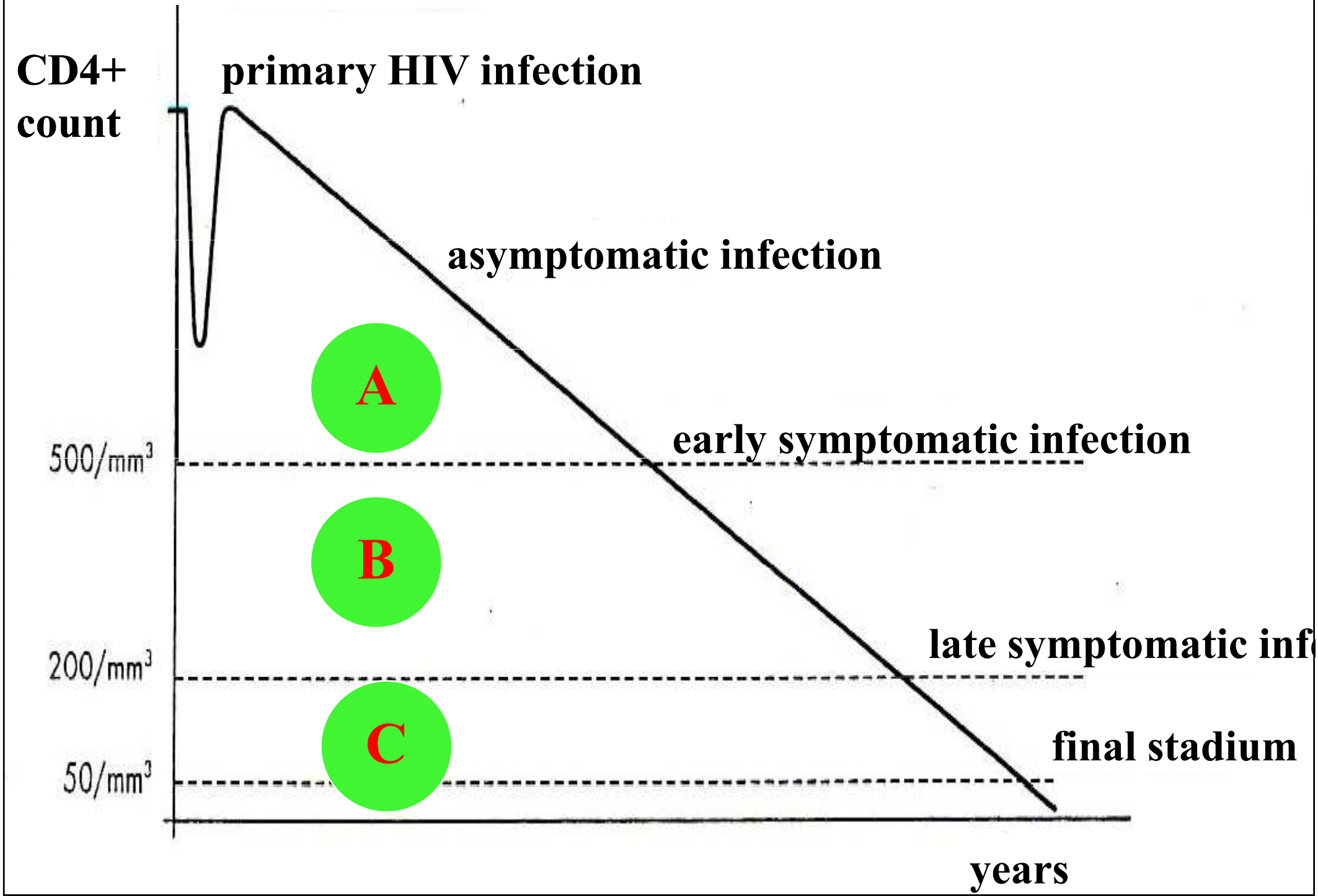
- **Is the end stage of long-standing, chronic infection with HIV**
- **Without antiretroviral therapy, approximately 50% of individuals develop AIDS within 10 years after HIV infection**

The AIDS syndrome is defined by various

- opportunistic infections
- malignancies
- other conditions

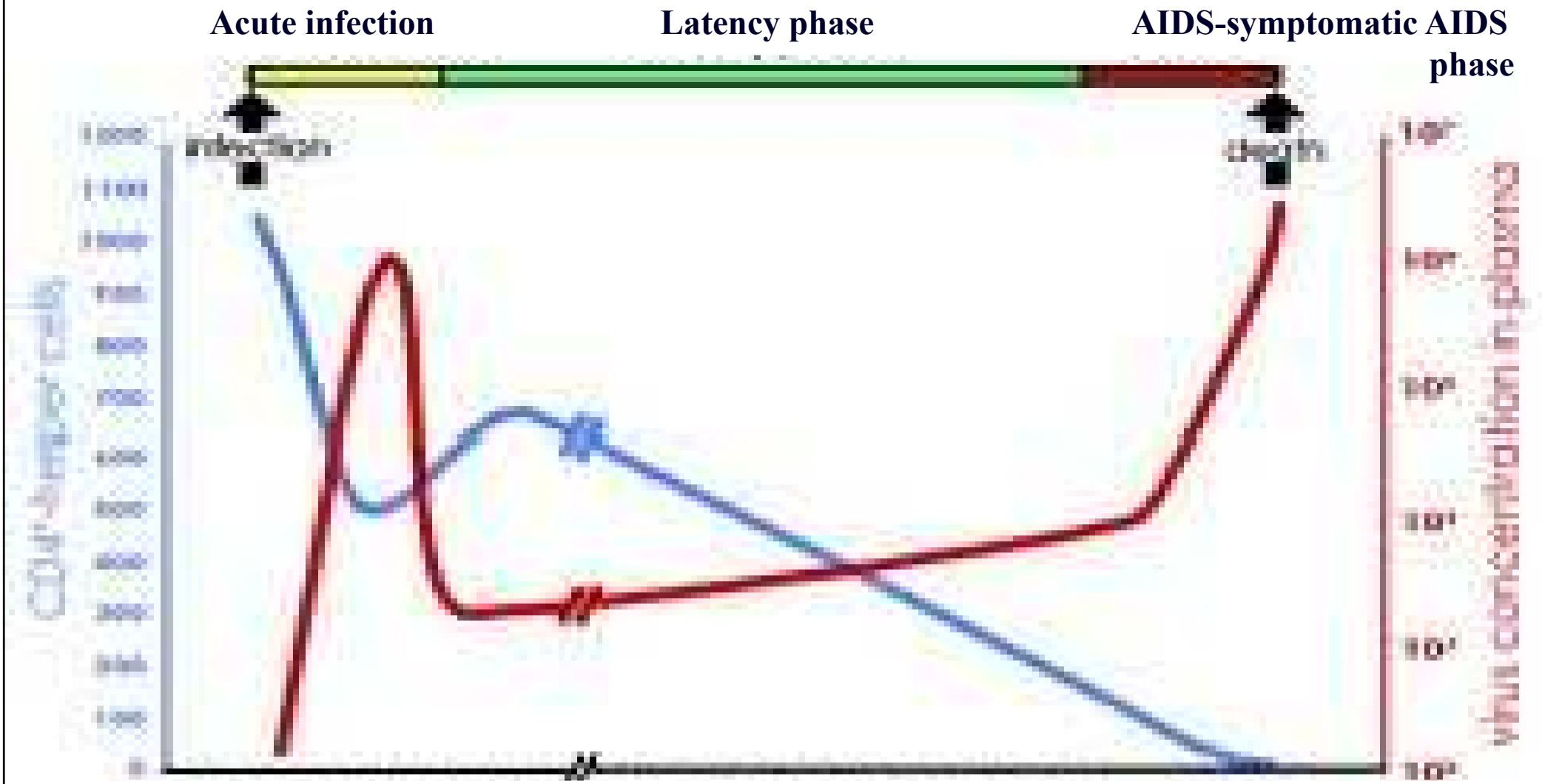
sumarized in the CDC definition.

CD4+ lymphocytes depletion



Natural course of HIV infection (without treatment)

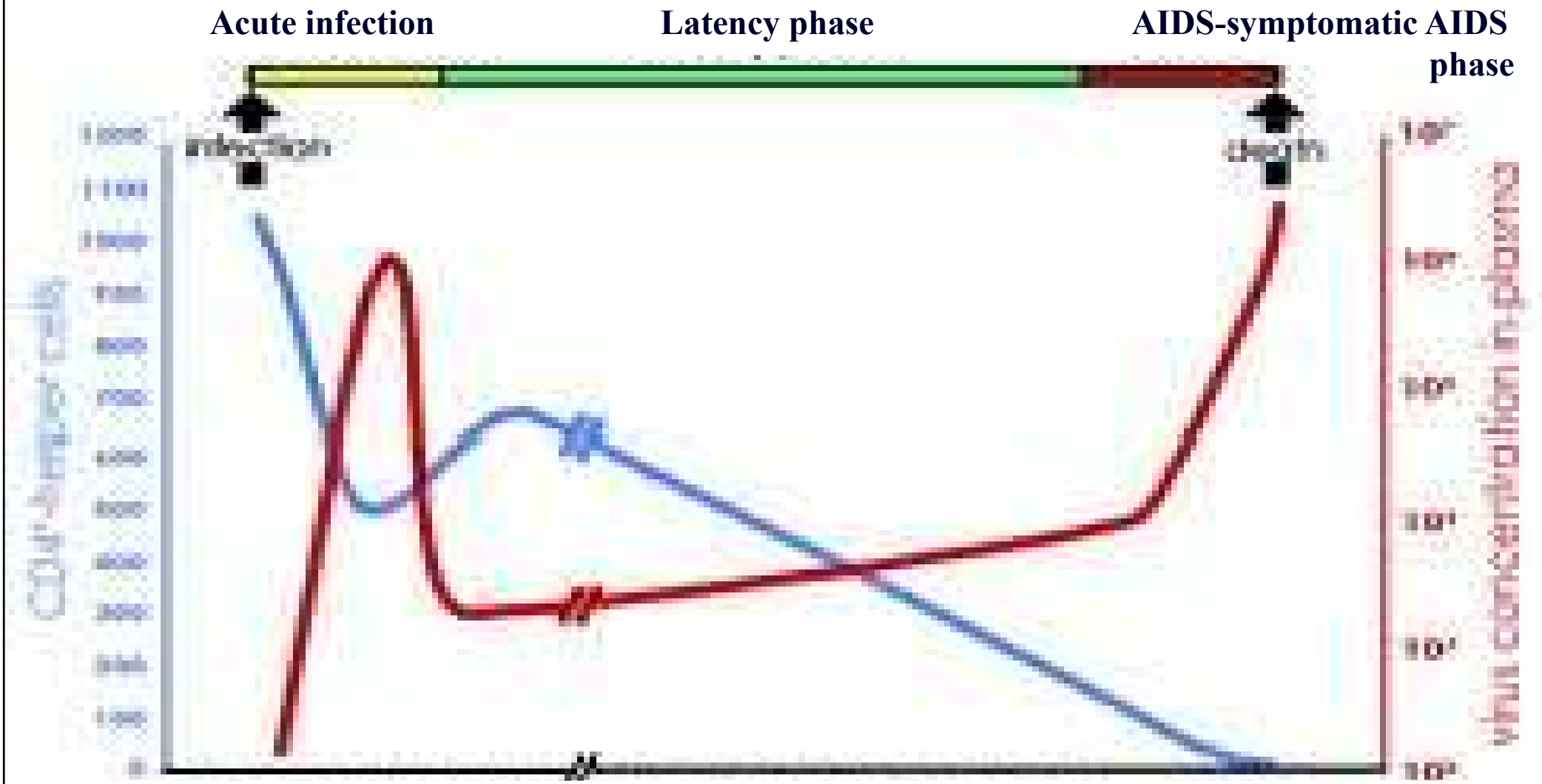
- Gradual loss of number of CD4 cells over time
- Gradual increase of number of viral copies (increase of viral load)



- **VL is extremely high** – possibly one million copies/ml or more
- **CD4 counts** usually **below 200** cells/mm3 and may fall **to zero**

Natural course of HIV infection (without treatment)

- **Gradual loss of number of CD4 cells over time**
- **Gradual increase of number of viral copies (increase of viral load)**



- Symptoms of very advanced infection include opportunistic infections, malignancies and other clinical conditions such as AIDS case definition

Category C - AIDS

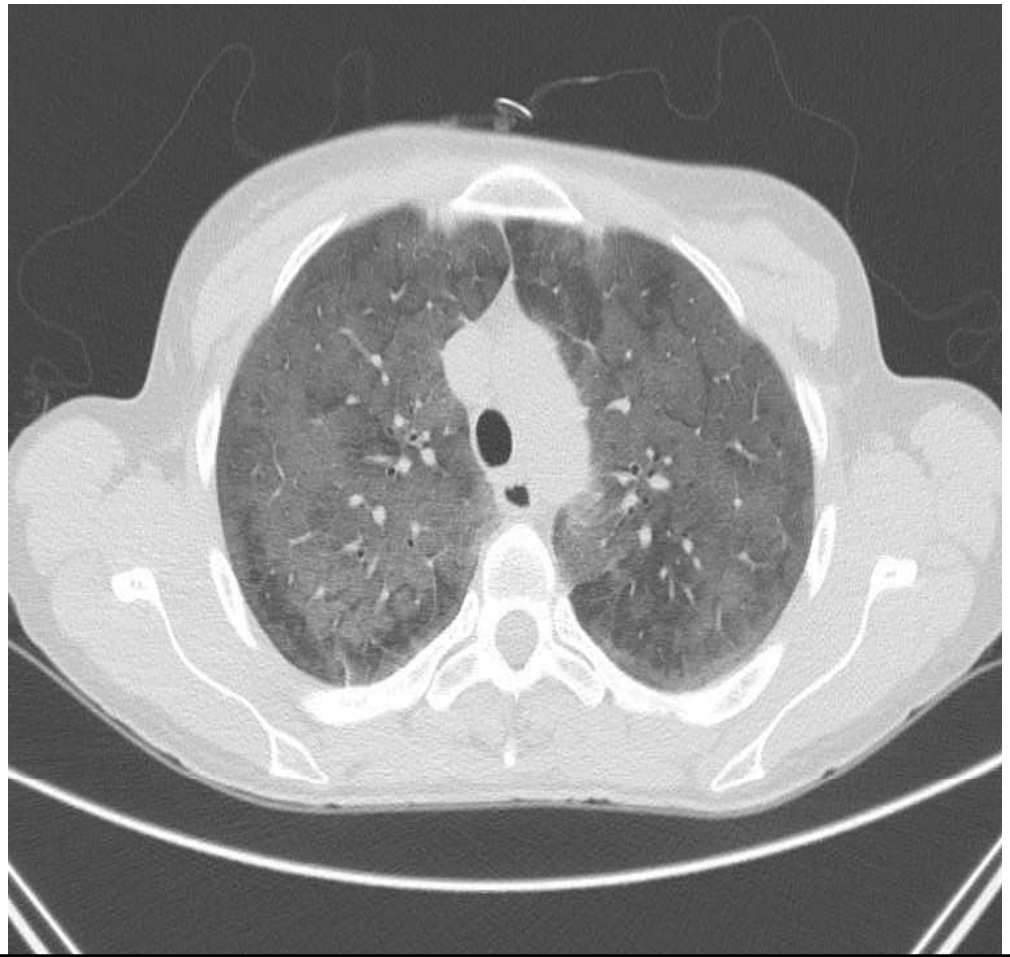
- **Includes the following clinical conditions as listed in the AIDS case definition**

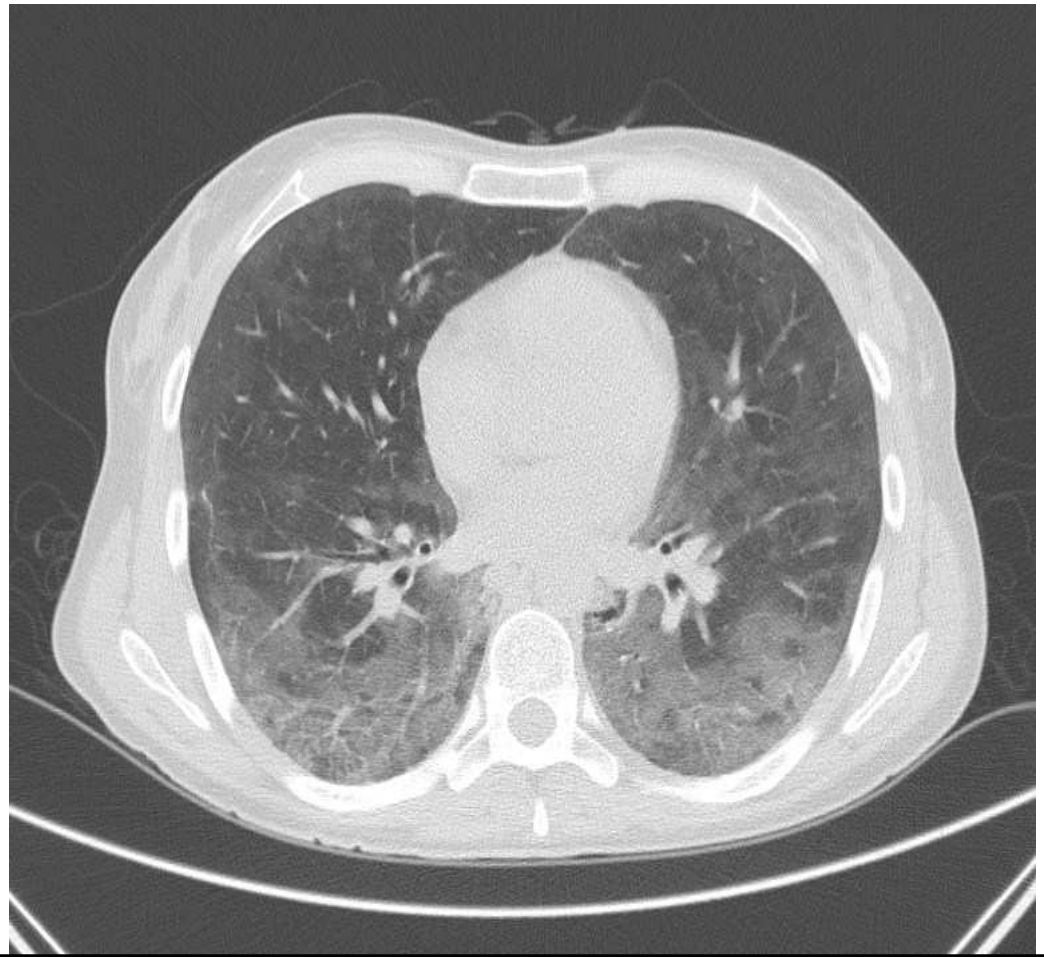
- **For classification purposes,**
  once a category C conditions has occured,
  the person will remain in category C
  untill the end of his life

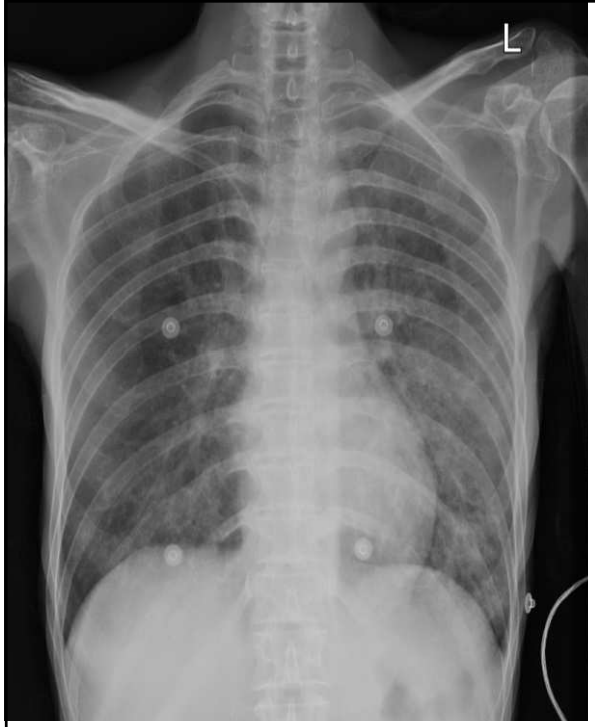
Opportunistic infections - Such as AIDS case definition

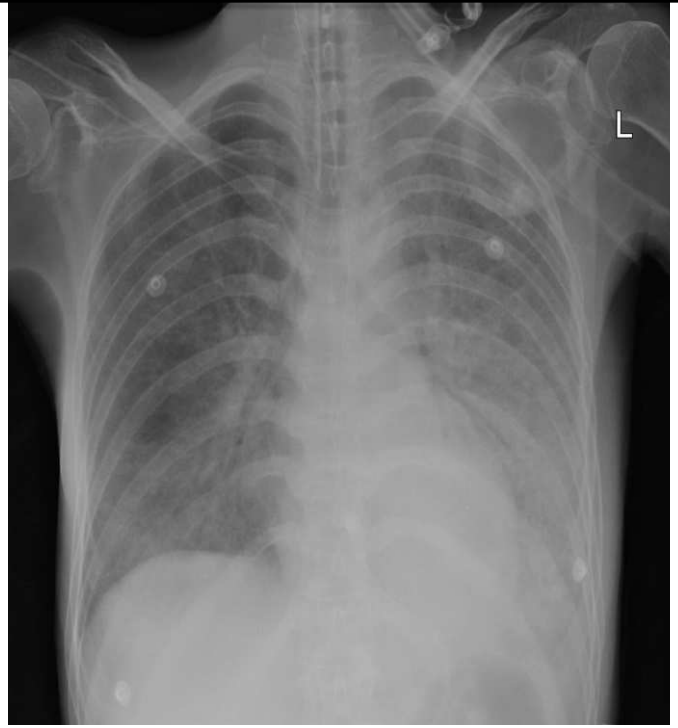
Pneumocystis jiroveci pneumonia – High-resolution CT scan

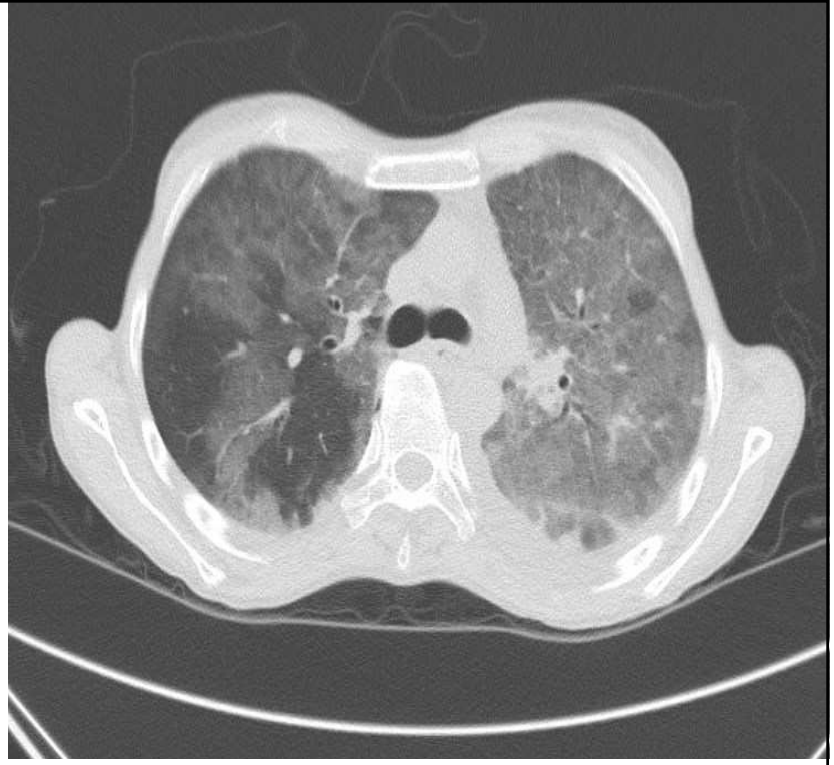
- Showing ground-glass appearance (image of milk glass)
- Destruction of pulmonary parenchymaT (HRCT) scan in 32-year-old woman with HIV infection showing ground-glass appearance due to Pneumocystis jiroveci pneumonia.
- CD4+ 4/µl
- *Jirovecii* > 100 000 000 kopií DNA/rekaci





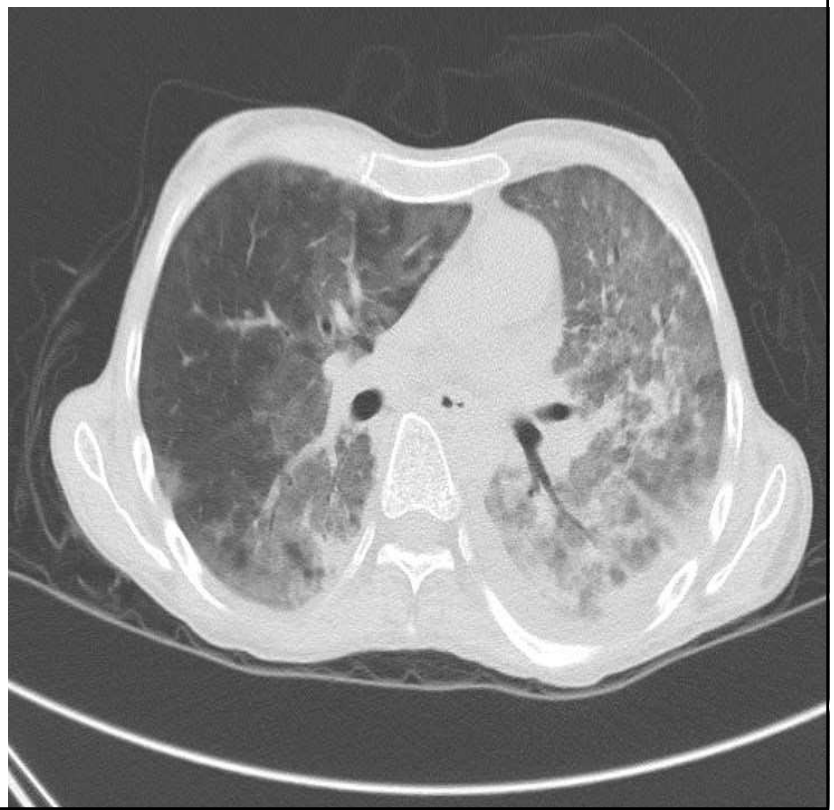






Pneumocystis jiroveci pneumonia (PCP)
showing ground-glass appearance

P. jirovecii
CD4 lymf. 2 bb/mm3
VL 468000 kopií/ml



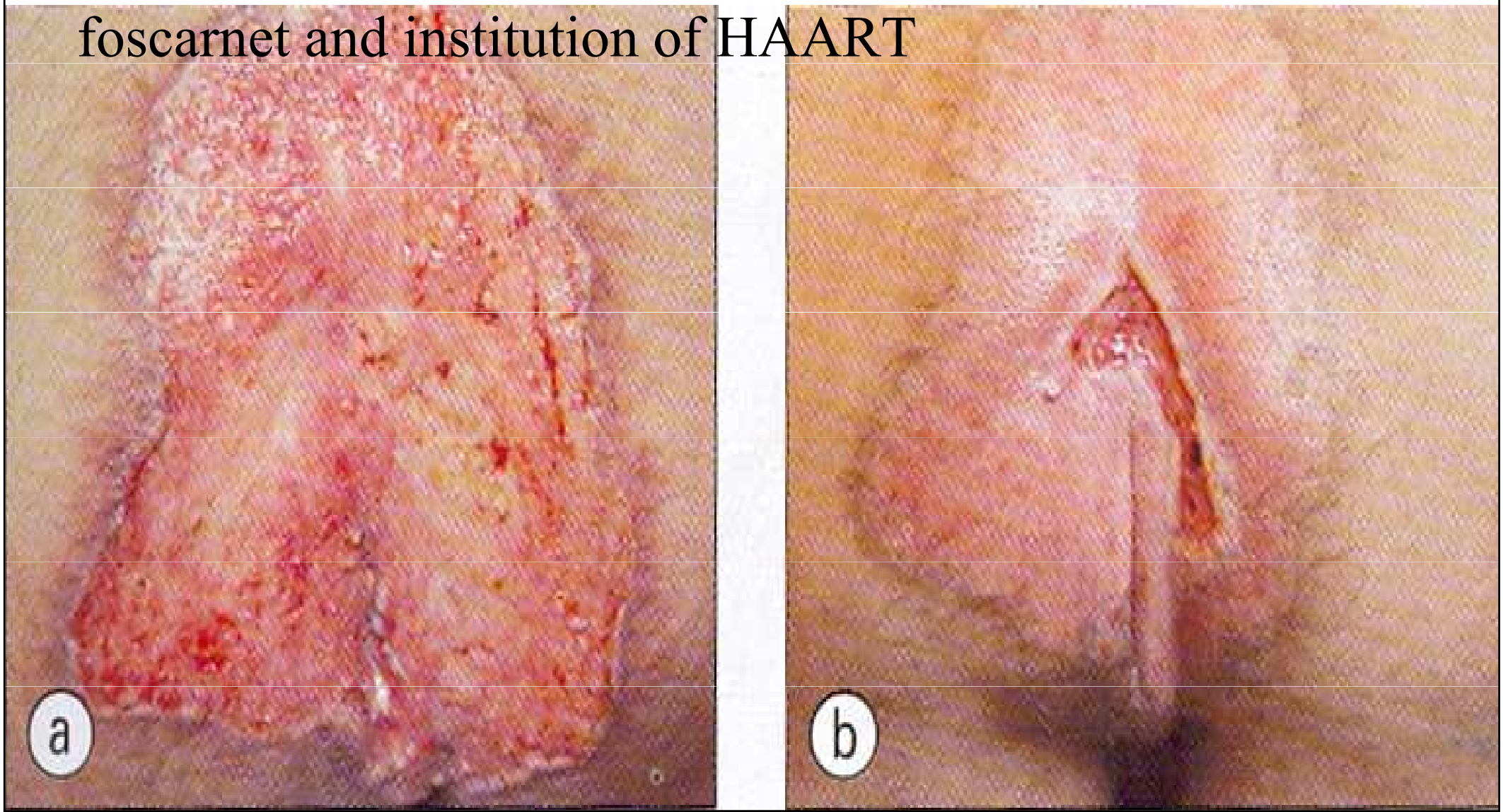
AIDS – Opportunistic infections

- Candidasis esophageal, tracheal, bronchial or pulmonary
- Herpes simplex with mucocutaneous ulcer > 1 month
- Herpes simplex esophagitis, bronchitis, pneumonia
- Recurrent pneumonia with > 2 episodes in 12 month
- Recurrent *Salmonella* bacteremia
- Chronic intestinal cryptosporidiosis (diarrhea > 1 month)
- Extrapulmonary cryptoccocosis
- CMV retinitis
- Generalized CMV infection (in other organ than liver, spleen, nodes)

Severe perianal aciclovir-resistant herpes simplex virus 2 infection

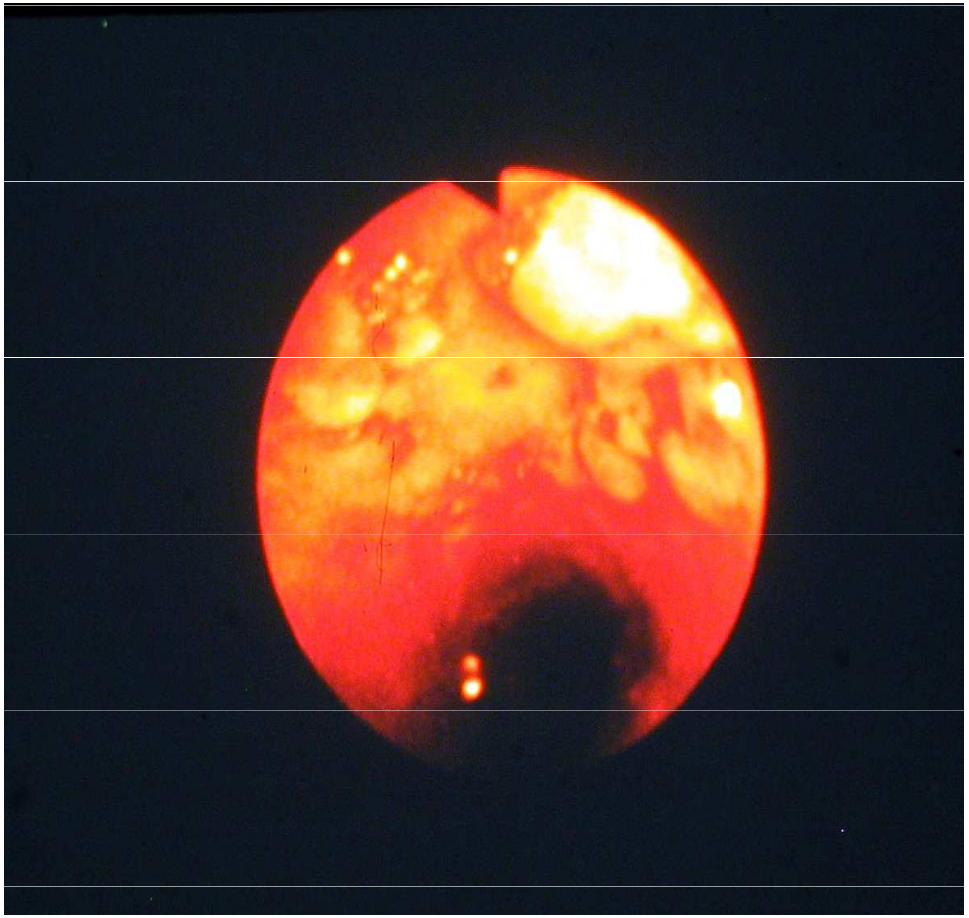
a-untreated appearance

b-healing and re-epithelialization after treatment with foscarnet and institution of HAART

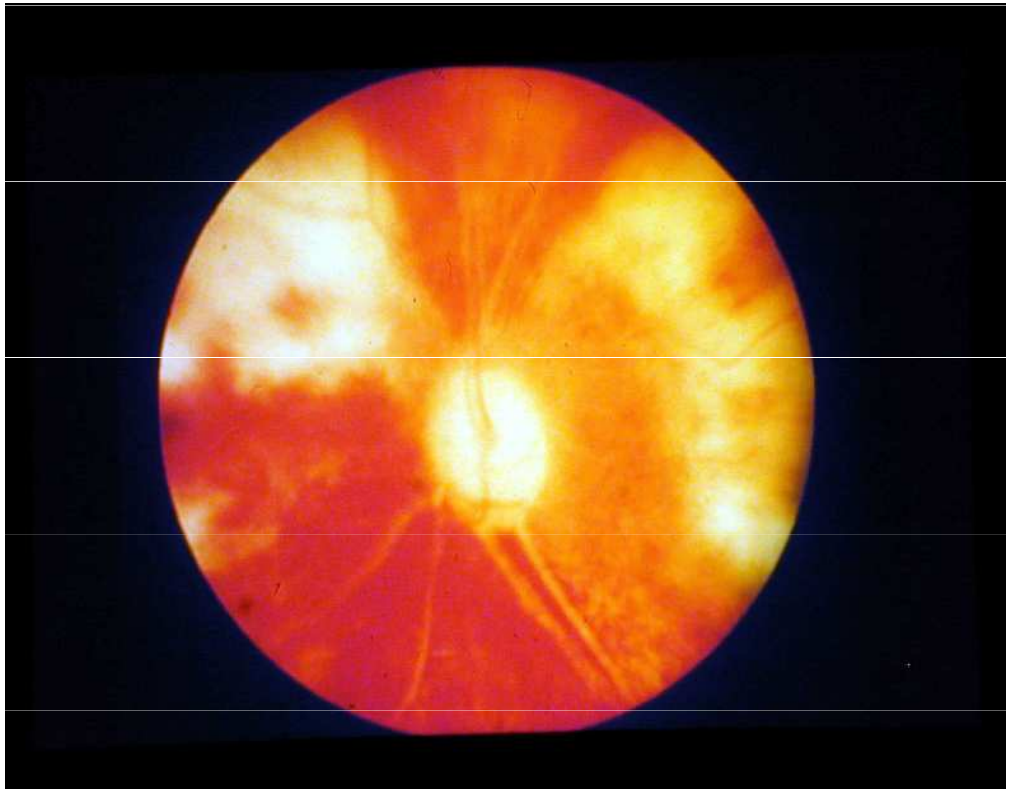


AIDS – clical caregory C

Herpes simplex esophagitis



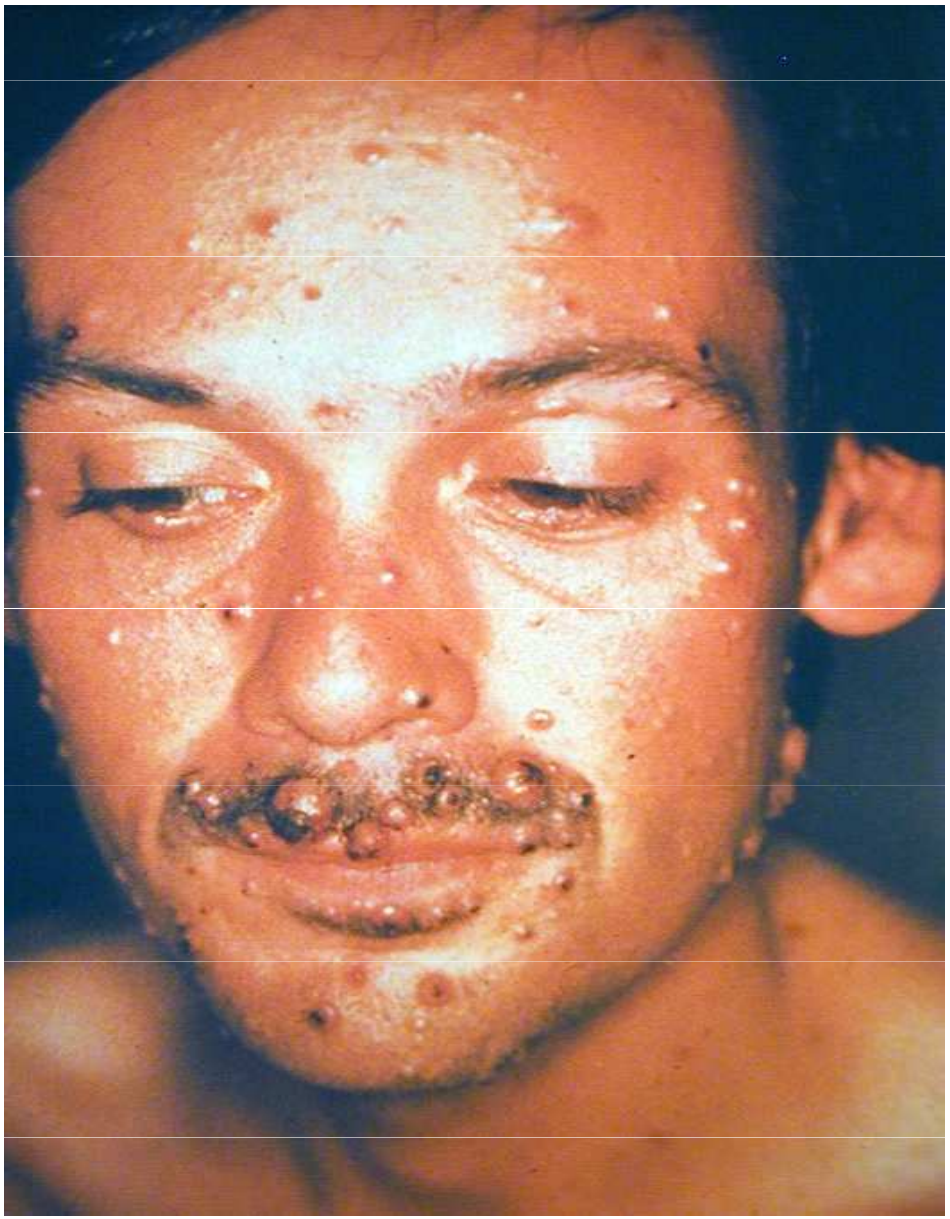
CMV retinitis

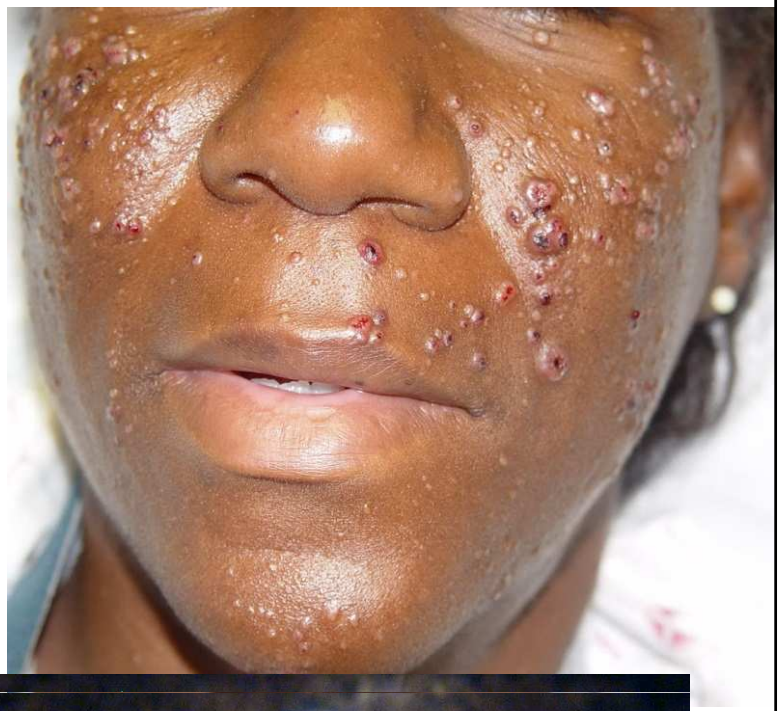


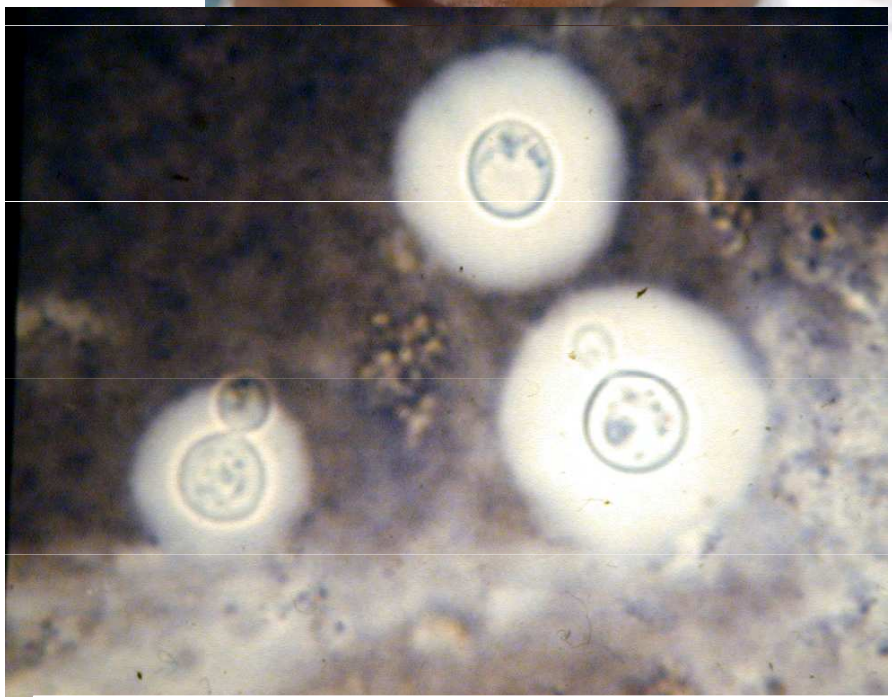
AIDS

- Extrapulmonary cryptoccocosis

- on the skin with cryptoccocomas







Cryptococcus neoformans
in cerebrospinal fluid

AIDS – Opportunistic infections

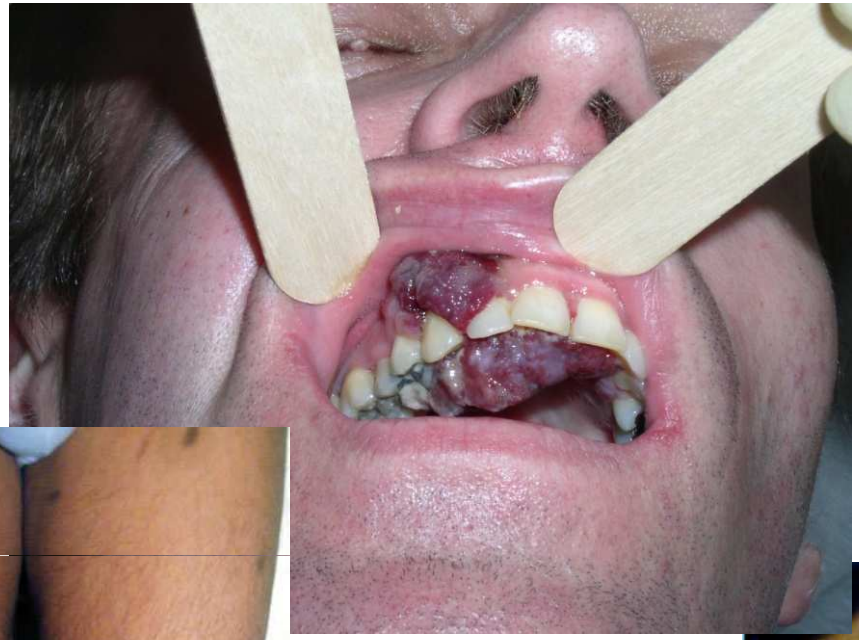
- Diseminated or extrapulmonary histoplasmosis
- Disseminated coccidioidomycosis
- Tuberculosis

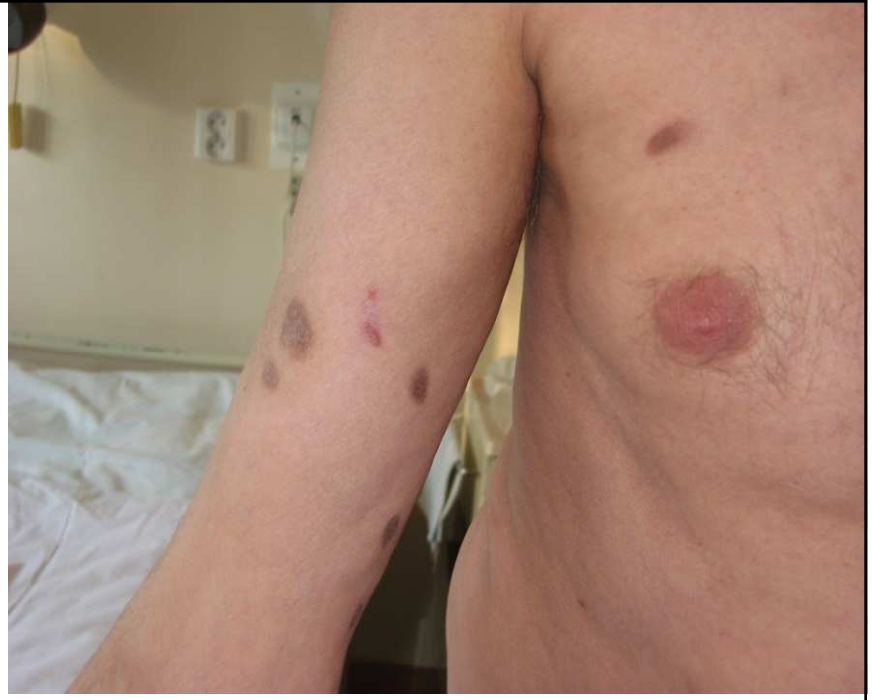
  (pulmonary or extrapulmonary)
- Disseminated or extrapulmonary *M. avium* or *M. kansasii* infection
- And others…

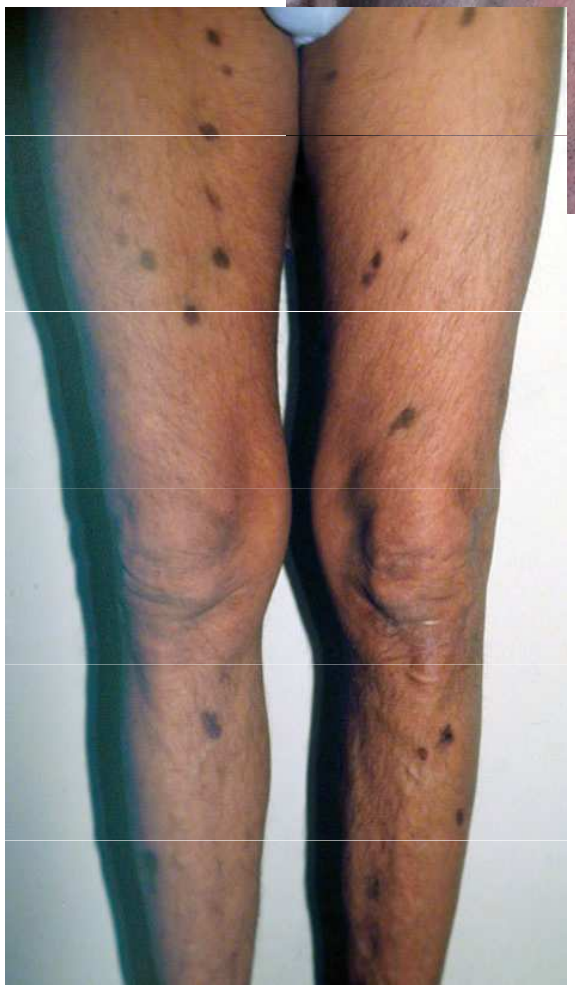
Malignancies – AIDS case definition

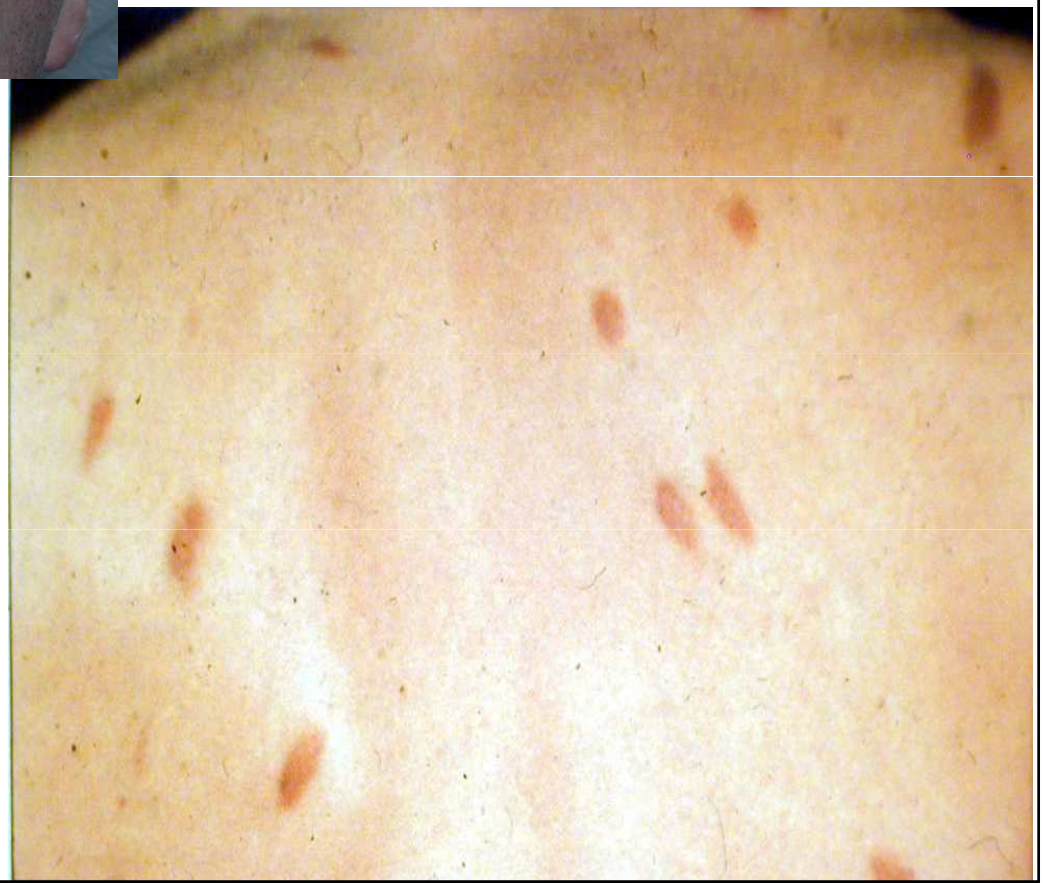
- Kaposi´s sarcoma
- Lymphoma
  - Burkitt´s
  - Non–Hodgkin lymphoma
  - Primary lymphoma in brain
- Invasive cervical cancer

Multiple lesions of Kaposis´s sarcoma

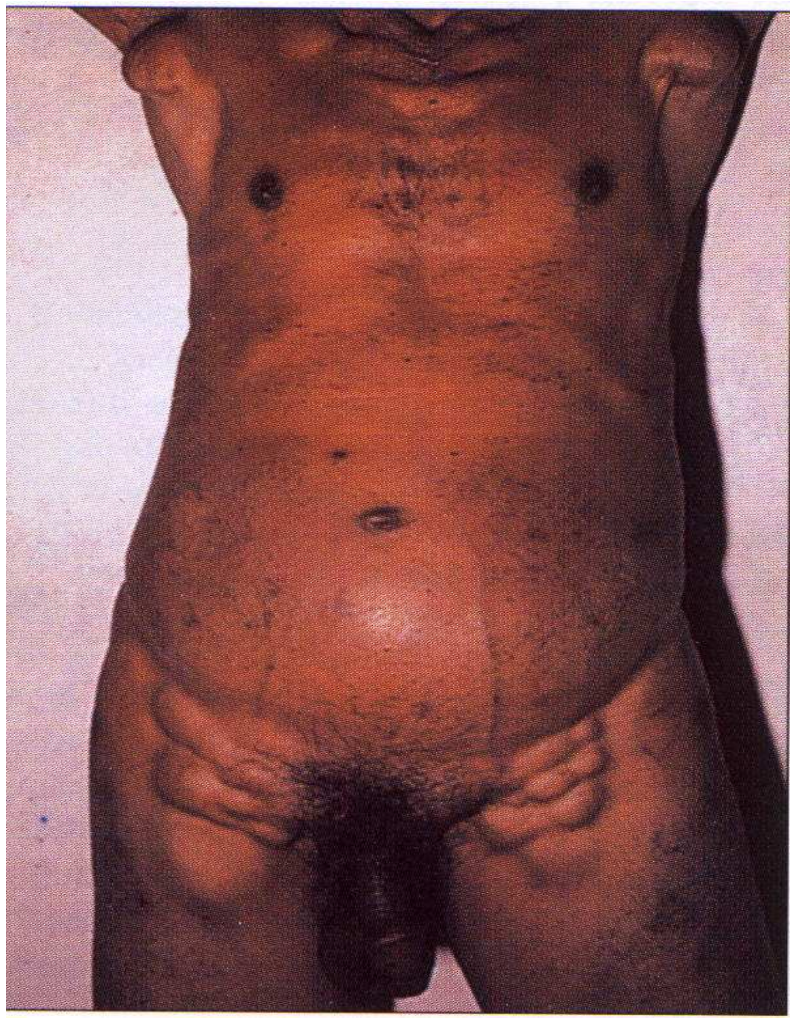








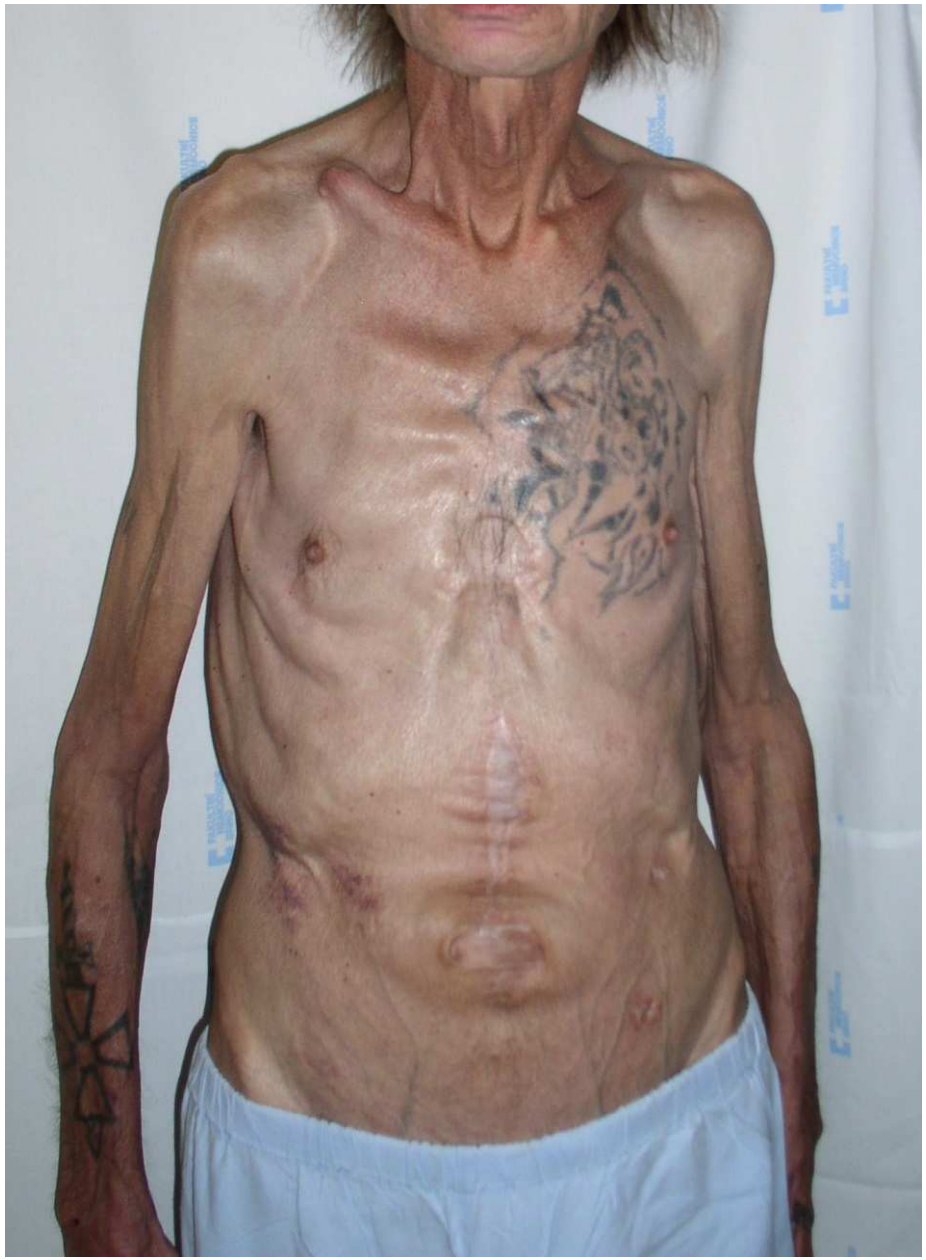
Non-Hodgkin lymfoma
(AIDS - category C)



Other conditions – such as AIDS case definition

- **HIV encephalopathia (dementia)**
- **Wasting syndrome („slim“ disease)**
  - **the introduction of ART has decreased the incidence of opportunistic infections and associated wasting**
  - wasting still remains a common problem in clinical practice
  - especially in middle income countries

Wasting syndrome associated with HIV/AIDS („slim disease)



HIV-associated wasting syndrome, „slim disease“

- Loss of body weight together with fever or diarrhea for more than 30 days
- In patient at the time of advanced infection
- In up to 50% of patients in Africa (less in industrialized countries)

Key etiologic factors

- Basal metabolic rate is generally increased at all stages of HIV infection
- Disturabances in intermediary metabolism
- A reduction in energy intake (nausea, taste disturbance, dysphagia, early satiety, depression, dementia…)
- Malabsorption – idiopathic (HIV enteropathy)
  - secondary (GI pathogens, OI)

Opportunistic infection in GIT

- **Protozoa (cryptosporidia, microsporidia…)**
- **Bacteria *(Shigella* spp., *Salmonella* spp., *Campylobacter* spp.,…)**

Profound anorexia

mediated by cytokine release

accompanies acute OI (not only in GIT)

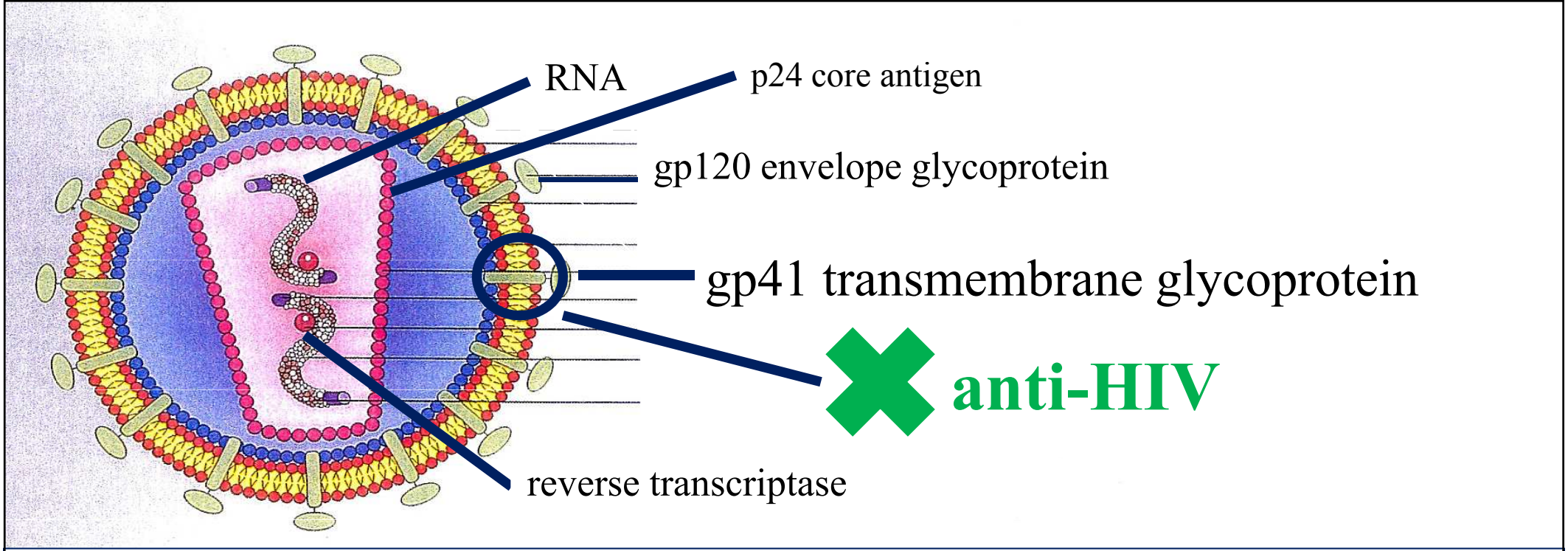
and results in rapid weight loss.

Main laboratory tests for dg.

- **Recommended for initial evaluation and follow-up of all patients**

1. **Anti-HIV** (antibodies to HIV)
   ELISA, WB
2. **Viral load** (the number of copies of RNA HIV-1)
3. **CD4+ lymphocyte count**

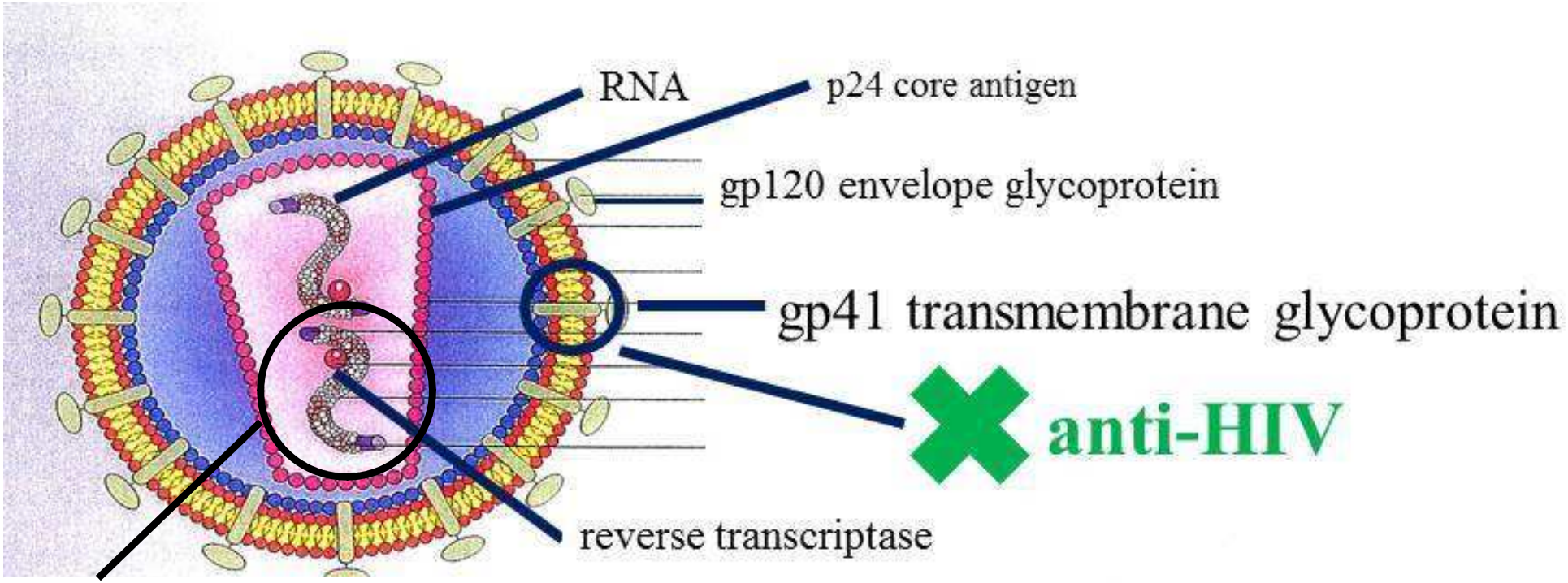
1. **Anti – HIV**
   - **enzyme-linked immunosorbent assay (ELISA)**
     - **antibodies to HIV**
     - **standard test**
     - **primary screening test for HIV infection**
   - **WB (Western Blot)**
     - **if the ELISA anti-HIV test is reactive, WB is done**
     - **more specific, less sensitive**



Anti-HIV

- Approximately 79% of people with HIV globally knew their HIV status.
- The remaining 21% (about 8.1 million people) still need access to HIV testing services.
- Testing is an essential gateway to HIV prevention, treatment, care and support services.

2. VL – viral load (viral detection)



RNA HIV-1 PCR

- quantitative plasma RNA HIV-1
- the number of copies of RNA HIV-1 per 1 ml plasma
- by technique PCR
- main virological marker
- the most reliable indicator of prognosis

Quantitative HIV RNA (VL) is useful for:

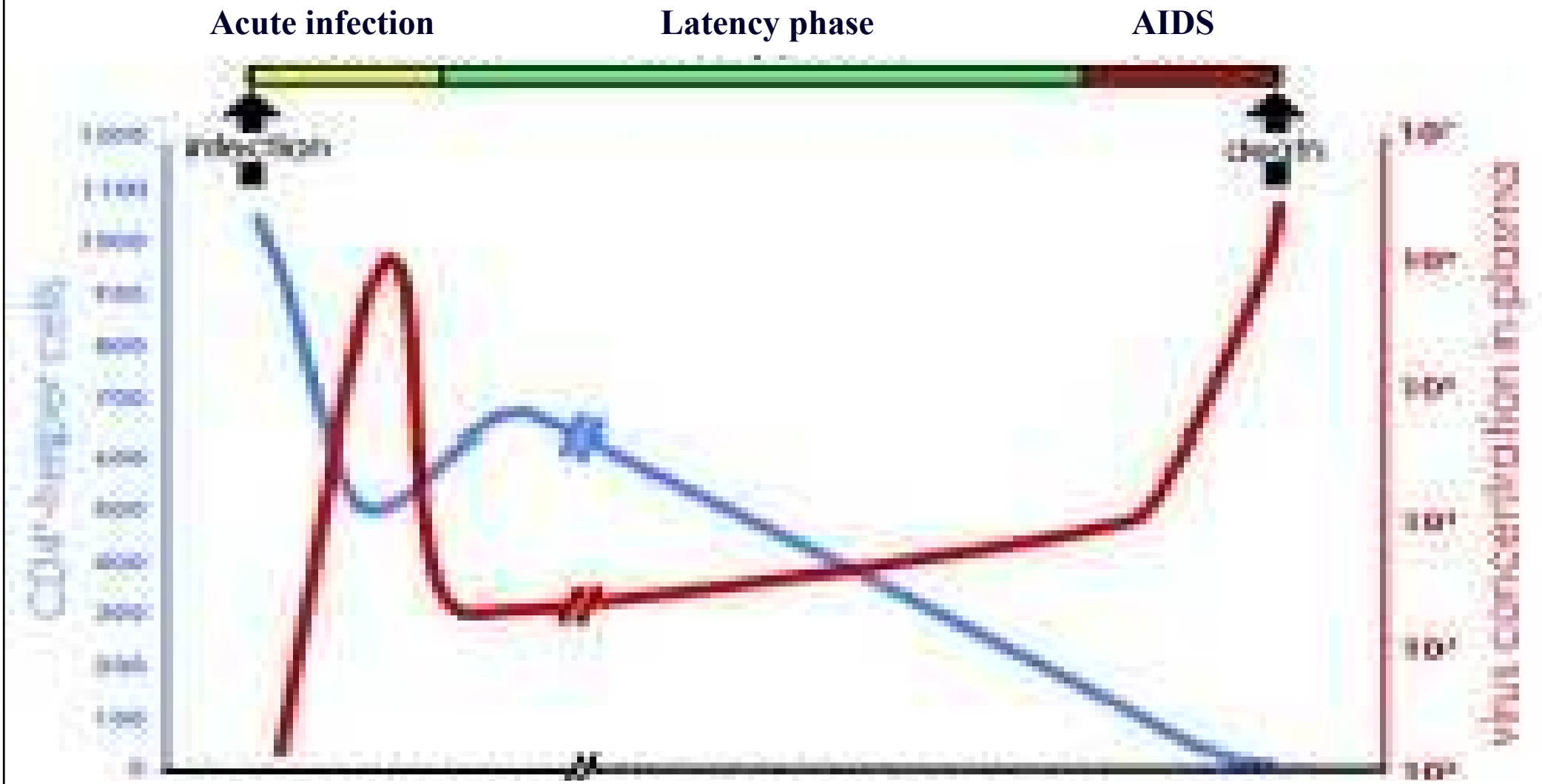
- Diagnosis acute HIV infection
- For predicting probability of transmission
- Predicting the rate of progression in chronically infected patiens
- For therapeutic monitoring
- is very senstitive
- was developed for monitoring the progression of the disease and the effectiveness of antiretroviral therapy
- is not for establishing the diagnosis of HIV infection
- should be repeated from 3- to 4-month intervals during therapy
- In stabile patients it should be repeated every 6 mounths

ART

- The objective of ART should be to maintain the lowest VL for as long as possible
- When an affective AR regimen is initiated in as asymptomatic patient with no previous ART, the VL should decrease to an undetectable level (< 50 copies/ml) within 24 weeks

Natural course of HIV infection

- **Gradual loss of number of CD4 cells over time**
- **Gradual increase of number of viral copies (increase of viral load)**



VL is extremely high (possibly one milion copies/ml and more)

- Primoinfection
- Advanced infection - AIDS

3. CD4+ Cell (lymphocyte) Count

This is a standard test:

- to assess prognosis for progression infection
- to formulate the differential diagnosis in a symptomatic patient
- to make therapeutic decisions regarding antiviral treatment and prophylaxis for opportunistic pathogens

- It was the most reliable indicator of prognosis until recently
- Number of copies RNA HIV (VL) is considered the most reliable indicator of prognosis currently

Natural course of HIV infection

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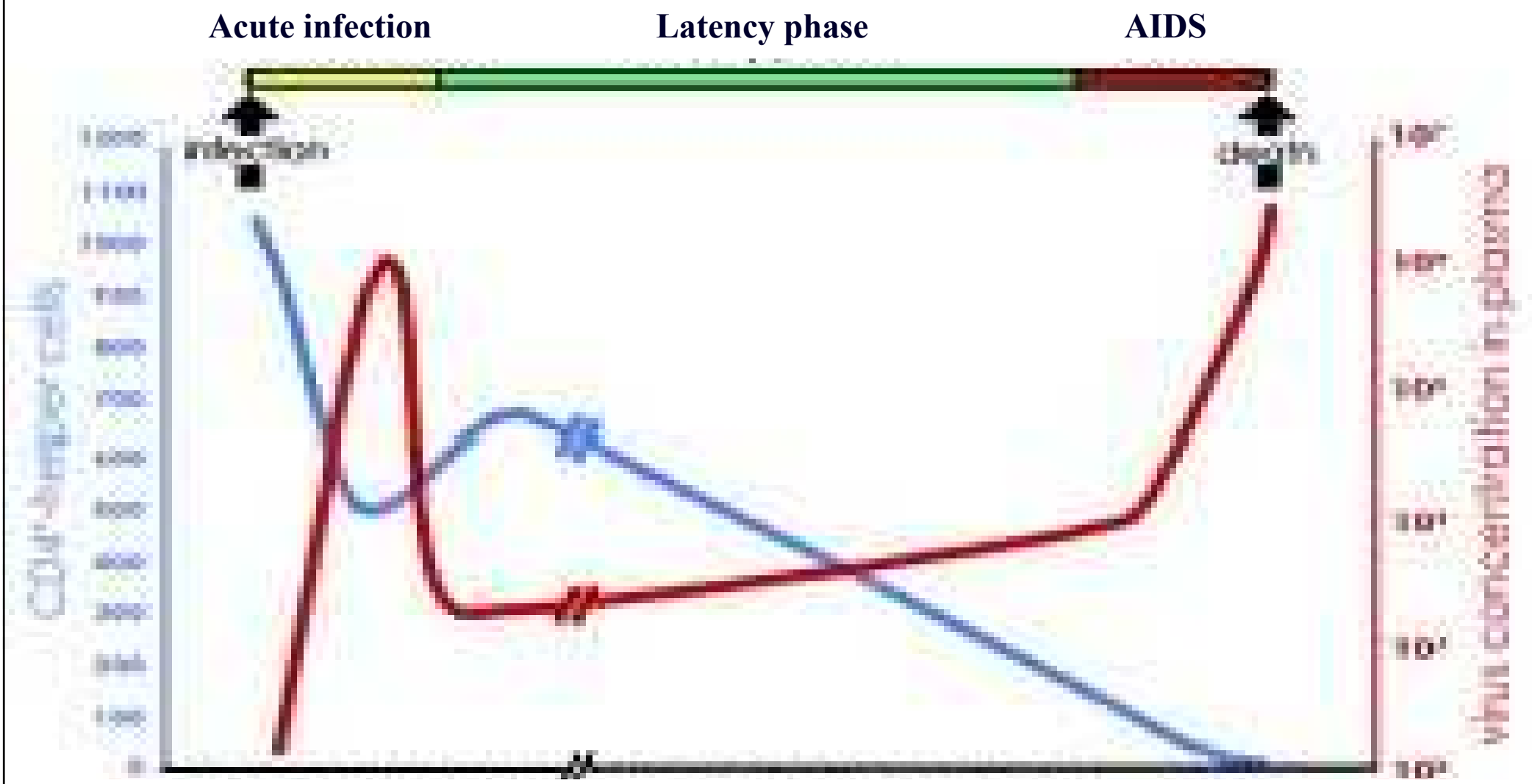

Another screening laboratory tests

- Complete blood count
- Serum chemistry panel
- Urine
- Syphilis serology
- Screening for other sexually transmitted diseases
- Tuberculin skin test (Mantoux)
- Serology
  - Hepatitis A, B, C, D, E
  - Toxoplasmosis
  - CMV
- Chest X-ray
- EKG
- Glucose-6-phosphate dehydrogenase levels (G6-PD)

Glucose-6-phosphate dehydrogenase deficiency

- is a genetic disease that predisposes to hemolytic anemia following exposure to oxidant drugs
  - Dapsone (x lepra, sec.prof. PCP)
  - Primaqine (x malaria, PCP)
  - TMP-SMX… (x PCP)
- Is found in 10% of black men and in 1% to 2% of black women, in men from Mediterranean area, India and Southeast Asia

Thank you for your attention…