HIV/AIDS Lecture.

فيروس العوز المناعي البشري

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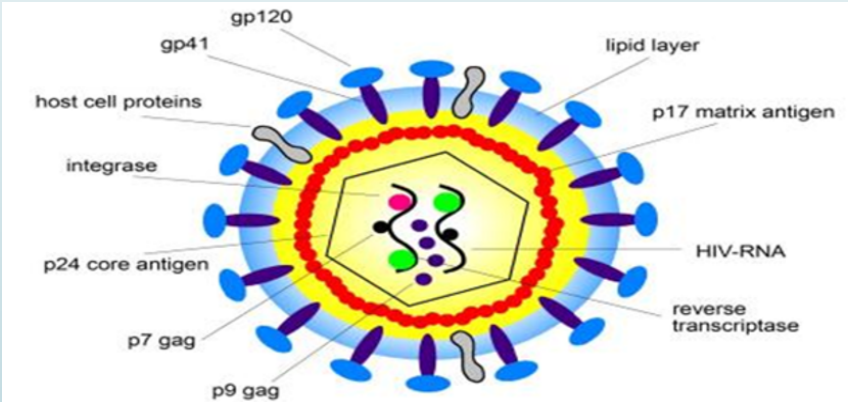
Infectious Diseases
1442 / 2021



HIV / AIDS

History

Epidemiology

Human immunodeficiency virus

Transmission

Pathogenesis and life cycle & replication.

Clinical features

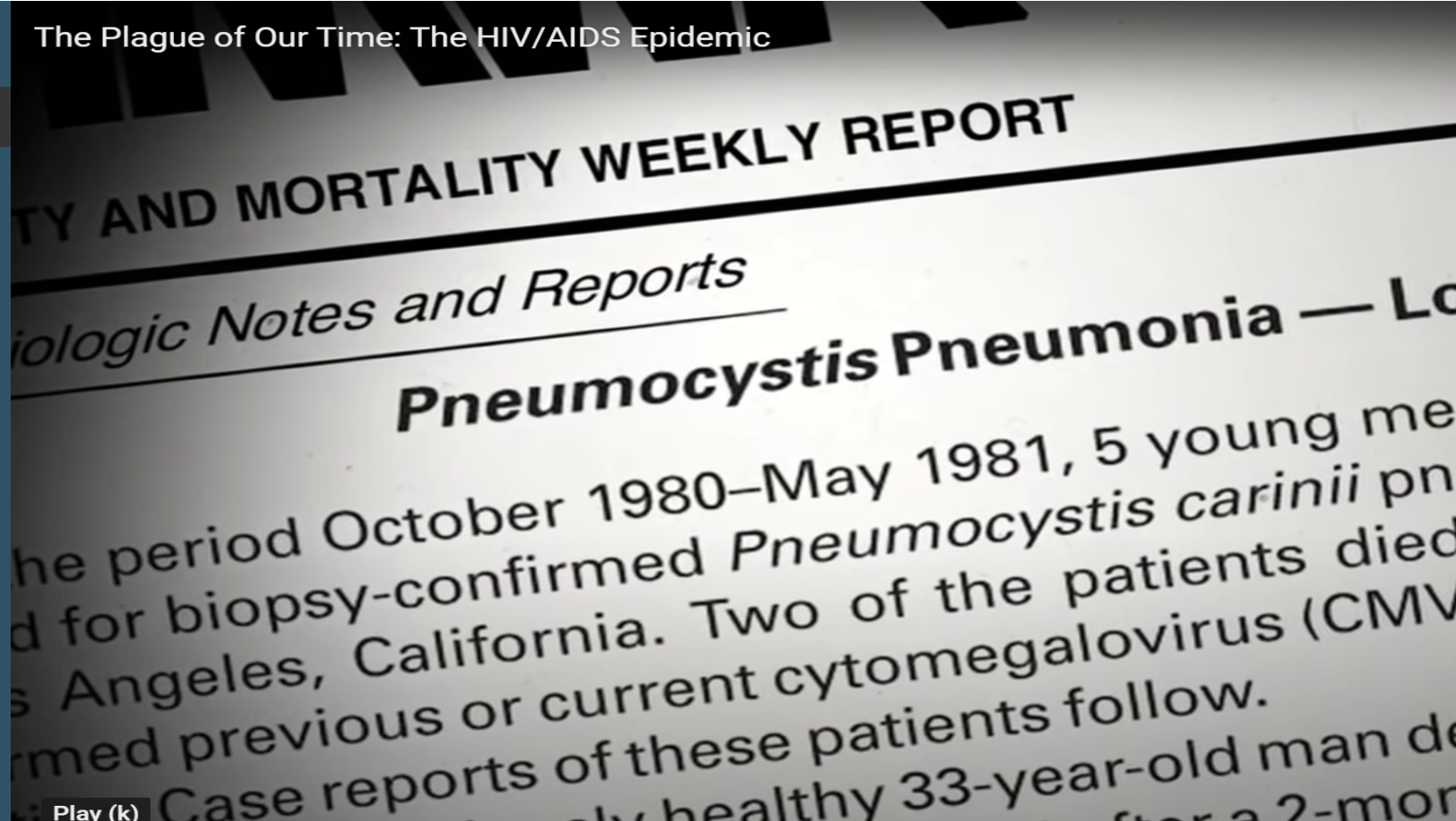
Laboratory diagnosis

Complications

Option of treatment

Natural history

Questions


The Plague of Our Time: The HIV/AIDS Epidemic
TY AND MORTALITY WEEKLY REPORT
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Pneumocystis Pneumonia — Lo
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d for biopsy-confirmed Pneumocystis carinii pn
s Angeles, California. Two of the patients died
rmed previous or current cytomegalovirus (CMV
Case reports of these patients follow.
healthy 33-year-old man de
Play (k)

Pneumocystis Pneumonia --- Los Angeles

In the period October 1980-May 1981, 5 young men, all active homosexuals, were treated for biopsy-confirmed *Pneumocystis carinii* pneumonia at 3 different hospitals in Los Angeles, California. Two of the patients died. All 5 patients had laboratory-confirmed previous or current cytomegalovirus (CMV) infection and candidal mucosal infection. Case reports of these patients follow.

Patient 1: A previously healthy 33-year-old man developed *P. carinii* pneumonia and oral mucosal candidiasis in March 1981 after a 2-month history of fever associated with elevated liver enzymes, leukopenia, and CMV viruria. The serum complement-fixation CMV titer in October 1980 was 256; in may 1981 it was 32.* The patient's condition deteriorated despite courses of treatment with trimethoprim-sulfamethoxazole (TMP/SMX), pentamidine, and acyclovir. He died May 3, and postmortem examination showed residual *P. carinii* and CMV pneumonia, but no evidence of neoplasia.

Patient 2: A previously healthy 30-year-old man developed *p. carinii* pneumonia in April 1981 after a 5-month history of fever each day and of elevated liver-function tests, CMV viruria, and documented seroconversion to CMV, i.e., an acute-phase titer of 16 and a convalescent-phase titer of 256 in anticomplement immunofluorescence tests. Other features of his illness included leukopenia and mucosal candidiasis. His pneumonia responded to a course of intravenous TMP/.SMX, but, as of the latest reports, he continues to have a fever each day.

Patient 3: A 30-year-old man was well until January 1981 when he developed esophageal and oral candidiasis that responded to Amphotericin B treatment. He was hospitalized in February 1981 for *P. carinii* pneumonia that responded to TMP/SMX. His esophageal candidiasis recurred after the pneumonia was diagnosed, and he was again given Amphotericin B. The CMV complement-fixation titer in March 1981 was 8. Material from an esophageal biopsy was positive for CMV.

Patient 4: A 29-year-old man developed *P. carinii* pneumonia in February 1981. He had had Hodgkins disease 3 years earlier, but had been successfully treated with radiation therapy alone. He did not improve after being given intravenous TMP/SMX and corticosteroids and died in March. Postmortem examination showed no evidence of Hodgkins disease, but *P. carinii* and CMV were found in lung tissue.

Patient 5: A previously healthy 36-year-old man with clinically diagnosed CMV infection in September 1980 was seen in April 1981 because of a 4-month history of fever, dyspnea, and cough. On admission he was found to have *P. carinii* pneumonia, oral candidiasis, and CMV retinitis. A complement-fixation CMV titer in April 1981 was 128. The patient has been treated with 2 short courses of TMP/SMX that have been limited because of a sulfa-induced neutropenia. He is being treated for candidiasis with topical nystatin.

One month later..MMWR.

miologic Notes and Reports

MMWR

Kaposi's Sarcoma and *Pneumocystis* Pneumonia Among Homosexual Men – New York City and California

ring the past 30 months, Kaposi's sarcoma (KS), an uncommonly report
in the United States, has been diagnosed in 26 homosexual men (20 in N
NYC]; 6 in California). The 26 patients range in age from 26-51 years
. Eight of these patients died (7 in NYC, 1 in California)--all 8 within 2

Pneumocystis Pneumonia

Kaposi's sarcoma

History

By the end of 1981, total of **270 reported cases** of severe immune deficiency among gay men, and **121 of those individuals had died**.

In 1983, Luc Montagnier and Françoise Barré-Sinoussi reported the discovery of a new virus (later called HIV) that is the cause of AIDS.

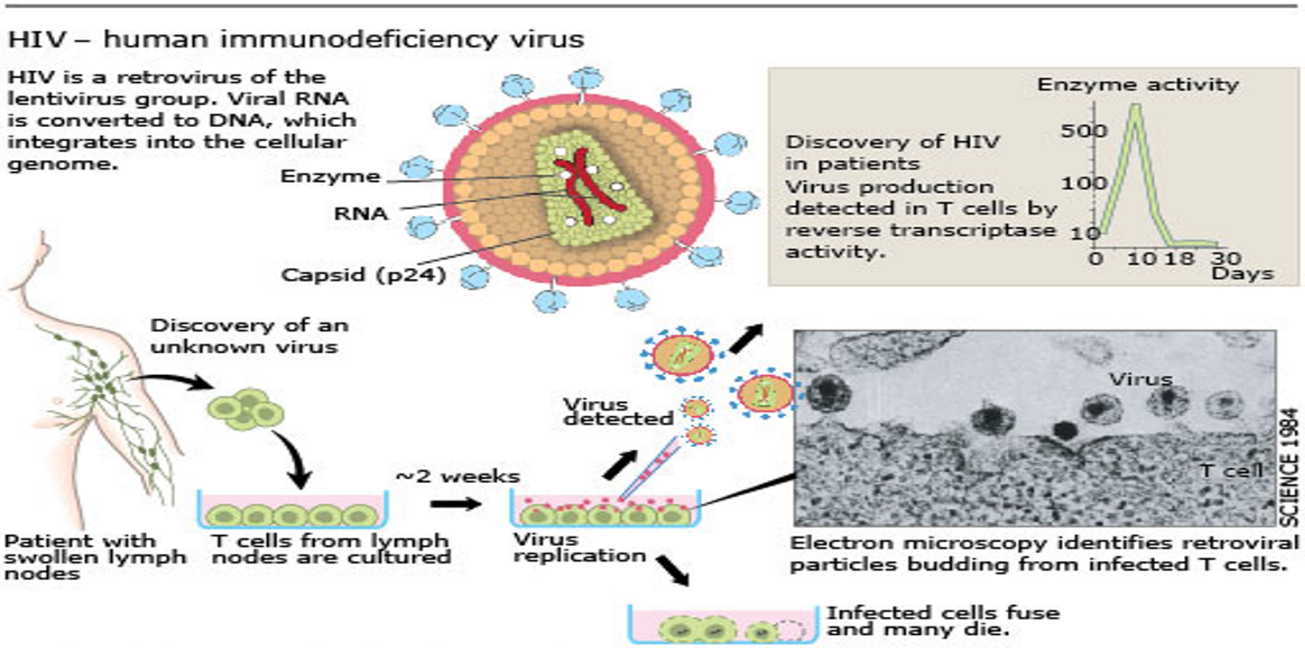
1984: Blood test was developed.

Electron microscopy and genome sequence analysis revealed that this virus (HIV) to be a lentivirus, known group of **retroviruses.**

HIV started in Human in USA (1981) and then spread rapidly to all over the world.

History

1983- Identification of the HIV virus- Françoise Barré-Sinoussi and Luc Montagnier (Shared 2008 Nobel Prize in Physiology or Medicine)



Epidemiology

WORLDWIDE STATISTICS

HIV Has **literally** exploded over the past three decades to become **the worst epidemic of the twentieth century**. The epidemic has reached every country

With more than 35 million fatalities, the AIDS epidemic now ranks alongside the **influenza pandemic of the early 1900s: 20 to 50 million death**

and the **plague of the 14th century : 75 to 100 million death in terms of fatalities**.

In some countries in sub-Saharan Africa, the AIDS epidemic **had caused a dramatic decline on life expectancy.**

Epidemiology

38.0 million people globally were **living with HIV in 2019.**

1.7 million people became **newly infected with HIV in 2019.**

690 000 people died from AIDS-related illnesses in 2019

75.7 million people have become infected with HIV since the start of the epidemic (end 2019).

32.7 million people have died from AIDS-related illnesses since the start of the epidemic (end 2019).

Epidemiology

	2000	2005	2010	2015	2016	2017	2018	2019/*2020
People living with HIV	**24.0 million** [20.0 million–28.2 million]	**27.3 million** [22.8 million–32.1 million]	**30.7 million** [25.6 million–36.1 million]	**34.9 million** [29.1 million–40.9 million]	**35.7 million** [29.8 million–41.9 million]	**36.5 million** [30.4 million–42.8 million]	**37.3 million** [31.0 million–43.6 million]	**38.0 million** [31.6 million–44.5 million]
New HIV Infections (total)	**2.7 million** [2.0 million–3.7 million]	**2.4 million** [1.8 million–3.2 million]	**2.1 million** [1.6 million–2.9 million]	**1.9 million** [1.4 million–2.5 million]	**1.8 million** [1.3 million–2.4 million]	**1.8 million** [1.3 million–2.4 million]	**1.7 million** [1.2 million–2.3 million]	**1.7 million** [1.2 million–2.2 million]
New HIV infections (aged 15+)	**2.2 million** [1.7 million–3.0 million]	**1.9 million** [1.4 million–2.6 million]	**1.8 million** [1.4 million–2.5 million]	**1.7 million** [1.2 million–2.3 million]	**1.6 million** [1.2 million–2.2 million]	**1.6 million** [1.2 million–2.1 million]	**1.5 million** [1.1 million–2.1 million]	**1.5 million** [1.1 million–2.0 million]
New HIV infections (aged 0–14)	**480 000** [300 000–750 000]	**440 000** [280 000–700 000]	**310 000** [200 000–500 000]	**190 000** [120 000–290 000]	**180 000** [110 000–280 000]	**170 000** [110 000–270 000]	**160 000** [99 000–250 000]	**150 000** [94 000–240 000]
AIDS-related deaths	**1.4 million** [1.0 million–2.0 million]	**1.7 million** [1.2 million–2.4 million]	**1.1 million** [830 000–1.6 million]	**830 000** [610 000–1.2 million]	**800 000** [580 000–1.1 million]	**760 000** [550 000–1.1 million]	**730 000** [530 000–1.0 million]	**690 000** [500 000–970 000]
People accessing antiretroviral therapy*	**590 000** [590 000–590 000]	**2.0 million** [2.0 million–2.0 million]	**7.8 million** [6.9 million–7.9 million]	**17.2 million** [14.7 million–17.4 million]	**19.3 million** [16.6 million–19.5 million]	**21.5 million** [19.5 million–21.7 million]	**23.1 million** [21.8 million-23.4 million]	**25.4 million** [24.5 million-25.6 million]/ **26.0 million** (mid 2020)

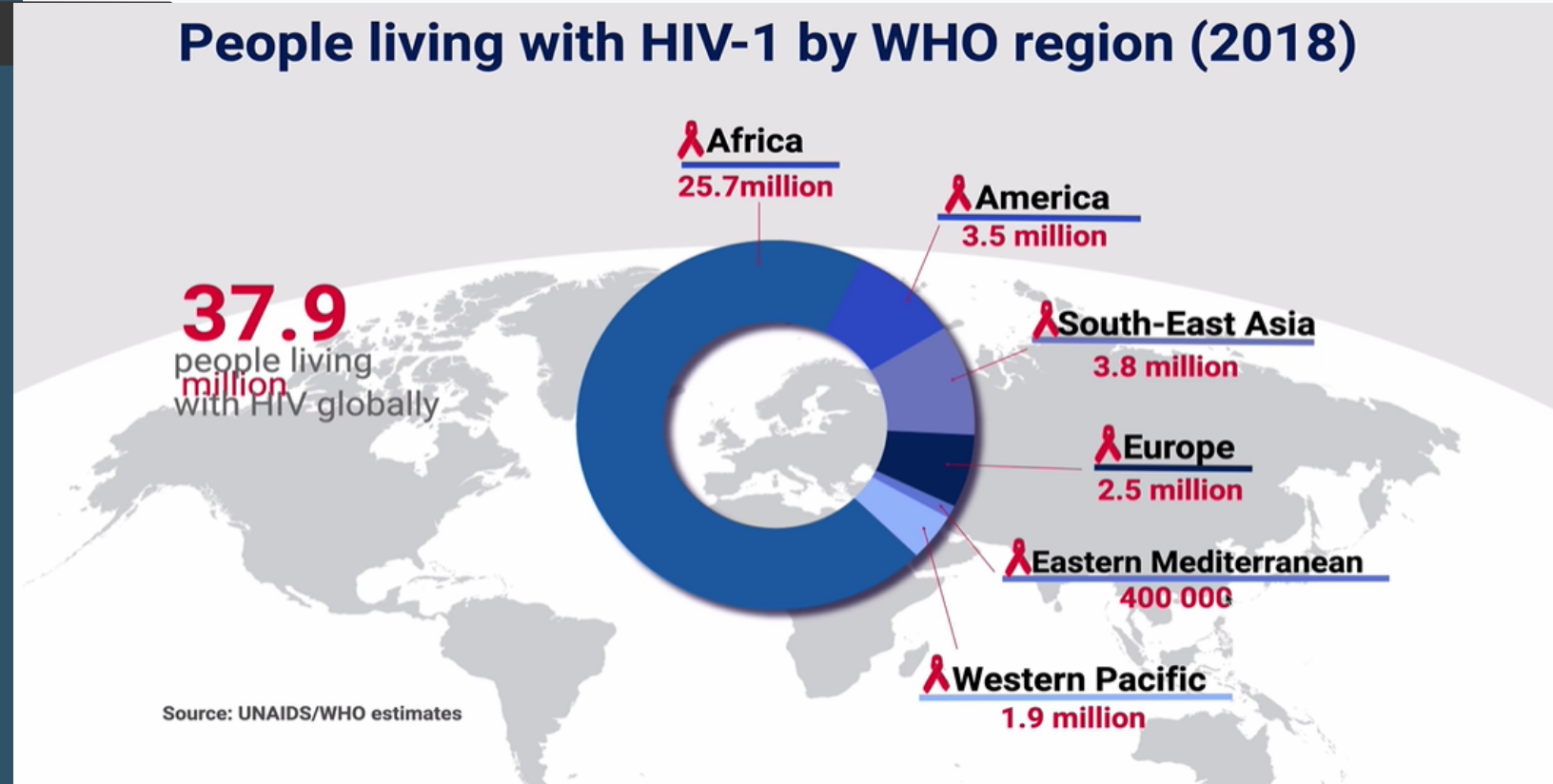
Epidemiology

Global summary of the HIV-1 pandemic (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]

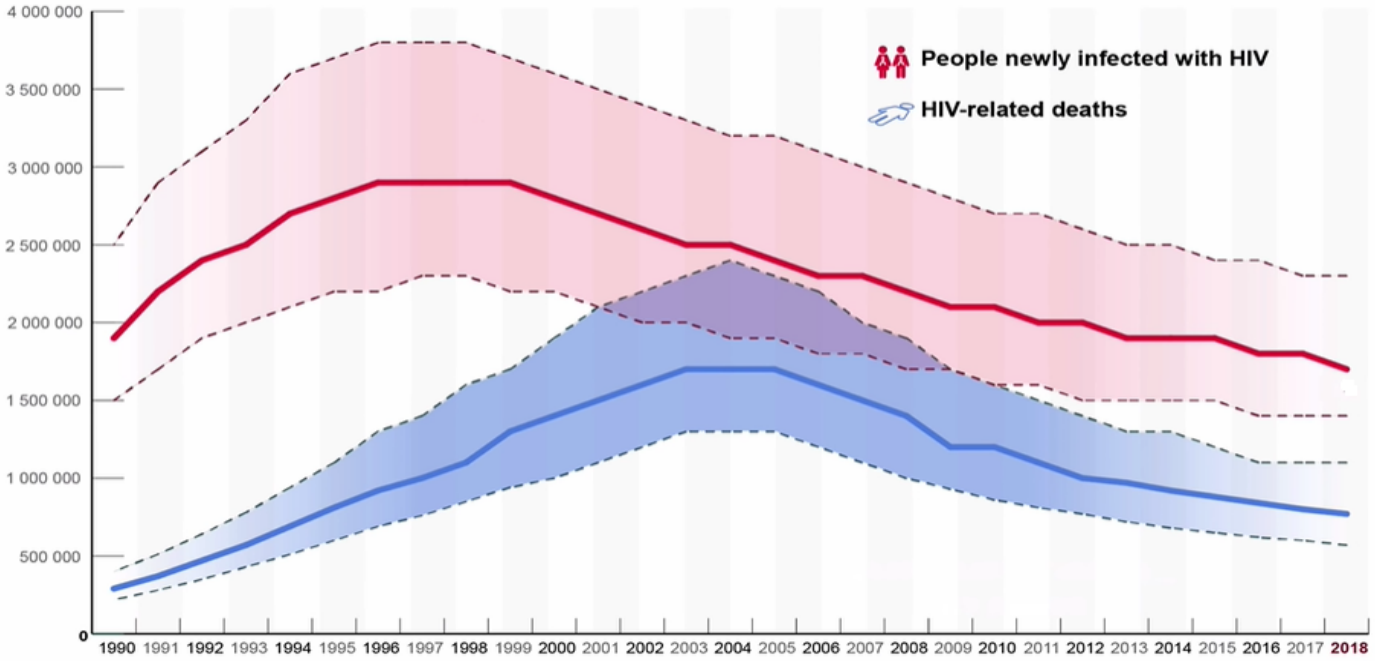
Source: UNAIDS/WHO estimates

Epidemiology



Epidemiology

Decline in HIV-1 incidence and mortality over time



Source: UNAIDS/WHO estimates

Human immunodeficiency virus.

Is a member of the lentivirus family, a subgroup of **retroviruses**,

and it is an **RNA viruses** that replicate via a DNA intermediate.

Is a virus that **target the cells of the immune system** and **viral replication within T-lymphocyte expressing the CD4 antigen** resulting OVER TIME in :

Progressive depletion in CD4 cell counts with increased risk of:

1] Opportunistic infections (OIs) such as Pneumocystis Jiroveci, CMV….etc

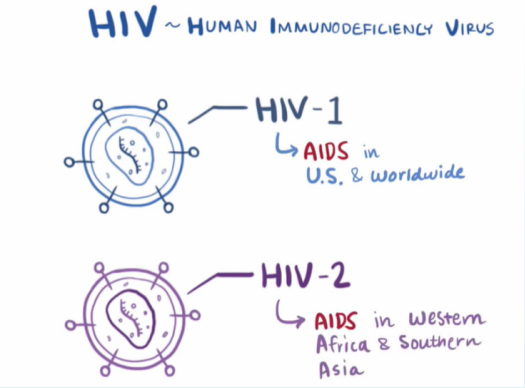
2] Malignancy such as Lymphoma and Kaposi sarcoma

This is called:

AIDS (Acquired immunodeficiency syndrome)

It is defined by a loss of CD4 T lymphocytes (< 200 cell/) or the occurrence of opportunistic infections or cancers in HIV infected Patient.

HIV/AIDS.



There are two HIV viruses :

HIV1 : **Predominate world wide**

HIV2 : Closely resemble HIV-1, but is a **much slower progression** to AIDS than HIV1.

It Predominate in **western Africa** and Southern Asia.

HIV STRCTURE.

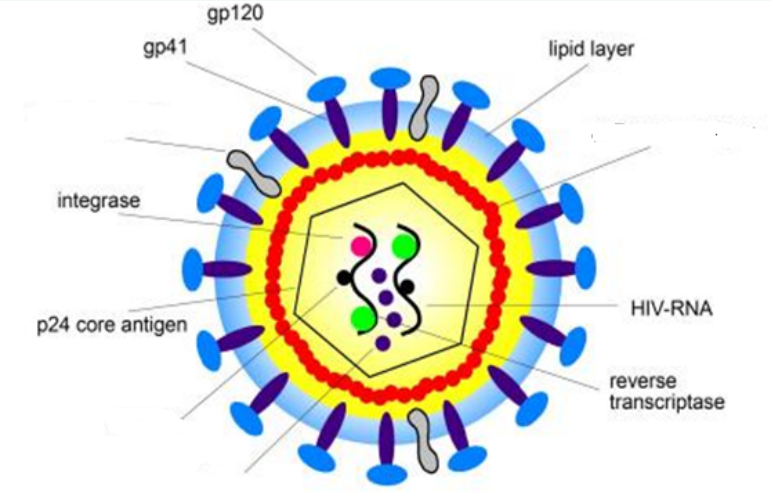
It is an RNA virus

1)The core: contain the **genetic material** [RNA] and Reverse transcriptase [enzyme]

2) The capsid: outer protein coat.

3) Lipid Envelope (env) derived from infected cell, containing numerous external spikes formed by two major envelope proteins :

a) **The external gp 120**
b) **The trans membrane gp 41**



Epidemiology: Transmission

- HIV is a fragile virus .It cannot live outside the body
- HIV is primarily found in the infected person :
- Blood.
- Semen and Vaginal fluid.

VIRAL TRANSMISSION

Major risk categories:

Sexual contacts (heterosexual and homosexual)..Repeated exposure↑ Risk.

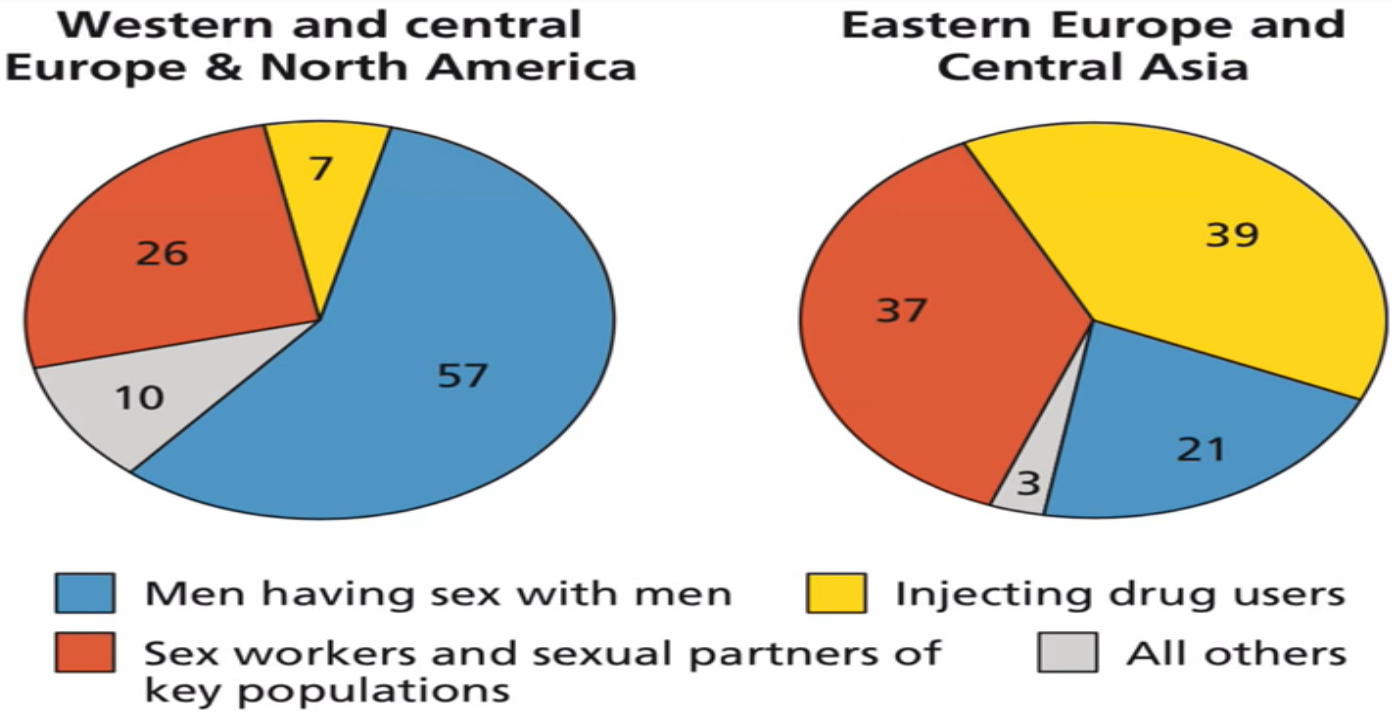
People who inject drugs.

Blood product recipients.

Health care workers with a needle-stick exposure.

Perinatal transmission. [MTCT].

Epidemiology: Transmission



Mother to child at birth, ~5%

Epidemiology: Transmission

Risk factors for HIV transmission:

High viral load.(Acutely infected or chronically untreated patient)

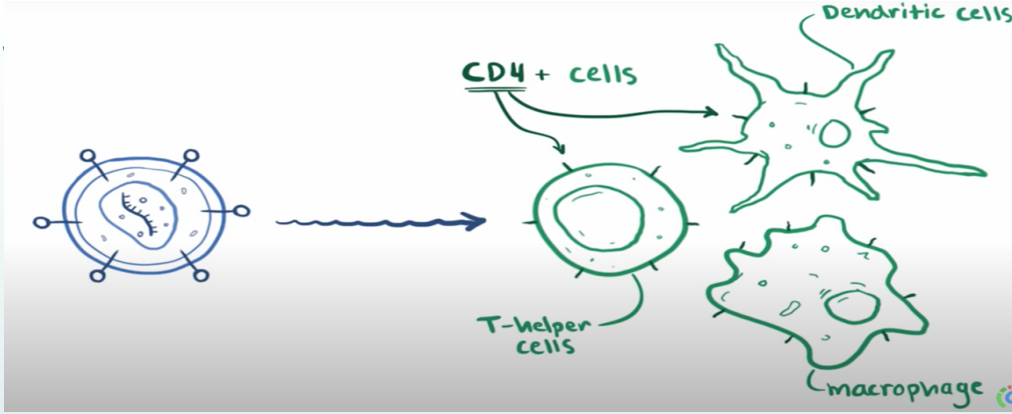
Certain sexual behaviours.(MSM is more)

Presence of ulcerative sexually transmitted infections.

lack of circumcision.

Certain other host and genetic factors.

PATHOGENESI

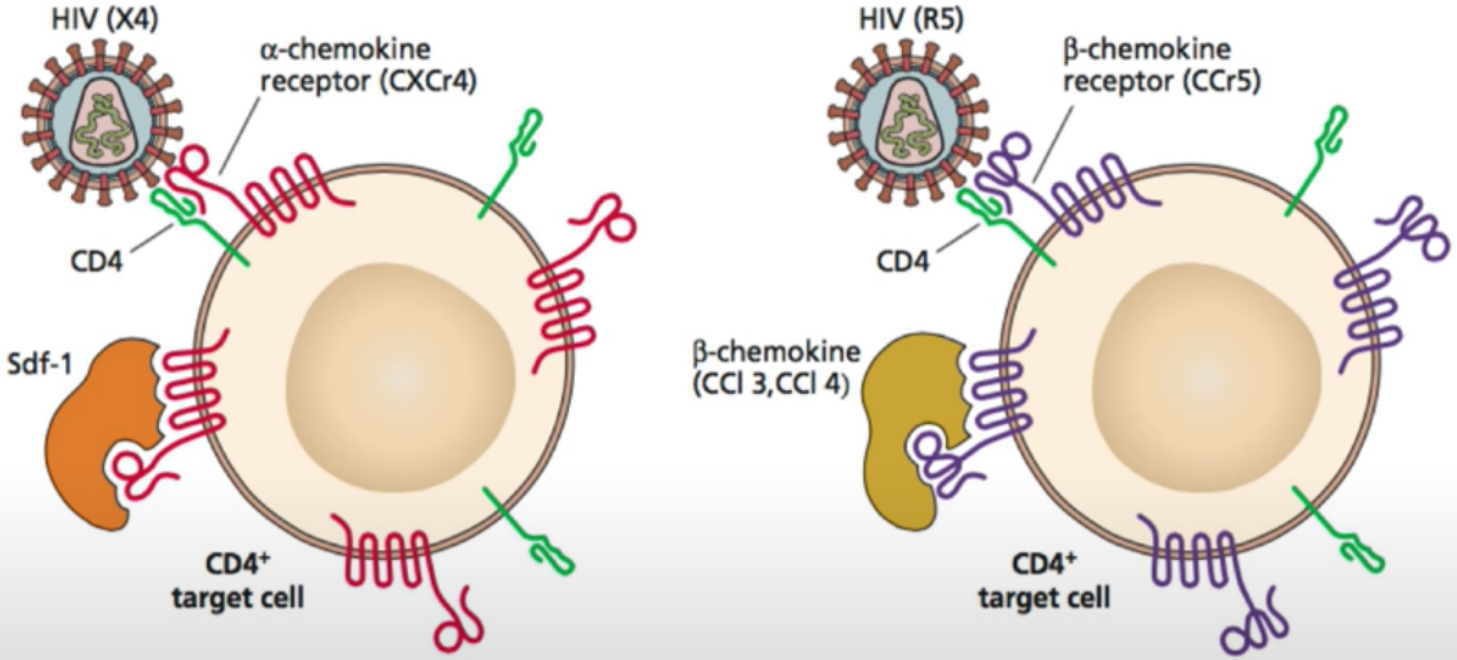


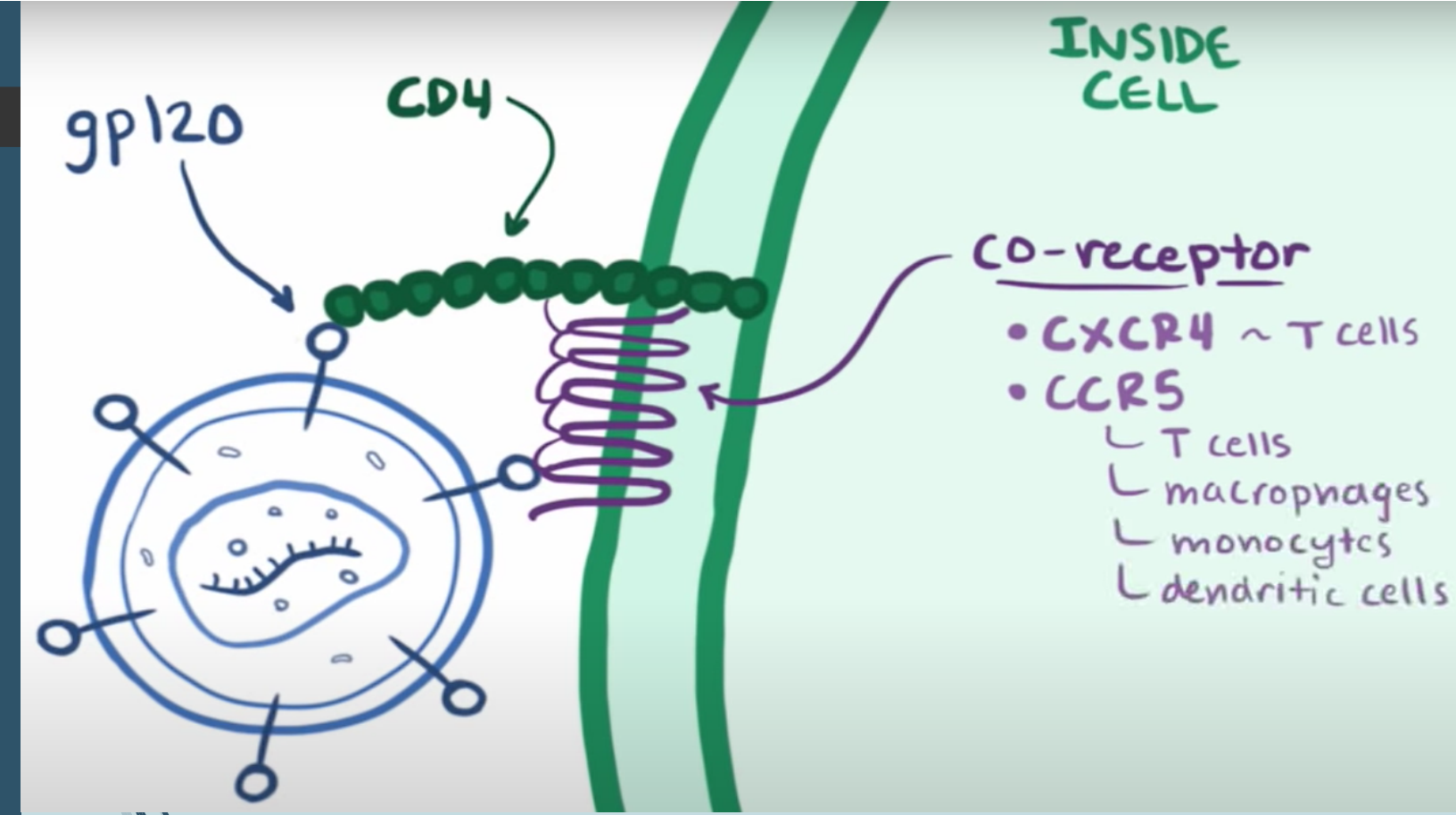
Target cells: CD4+ cells.

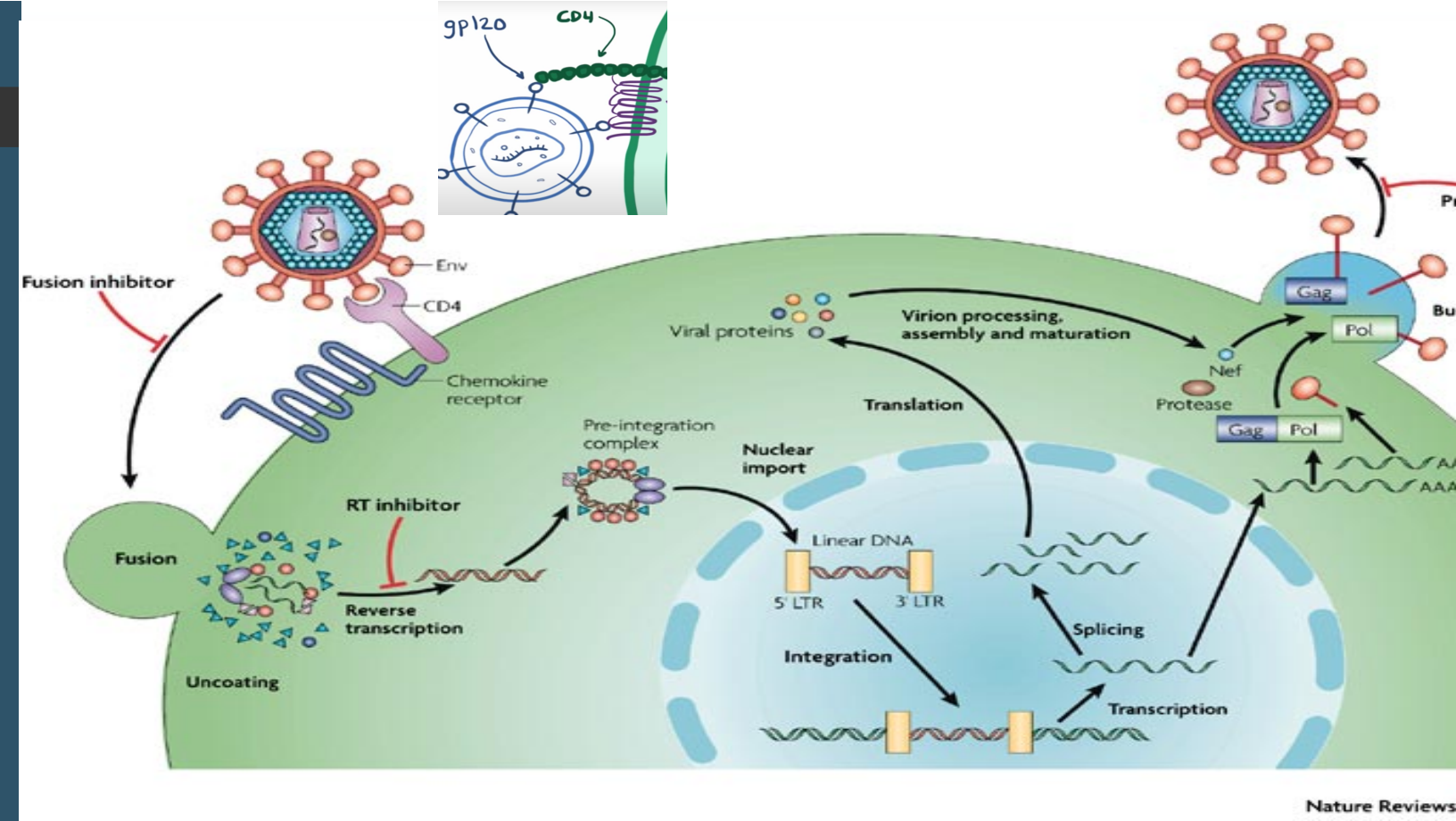
Has several targets including dendritic cells, macrophages, and CD4+ T cells.

Target cells — HIV-1: most often enters the host through the anogenital mucosa.

CO-RECEPTORS: Viral entry into these cells is mediated by different receptors. **GP-120 must bind to CD4+ receptor as well as to the chemokine receptor CCr5 or CXCr4**




gp120
CD4
INSIDE CELL
co-receptor
• CXCR4 ~ T cells
• CCR5
└ T cells
└ macrophages
└ monocytes
└ dendritic cells


gp120
CD4
Fusion inhibitor
Env
CD4
Chemokine receptor
Fusion
Uncoating
RT inhibitor
Reverse transcription
Pre-integration complex
Nuclear import
Linear DNA
5' LTR
3' LTR
Integration
Transcription
Splicing
Translation
Viral proteins
Virion processing, assembly and maturation
Nef
Protease
Gag
Pol
Gag
Pol
Nature Reviews

Video…Pathiogenesis

Pathogenesis

HIV RNA levels rapidly increase from the earliest quantifiable measure to a peak level that usually coincides with seroconversion.

Cellular immune response

At the time of initial infection with HIV, patients have a large number of susceptible CD4+ T cells and no HIV-specific immune response. **Therefore**

Viral replication is rapid; plasma HIV RNA levels may climb to more than 10(7) copies/mL.

Concomitant with the evolution of HIV specific immunity (**virus-specific CD8+ cytotoxic T lymphocytes**) This will lead to:

a fall in plasma RNA levels precipitously by 2 to 3 logs, and symptoms of the acute retroviral syndrome resolve.

Elite controllers:

A few individuals with HIV may, even in the absence of antiretroviral therapy, retain normal CD4 counts and low or undetectable plasma viremia.

Genetic susceptibility:

The most extensively studied of these genetic factors is the C-C chemokine receptor 5 (CCR5), **a major receptor for HIV……and**

CCR5 (delta) 32 homozygotes genotype: people who inherited the Delta 32 mutation, resulting in the genetic deletion of a portion of the CCR5 gene are **highly resistant** to HIV infection.

Epidemiology: Transmission

Sexual transmission:

Heterosexual transmission :

More than 80 percent of infections worldwide. (Transmission is more from man to women).

Sub-Saharan Africa houses the majority of the world's HIV-infected population and **heterosexual transmission** is the main contributor to the HIV epidemic…BUT IN OTHER PART OF THE WORLD (especially USA): more men than women are infected with HIV.

United States, the number of newly diagnosed HIV infections attributed to **MSM** sexual contact **increased** from 2009 to 2015, while those attributed to injection drug use and heterosexual contact **decreased**.

68% of newly diagnosed HIV in USA are among men (Homosexuality).

Epidemiology: Transmission

Injection drug use :

Outside of sub-Saharan Africa, injection drug use (IDU) accounts for approximately **30 percent of new HIV infections** in Central and Eastern Europe and in some countries of Asia.

Needle exchange programs has resulted in reducing the number of new HIV infections by up to **70 percent like in Australia.**

Unfortunately, 40 percent of countries with documented injecting drug use do not have needle-syringe programmes in place.

Mother-to-child transmission:

Over two million infants are born to HIV-infected women annually.

These children are vulnerable to HIV transmission:

in utero (30%) , **at birth (60%)** , or through **breastmilk (10%)**…..and

Without antiretroviral preventive interventions, the risk of perinatal HIV transmission has varied between **15 and 45 percent**.

Mother-to-child transmission accounts for 90% of HIV infections among children worldwide.

Certain countries in sub-Saharan Africa, **20 to 40 %** of pregnant women are HIV-infected, and **one-third of their babies become infected.**

Clinical manifestations.

Acute HIV infection : (two to four weeks after exposure)

Mononucleosis syndrome : Diagnosis can frequently be **missed by clinicians.**

Fever, fatigue, and myalgia/arthralgia : the most common symptoms

lymphadenopathy, sore throat, rash,, diarrhea, weight loss.

None OF THESE SYMPTOME is specific **But**:

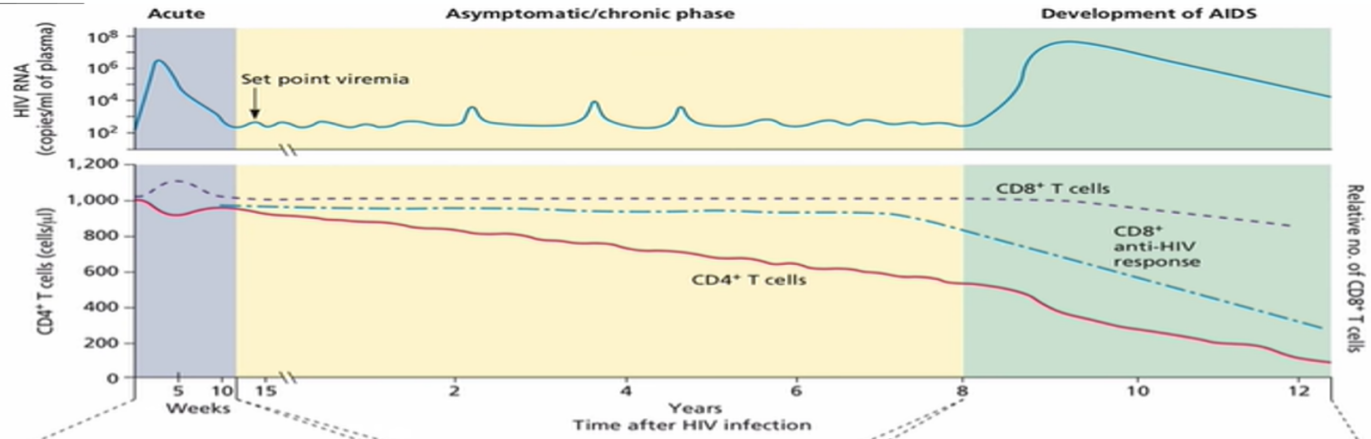
Prolonged duration of symptoms.

Presence of mucocutaneous ulcers, are suggestive of the diagnosis

Most symptoms associated with acute HIV infection are **self-resolving**.

Asymptomatic infection — An estimated **10 to 60 percent** of individuals with early HIV infection will not experience symptoms

Progression of HIV infection



Acute phase.

Symptoms
Fever.
Diarrhoea.
Lymphadenopathy.

At cellular level
$CD4^+$ T cell decline temporarily.
$CD8^+$T cell increase temporarily.

Chronic phase

Symptomes
Usually: No symptoms
Sporadically: fatigue, weight loss,
Lymphadenopathy. Shingles.

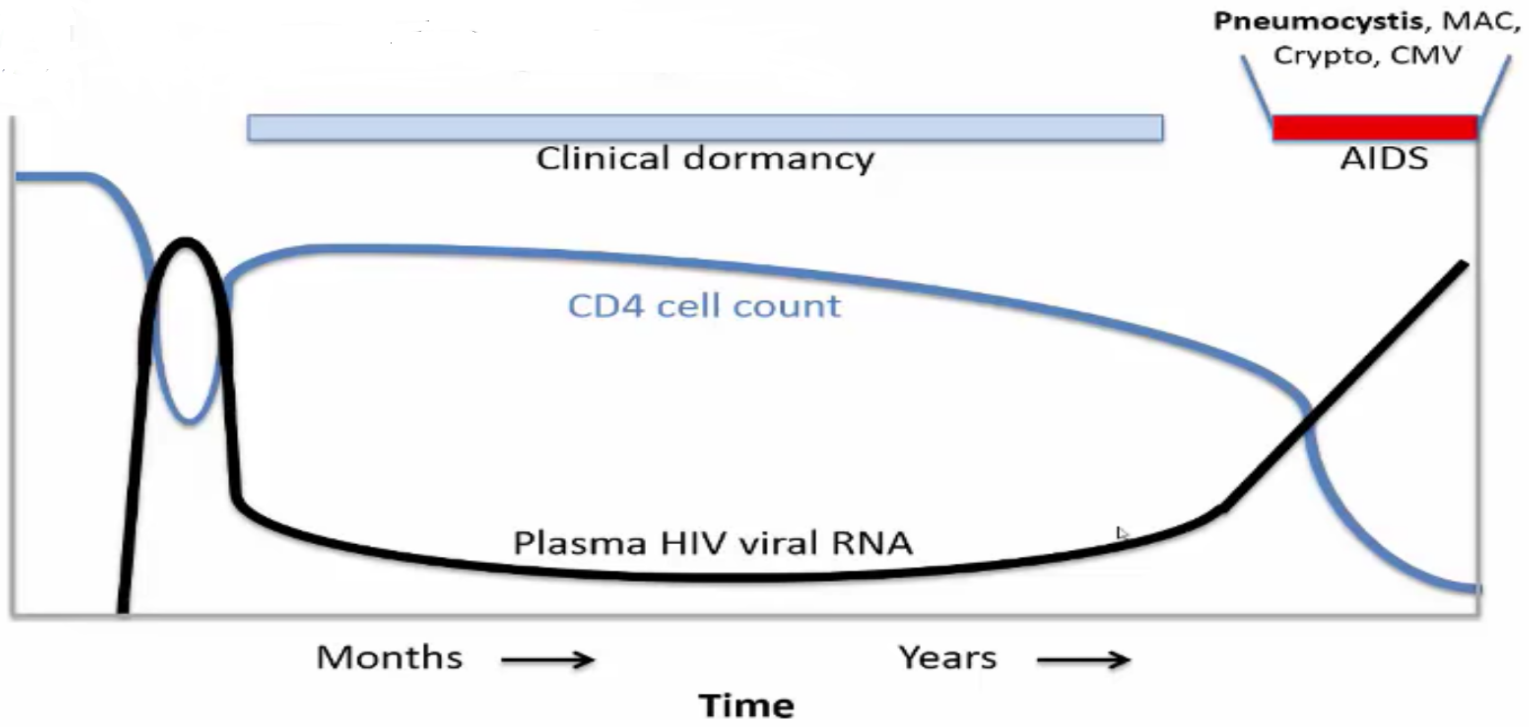
At cellular level:
CD4+ T cells: gradually decline.
CD8+T cells: remain high.

Symptomatic phase

CD4+ T cells count:
200-500 CD4+ T cell/ml
Reactivation of latent tuberculosis
Kaposi Sarcoma.

< 200 CD4+ Tcell/ml
Opportunistic infections.
Malignancies
Neurological symptoms.

Natural history.



Clinical features:

Physical examination:

Skin: condition associated with HIV

Seborrheic dermatitis,

Oropharynx:

1) **oral trush** 2) **hairy leukoplakia**

3) **mucosal kaposi sarcoma**

Lymph node:

Generalized lymphadenopathy.

Eyes:

Fundoscopy : **CMV retinitis.**

Génital exam:

Condylomatous lesions :

Condyloma acuminatum: A wart, found on the genitals It is caused by human papilloma virus. (STD).

Condyloma latum: wart-like lesions on the genitals due to syphilis (STD).

kaposi sarcoma

Complication.

1] Infections:

Pneumocystis jirovecii Pnumonia.

One of the leading causes of **opportunistic infections** among persons with HIV and low CD4 cell counts.

such as those who are unaware of their HIV diagnoses or are not receiving medical care.

Pneumocystis is currently recognized as a fungus.(atypical fungi). based upon ribosomal RNA and other gene sequence homologies.

transmission of P. jirovecii is via the airborne route.

It causes lower respiratory tract infection in seveferly immunosuppressed patients .(in the past it used to be an infection in leukaemia patient).

Case discussion

22 years old young male who presented with :

Progressive shortness of breath, cough and dyspnoea for 2 wks.

Examination: looks in respiratory distress with RR : 28/m

No focal lung findings

Oral thrush

Decreased oxygen saturation.

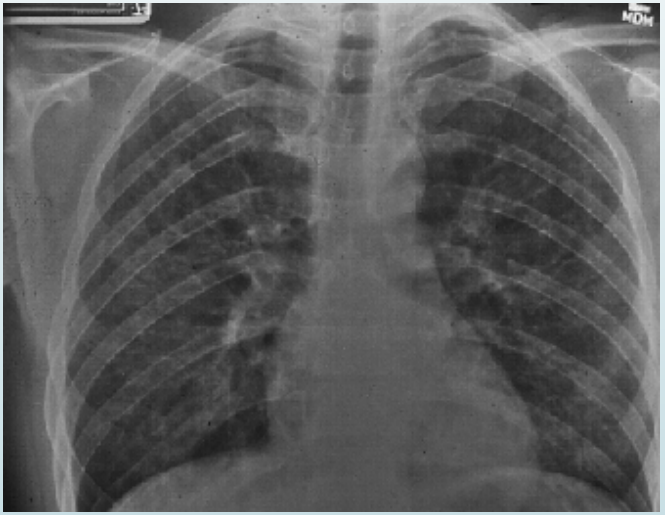
Chest x-ray: diffuse lung infiltrate:

HIV antibody: Reactive . CD4: 27cells/microL.

Elevated LDH.

DX: AIDS with Pneumonia..likely to be Pneumocystis jirovecii Pnumonia.

Give reasons?



Diagnosis:

Consider pneumocystis pneumonia in certain populations:

1] AIDS with CD4 < 200 cells.

2] Organ transplant

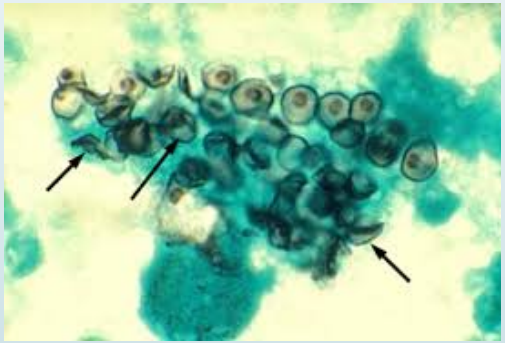
3] High dose of corticosteroid

Laboratory DX: Definitive diagnosis of PCP requires visualization of the cystic or trophic forms in respiratory secretions by:

methenamine silver stain.

Treatment:

Trimethoprim-sulfamethoxazole.



Pneumocystis cysts.

Complication

2] **Malignancy**:...**AIDS-defining conditions**

- **Kaposi sarcoma: HIV IS 500 times more likely to be diagnosed with KS.**
- **Non-Hodgkin lymphoma: 12 times.....**
- **Cervical cancer : 3 times.....**

Kaposi sarcoma(KS):

Is a vascular tumour that is etiologically associated with human herpesvirus 8 (HHV-8).

It is the most common tumour arising in HIV-infected persons.

It is most common in homosexual or bisexual men, and is much less common among injection drug users, transfusion recipients, women or children, and haemophiliacs.

KS is considered an AIDS-defining illness and is predominantly a disease of men.

Incidence has declined substantially since widespread use of potent antiretroviral therapy (ART).

An erythematous to violaceous plaque on the nose.

Nodules of Kaposi sarcoma on the palate

Multiple violaceous papules on the lower leg.

Diagnosis.

Nearly 15 percent of HIV-infected persons in the United States remain unaware of their HIV infection.

WHOM TO TEST:

1] Symptoms of HIV infection:

Signs and symptoms of acute or chronic HIV infection should be tested.

testing for HIV RNA may be needed.

2] Possible HIV exposure:

Patients after a known high-risk exposure to HIV (eg, sexual or percutaneous).

3] Patient with sexually transmitted disease (STD).

4] pregnant women should be tested for HIV early in each pregnancy.

5]

1] HIV **antibody tests** only look for antibodies to HIV . Detect HIV infection **23 to 90 days** after an exposure

2] An **antigen/antibody test:** looks for both HIV antibodies and antigens. detect HIV infection **18 to 45 days after an exposure**

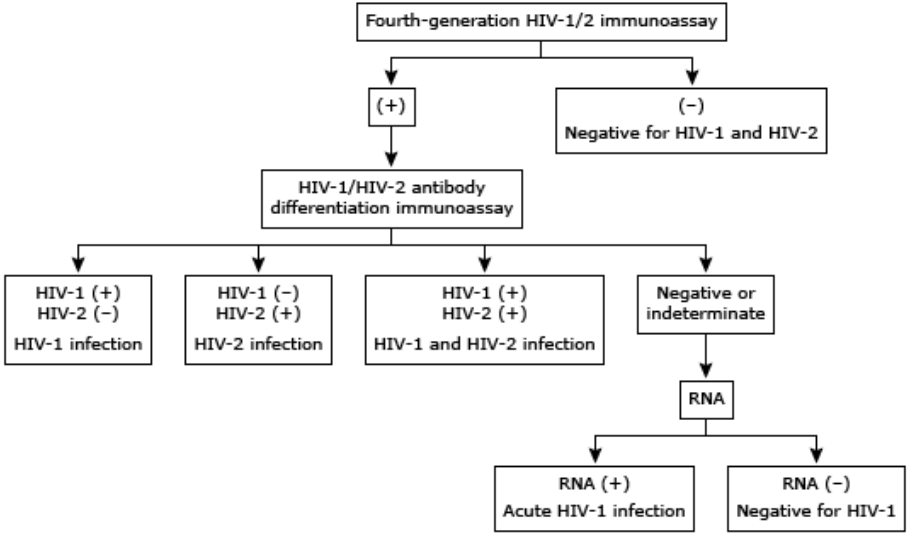
3] A **NAT** looks for the actual virus in the blood. **10 to 33 days after an exposure.**

Rapid tests:

1) The rapid antigen/antibody test with a finger prick and takes 30 minutes.

2) The oral fluid antibody self-test provides results within 20 minutes.

Recommended algorithm for HIV diagnosis



HIV: human immunodeficiency virus.

Modified from: CDC and Prevention and Association of Public Health Laboratories. Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations. Available at http://stacks.cdc.gov/view/cdc/23447. Published June 27, 2014.

Test	Target of detection	Approximate time to positivity (days)
Enzyme-linked immunoassay		
First generation	IgG antibody	35 to 45
Second generation	IgG antibody	25 to 35
Third generation	IgM and IgG antibody	20 to 30
Fourth generation	IgM and IgG antibody and p24 antigen	15 to 20
Western blot		
	IgM and IgG antibody	35 to 50 (indeterminate)
		45 to 60 (positive)
HIV viral load test		
Sensitivity cutoff 50 copies/mL	RNA	10 to 15
Ultrasensitive cutoff 1 to 5 copies/mL	RNA	5

Positive result with **third**-(HIV- antibody only) and/or **fourth**-generation (HIV antigen and antibody) HIV serologic assays hould be confirmed by :

Confirmatory HIV-1/HIV-2 antibody differentiation immunoassay.

Treatment

HIV can be suppressed by treatment regimens

Current ART does not cure HIV infection but highly suppresses viral replication and allows an individual's immune system recovery to strengthen and regain the capacity to fight off infections.

Combination antiretroviral therapy (ART) regimens have led to remarkable declines in morbidity and mortality among persons with HIV.

The standard of care today is to treat nearly all HIV-infected individuals with ART, regardless of CD4 count.

RATIONALE FOR UNIVERSAL TREATMENT:

Reduce HIV infection–related morbidity and prolong duration and quality of life

Restore and preserve immunologic function.

Maximally and durably suppress viral load (plasma HIV RNA)

Prevent HIV transmission.

Treatment

Patients with a CD4 count ≤350 :

Initiating ART results in a significant decline in the risk of AIDS-related morbidity and mortality .

Patients CD4 count <200 cells **[AIDS] :** ART improves survival and delays disease progression.

Medication

Antiretroviral drugs:

Fusion / Entry inhibitors: not used currently :parentral inj.

Reverse transcriptase inhibitor:

A] Nucleoside Analogue RTI.

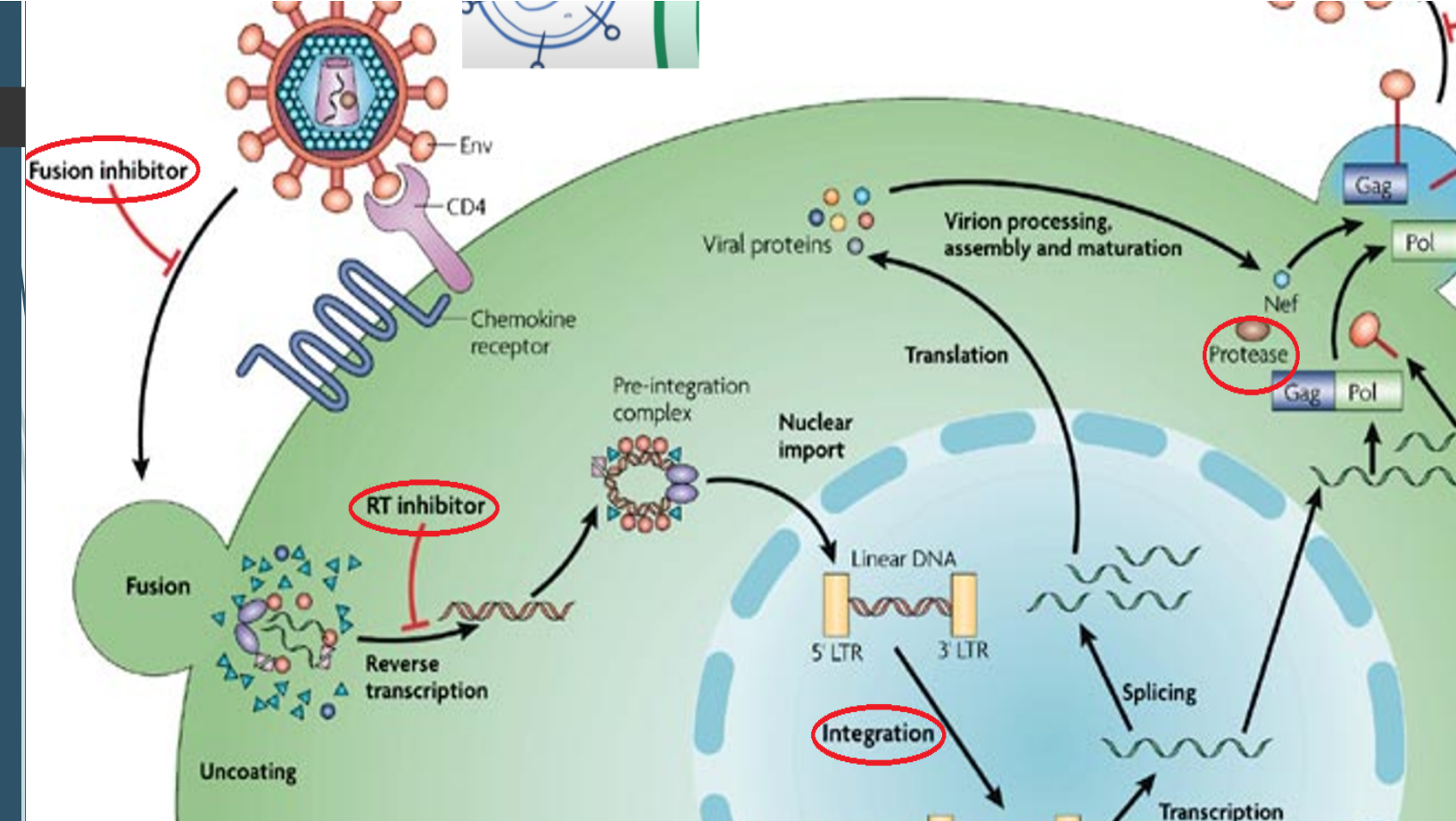
- **Abacavir(ABC)**
- **Emtricitabine(FTC)**
- **Lamivudine(3TC)**
- **Tenofovire**

B] Non-nucleoside RTI

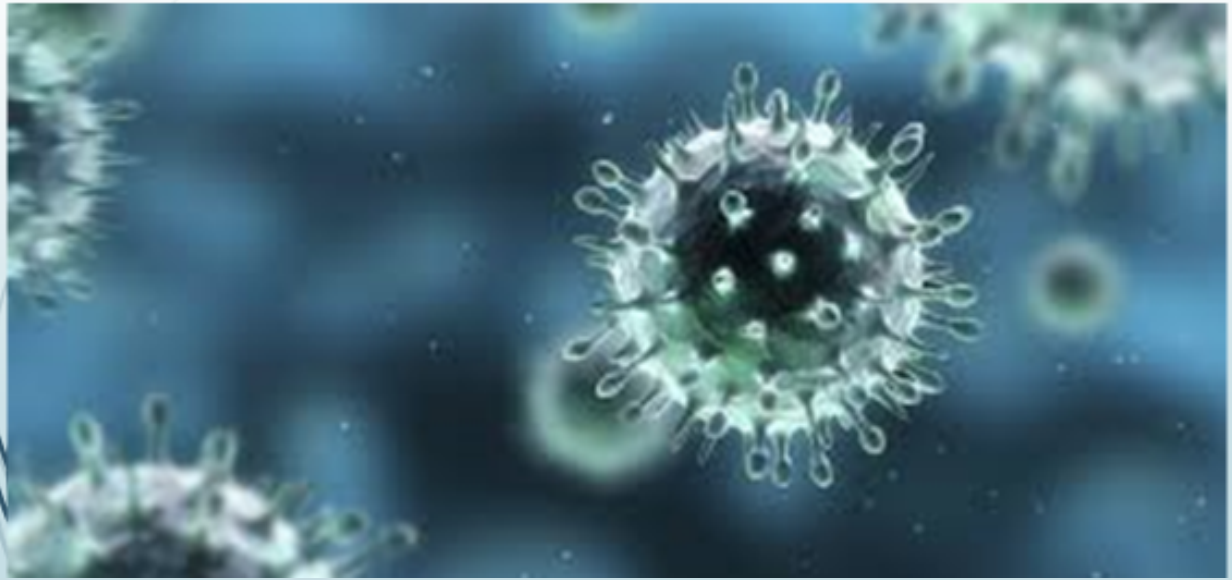
- **Delavirdine**
- **Efavirenz**
- **Nevirapine**

Integrase inhibitors : Raltegravir & dolutegravir

Protease inhibitors : Atazanavir & Darunavir


Fusion inhibitor
Env
CD4
Chemokine receptor
Viral proteins
Virion processing, assembly and maturation
Gag
Pol
Nef
Protease
Gag Pol
Translation
Pre-integration complex
Nuclear import
RT inhibitor
Fusion
Linear DNA
5' LTR
3' LTR
Reverse transcription
Integration
Splicing
Uncoating
Transcription

Video…Pathiogenesis



Prevention

- The only absolute way to **Prevent sexual transmission** of HIV infection is :

Abstinence from sexual relation completely

{ وَلَا تَقْرَبُوا الزِّنَى إِنَّهُ كَانَ فَاحِشَةً وَسَاءَ سَبِيلًا }

- **Safer sexual contact** :
  Correct and consistent use of condoms during sexual contacthave an 85% or greater protective effect against HIV and other STIs .[**10 – 15 % failure rate**] .
- **Circumcision** : results in 50% reduction of HIV acquisition and other STD.
- **Stop using IDUs**
- **Screen all blood** and blood products
-

Prevention: Use of ARVs for prevention.

Use of ARVs for prevention

Secondary prevention benefits of ART

Several studies confirmed that if an HIV-positive person is taking ART and is virally suppressed they do not transmit HIV to their uninfected sexual.

Pre-exposure prophylaxis (PrEP) for HIV-negative partner.

Oral PrEP of HIV is the daily use of ARVs by HIV-negative people to block the acquisition of HIV. **Its effective in reducing HIV transmission.**

Post exposure Prophylaxis:

Sexual contact (unprotected)

Health care associated percutaneous exposure.

PEP is not recommended when care is sought > 72 hours after potential exposure.

Prevention: Elimination of mother-to-child transmission of HIV

Pregnant women infected with HIV infection caries risk to infect her baby by:

1) In utero ...25-40%
2) **Intrapartum ...60-75%**
3) Breast feeding : 1) Established infection 14%
   2) Primary infection 29%

In the **absence of any interventions** during these stages, rates of HIV transmission from mother-to-child can be between **15% and 45%**

Today the risk of perinatal transmission is :

Less than 2% with :

✓ **Effective antiretroviral therapy (ART)**

✓ **Formula feeding**.

Thank you all.

Any comment or question .