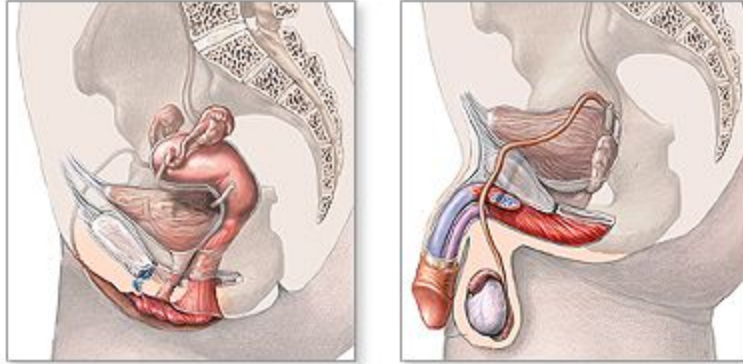


4- HIV & AIDS

Microbiology 435's Teamwork
Reproductive Block



إِنَّا كُلُّ شَيْءٍ خَلَقْنَاهُ بِقَدَرٍ ٤٩

Learning Objectives:

- HIV main structural components
- Mode of transmission
- Stages of HIV infection
 - Main clinical features of each stage of HIV infection
 - Serological profile during the stages of HIV infection
- Diagnosis
- Management & treatment

Please note that the summary was revised by Dr. Mona Badr and should be enough as a source for studying...

- Important
- Males notes
- Females notes
- Extra

Revised by
خولة العماري & هشام الغفيلي

Resources: 435 females & males slides and notes.

Editing file: [Here](#)

Credit: [Team members](#)

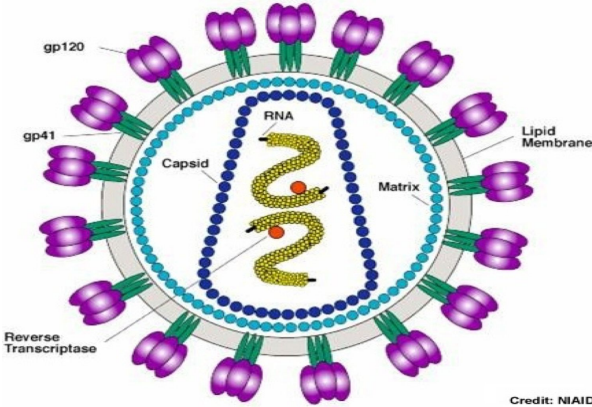
HIV & AID

في البداية لازم نعرف انه ممنوع نقولي ان هالبيشنت ايدز بيشتت بس نقولي HIV infected patient and determine the stage ليه؟ لأن لما نقول ايدز بيشتت نقصد End stage

Human Immunodeficiency Virus (HIV):

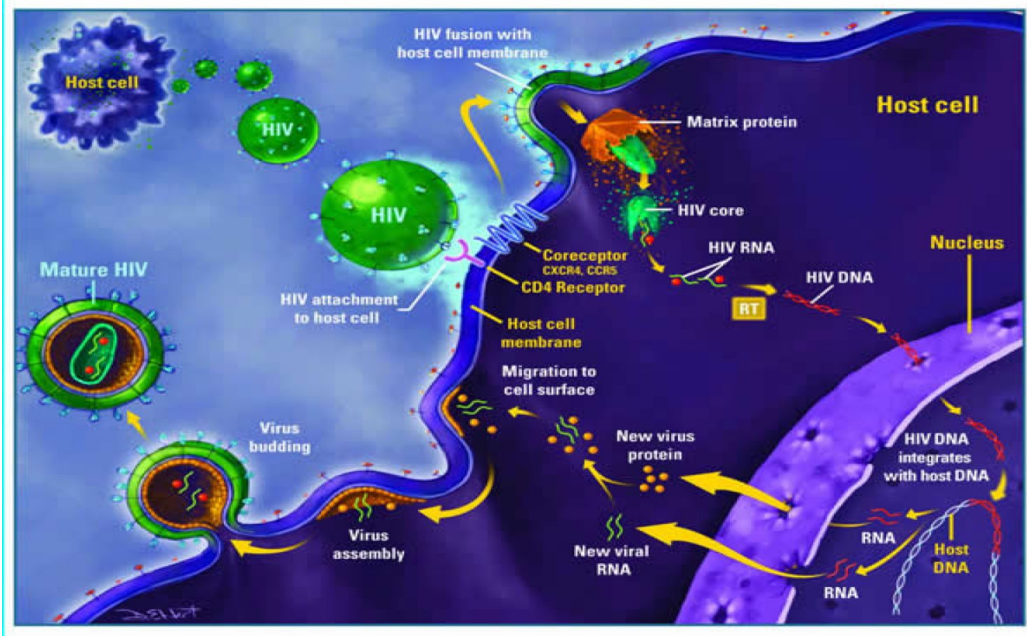
- HIV is known to infect mainly **T-helper cells (CD4)**, macrophages and monocytes.
- Destroying **T-helper cells (CD4)** resulting in the loss of cell mediated immunity which leads to severe immunologic impairment, leading to **multiple opportunistic infections, unusual cancers and death.**

وزي ما انتم عارفين السل ميديا تد اميونتي هي اللي تتحكم بكل الاميونتي فلو خربت من الفايروس حيبخرب معها كل باقي الاميون سستم

HIV	
Characteristics & structure	<ul style="list-style-type: none"> • Family of <i>Retroviridae</i>. • Virion consist of: <ul style="list-style-type: none"> ○ Glycoprotein envelope (gp120, gp41). ○ Matrix layer (p17) ○ Capsid (p24) ○ Two copies of ssRNA. ○ Enzymes: مهمة كتيبيبير <p>1-reverse transcriptase: converts viral RNA into DNA. لما يدخل الفايروس جوا الهوست سل يحتاج يتحول عن طريق هالانزاييم from RNA to DNA</p> <p>2- integrase: integrates viral DNA with host DNA (provirus), persisting infection تحسن الفايروس وتحوله ثاني ل ان اي</p> <p>3- protease: viral protein maturation.</p>
	
Types of HIV viruses:	
HIV-1:	HIV-2:
<ul style="list-style-type: none"> - Causes HIV infection worldwide. - Highly virulent. - Highly susceptible to mutations. 	<ul style="list-style-type: none"> - Causes the infection in specific regions e.g. West Africa - Relatively less virulent. - Relatively less susceptible to mutations.

HIV life cycle

Also explained in pathology & immunology



HIV needs CD4 receptors to enter the cell, it will leave the envelope outside and enter as ssRNA, after entering the cell, reverse transcriptase will convert the viral RNA into DNA.

So, if we do anti-reverse transcriptase in the treatment we will prevent this step.

Then the pro DNA (viral DNA) enter the nucleus to integrate with the host DNA by the integrase enzyme which will make them dsDna, after that it will multiply inside the cell making the cell produce large amount of the provirus (millions) which will use the protease enzyme to convert it back to RNA then it will release and infect other cells

Transmission of HIV

المحدثه من رحمة ربنا ان هالفايروس is very sensitive to environment يعني بمجرد ما يتعرض للبيئة يموت so it needs direct contact

- **Sexually:**

The most common mode of HIV infection is sexual transmission at the genital mucosa through direct contact with infected blood, semen and vaginal secretion.

- **Parenterally:** هذي الأشياء لما تتشف بعد فترة يكون الخطر أقل

- 1- **Direct exposure** to infected blood and blood products.
- 2- Use of contaminated needles and syringes as in drug abusers and Tattooing.
- 3- Through contaminated surgical and **dental instruments** (through incision/ abrasion)
- 4- Sharing contaminated razors, toothbrushes, and nail cutters.

HIV is easily inactivated by treatment for 10 min at 37oC with any of the following: 10% household bleach, Sodium Hypochlorite- 50% ethanol, 35% isopropanol, 0.5% Paraformaldehyde, 0.3% hydrogen peroxide

- **From mother to child:** ممكن ينتقل للبيبي فترة الحمل بس الاكثر أثناء عملية الولادة

- Infected mother transmit HIV to their babies transplacentally (vertical 25%), but Treatment of the mother with antiretroviral **Anti-reverse transcriptase** (Zidovudine) during **pregnancy** can reduce transmission in most cases.
- Virus spread to child mainly (50%) during delivery (perinatally). Giving **Anti-reverse transcriptase** (Nevirapine) as single dose during **delivery** can reduce the transmission .
- Breastfeeding is also an important way of viral transmission (25%). **Antiretroviral treatment** of the mother and infant **after birth** can also significantly decrease the risk of HIV infection in the newborn.

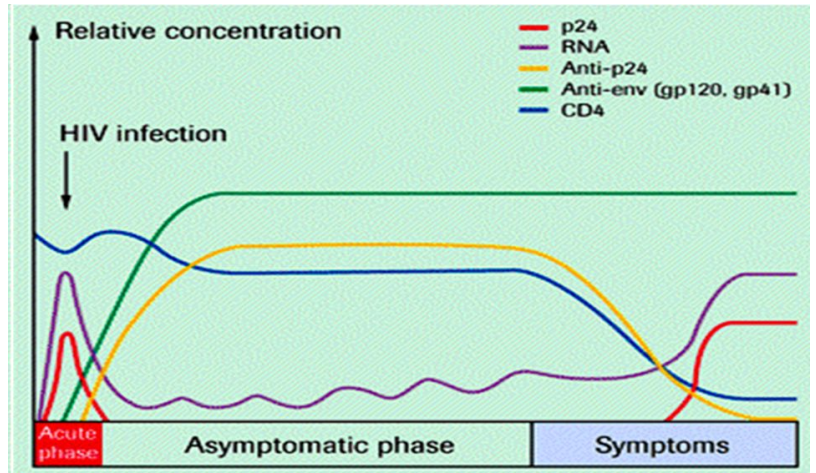
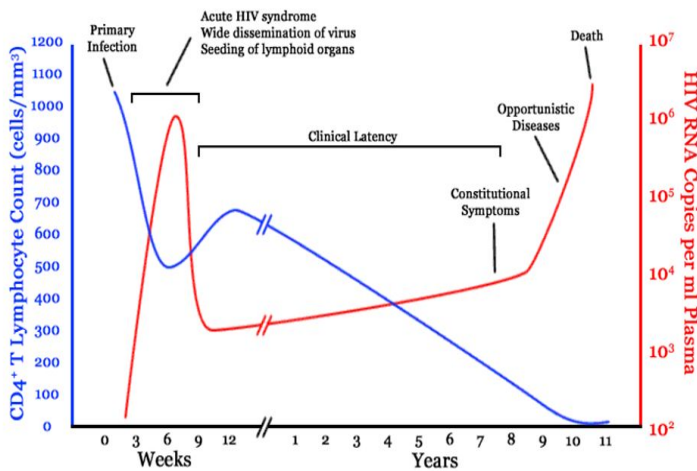
أسماء الأدوية مثل مهمة أهم شي تعرفوا إيش الميكازم (أنتي ريفيرز ترانزكريبتاز)

رکزوا ع الاحمر The Course of HIV-infection

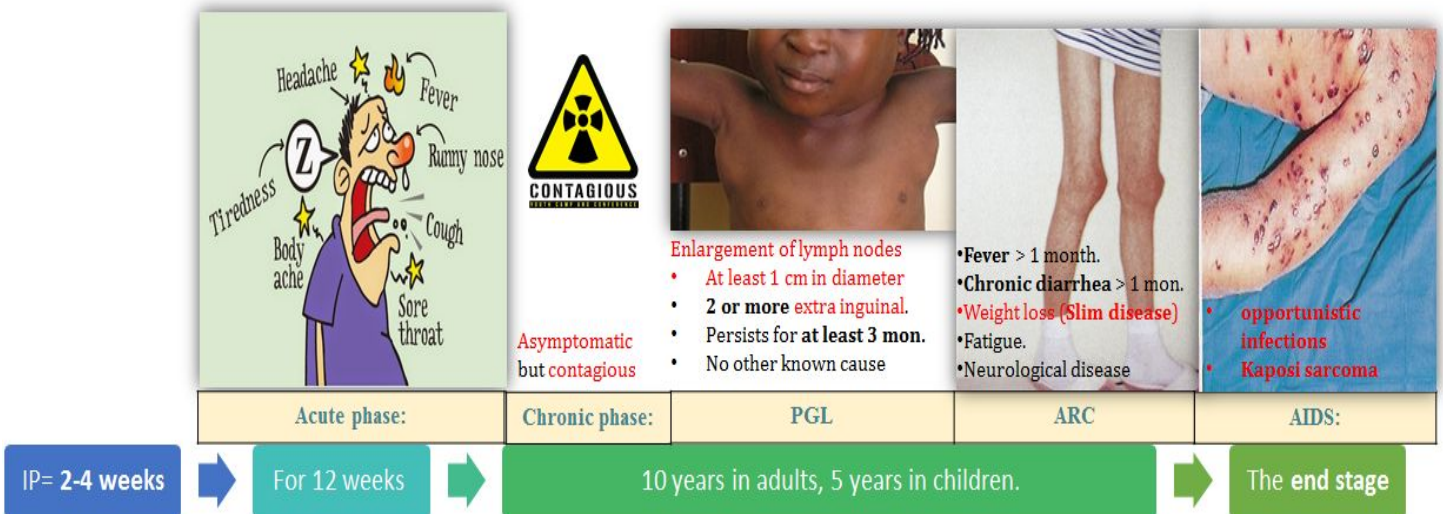
Phase	Acute phase:	Chronic phase:	AIDS:
Duration	Incubation period (2-4 weeks) - This phase (acute phase) lasts for about 12 weeks .	10 yrs in adults, 5 years in children.	The end stage of the disease.
Symptoms	Mostly asymptomatic , if there is symptoms will be mild... → 25-65% of patients develop symptoms that resemble infectious mononucleosis or Flu like syndrome (fever, headache, anorexia, fatigue, lymphadenopathy & skin rash). → Some of patients may develop aseptic meningitis (rare)	Totally asymptomatic but the patients still contagious . يضل هالفتره زي الإنسان الطبيعي ما يبين عليه اي شي، اللهم اذا صار في دايركت كونتاكت مع احد بيوزع الفايروس At the end of this stage patients start to develop: <ul style="list-style-type: none"> ● PGL ● ARC. <i>see next page</i>	1. Persistent or frequent multiple opportunistic infections e.g - Pneumocystis pneumonia - toxoplasmosis - extra pulmonary mycobacteriosis 2. Development of unusual cancer (Kaposi sarcoma) only in aids pt. more (FYI)
Serological picture/ blood markers			
Diagnosis	PCR-RNA is the recommended test for acute HIV infection لأن لسه ما طلعت الانتيبيديز فما راح نقدر نستعمل ELISA* مررررره مهم	Diagnosis mainly by <ul style="list-style-type: none"> ● ELISA, ● Western Blot or PCR 	
Viral load	viral RNA is the first to appear , showing Rapid viral replication (high viral load RNA in the serum). You'll notice high viral load in this phase due to rapid viral replication علاقه عكسية بين الفايرل لود و CD4	Low viral load, but at the end of this phase (PGL and ARC): high load of viral RNA and core Ag. p24 (indicate active viral replication)	Continuous viral replication (Marked increase in viral load viral RNA in the serum)
CD4 cell count	Gradual decrease in CD4 cell count (Normal to slightly decreased in serology)	CD4 count > 500/ml , further decreased in PGL and ARC but still more than 200 cells/mm ³	Marked decrease in CD4 cell count < 200 عشان اقول ايدز بيشتت لازم يكون cd4 اقل من 200
Ag. & Ab.	Detection of core antigen (p24), followed by (later in the phase) the appearance of anti envelope (anti p120, anti p41) and anti core (anti p24) مو مهم تعرفون دورهم في الدايقنوسس	Core antigen (p24) decrease but increase again in PGL and ARC. Continuous detection of anti p120, anti p41, anti p24	Increased core antigen (p24) and anti envelope (Anti-gp120 +ve) Anti p24 decrease

At the end of Chronic phase:

A- Persistent generalized lymphadenopathy (PGL):	B- AIDS-related complex (ARC):
<p>Is defined as enlargement of lymph nodes for at least 1 cm in diameter, and must meet the following conditions:</p> <ul style="list-style-type: none"> ● In two or more extra inguinal area. <div style="font-size: small; color: #e91e63; margin-top: 5px;"> كذا مره يجي السؤال ويحطوا انقوينال اريا والطلاب يختاروه (انتبهوا اكسترا انقوينال) </div> ● Persists for at least 3 months. ● In the absence of any illness or medication known to cause PGL. 	<p>Is a group of clinical symptoms that come before AIDS “قاب قوسين أو أدنى” and may include the following:</p> <ul style="list-style-type: none"> ● Fever of unknown origin that persists > 1 month. ● Chronic diarrhea, persisting > 1 month. ● Weight loss (Slim disease) > 10% of the original weight. ● Fatigue. ● Neurological disease as myelopathies and peripheral neuropathy.



The Course of HIV-infection:



- Enlargement of lymph nodes**
- At least 1 cm in diameter
 - 2 or more extra inguinal.
 - Persists for **at least 3 mon.**
 - No other known cause

- Fever > 1 month.
- Chronic diarrhea > 1 mon.
- Weight loss (**Slim disease**)
- Fatigue.
- Neurological disease

- **opportunistic infections**
- **Kaposi sarcoma**

HIV (cont.)

Diagnosis:

- **Patient's history** with or without clinical symptoms may give hints for a physician whether the patient has ever been exposed to HIV or not.

1. Screening: Elisa, HIV Ab, HIV Ag (p24)

- **ELISA:** for screening patient's serum for both (HIV Ag & HIV Ab).
→ if the result is +ve we repeat the **specimen twice in duplicate** اعيد الاختبار مرتين اذا طلع بوزتيف
→ if still giving +ve result will do **confirmatory tests**

2. Confirmatory: W.B., Riba & PCR In confirmatory tests just know the names

- **Western Blot:** To confirm the presence of Anti-HIV to the structural proteins of the virus by ELECTROPHORESIS

Western blot indeterminate result, means that the test specimen not positive nor negative. The individual must be retested after 8-12 weeks. If the result is negative, report negative. If the result is positive, report positive. If the individual still indeterminate then the patient must be referred to medical evaluation and PCR are recommended to look for HIV-RNA genome.

- **PCR:** For detection of **HIV RNA** in the blood (viral load). This test is important for:

- 1- Diagnosis of Acute HIV infection
- 2- Diagnosis of HIV in infant of infected mother
- 3- To monitor the antiviral treatment
- 4- As confirmatory test.

Treatment

High Active Antiretroviral Therapy (HAART) is a combined therapy composed of **two reverse transcriptase inhibitors & one protease inhibitor**.

- NOTE: HAART **does not clear the virus**, and should be taken all life. Treated patients are still **contagious** even if their blood viral load below detection (< 50 copies/ μ L).

A. Reverse Transcriptase Inhibitors: no need to memorize them

AZT Zidovudine - ddC Zalcitabine - ddI Didanosine - d4T Stavudine - 3TC Lamivudine

B. Protease inhibitors: no need to memorize them

Saquinavir - Indinavir - Ritonavir - Nelfinavir

Goals of HIV treatment

- To inhibit viral replication.
- To control chronic immune activation and keep the immune system close to the normal.
- To prevent the development of opportunistic infection.
- To minimize the chance of viral transmission especially from mother to neonate.
- **Treatment will never eradicate the HIV virus. The goal of treatment is not to eradicate the virus but to increase the duration of chronic stage (25 years)**

Prevention & Control

- **There is no vaccine available yet for HIV**
- Practice safer sex .
- Do not share razors, toothbrushes, needles and syringes, etc ...
- Avoid direct exposure to body fluids
- Educate the public about HIV-infection

L4: SUMMARY OF HIV

HIV	
intro	<ul style="list-style-type: none"> HIV is known to infect mainly T-helper cells (CD4) Destroying T-helper cells (CD4) leading to multiple opportunistic infections, unusual cancers and death. (seen in the end stage 'AIDS')
Morphology	<ul style="list-style-type: none"> Two copies of ss-RNA. Enzymes: مهم جدا جدا كل انزيم نعرف وش تعمل <ul style="list-style-type: none"> <u>Reverse transcriptase</u>: converts viral RNA into DNA. <u>Integrase</u>: integrates viral DNA with host DNA (provirus), persisting infection. مهم كثير <u>Protease</u>: viral protein maturation.
types	<p>HIV-1: worldwide, ↑virulent & ↑susceptible to mutation.</p> <p>HIV-2: in specific regions, ↓virulent & ↓ susceptible to mutation.</p>
transmission	<ul style="list-style-type: none"> Sexually (the most common route) Parenterally: through DIRECT exposure to infected blood (<i>needles, contaminated surgical and dental instruments</i>). From mother to child: transplacentally, during delivery (most common) & breastfeeding.
course	Acute phase <ul style="list-style-type: none"> High viral load. Pt mostly asymptomatic or have flu like syndrome Diagnosed by: PCR to detect viral load
	Chronic phase <ul style="list-style-type: none"> Asymptomatic but contagious. Diagnosis mainly by ELISA, Western Blot. CD4 count > 500/ml. at the end of this stage patients start to develop: <ol style="list-style-type: none"> Persistent generalized lymphadenopathy: Enlargement of lymph nodes In two or more EXTRA inguinal area. (CD4 count decreased but still more than 200 cells) MCQ AIDS-related complex: occur before AIDS characterized by Weight loss (Slim disease) (CD4 count decreased but still more than 200 cells).
	AIDS <ul style="list-style-type: none"> The end stage of the disease. CD4 cell count < 200 (marked ↓). They suffer from: <ol style="list-style-type: none"> multiple opportunistic infections e.g Pneumocystis pneumonia ,toxoplasmosis, extra pulmonary myco-bacerosis . Development of unusual cancer (Kaposi sarcoma)
diagnosis	<ul style="list-style-type: none"> Pt history تلاسف اغلبيهم مايقولوا الحقيقة 1) Screening patient's serum by ELISA for both (HIV Ag p24 & HIV Ab) بس اعرفوها اسماء if the result is +ve we repeated the specimen twice in duplicate if still giving +ve result will do confirmatory tests (Western Blot)MCQ 2) Confirming: Western Blot, Riba, PCR Blood viral load by PCR is important. to diagnose acute phase, infant & also used as confirmatory test and to follow up patients response to treatment.
treatment	<ul style="list-style-type: none"> Is a combined therapy known as high active antiretroviral therapy (HAART), usually composed of two reverse transcriptase inhibitors and one protease inhibitor (very very imp). NOTE: HAART does not clear the virus (MCQ),
prevention	<ul style="list-style-type: none"> There is no vaccine available yet for HIV

1- Which of the following drugs given to a women with HIV during delivery to reduce the transmission?

- A- reverse transcriptase inhibitors
- B- protease inhibitor
- C- antiretroviral
- D- antibiotic

2- In AIDS, CD4 count is :

- A- less than 650 cells /mm³
- B- less than 500 cells /mm³
- C- normal count due improved immunity
- D- less than 200 cells /mm³

3- During the end stage, Kaposi sarcoma occurs due opportunistic infection by which of the following:

- A-HHV-1
- B-HHV-2
- C-HHV-9
- D-HHV-8

4- Which of the following blood markers is present in the acute phase and usually disappears in the chronic phase of HIV infection?

- A-HIV RNA
- B-HIV core antigen
- C-anti-gp120
- D-anti gp325

5- The role of integrase enzyme is...

- A- converting viral RNA into DNA.
- B- viral protein maturation
- C- persisting infection
- D- Attaching to CD4 cells

6- HAART therapy is usually composed of

- A- One reverse transcriptase inhibitors & one protease inhibitor.
- B- One reverse transcriptase inhibitors & two protease inhibitor.
- C- two reverse transcriptase inhibitors & one protease inhibitor.
- D- none of the above.

7- which of the following is used for screening of HIV

- A- ELISA
- B- Western Blot
- C- Riba
- D- PCR

8- Which of the following best describes AIDS-related complex...

- A- Fever
- B- Slim disease
- C- Kaposi sarcoma
- D- Enlargement of lymph nodes (more than 1 cm) In two or more extrainguinal areas persistent for 2 months.

Answers

A-D-D-B-C-C-A-B