

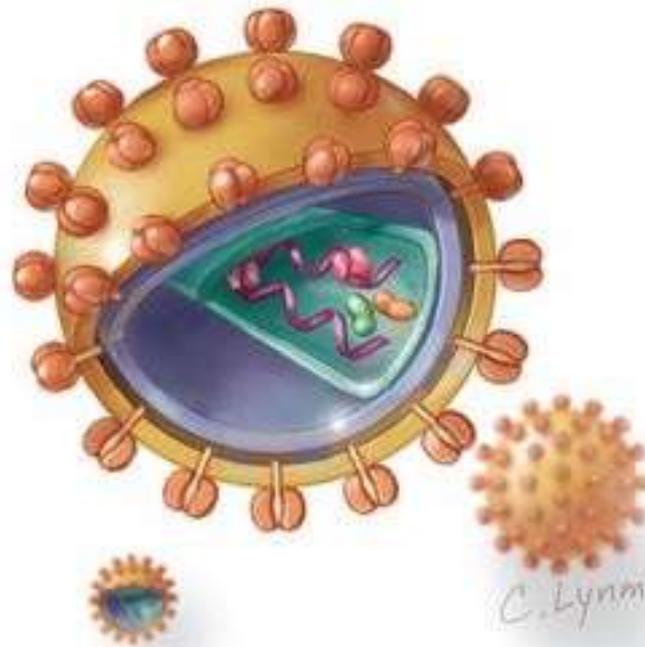
MIRACLE Academy

قال تعالى (يَزِفَعُ اللَّهُ الَّذِينَ آمَنُوا مِنْكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ)

تفريغ المناة
زميلتكم لين قطيشات



لجان الدفعات



Human Immunodeficiency Virus (HIV)

Introduction

1

- HIV is a viral infection that **destroy helper T cells of the immune system** long term transgene expression بتتميز انها بتعطي عشان هيك كثير بستخدموها بالمختبرات
- HIV is a lentivirus →
- Genus of the retroviridae family
- **Produce multi-organ diseases** 2
- Characterized by **long incubation periods** and persistent infection 3
- Infect a wide range of prime hosts, as well as some non-primate mammals

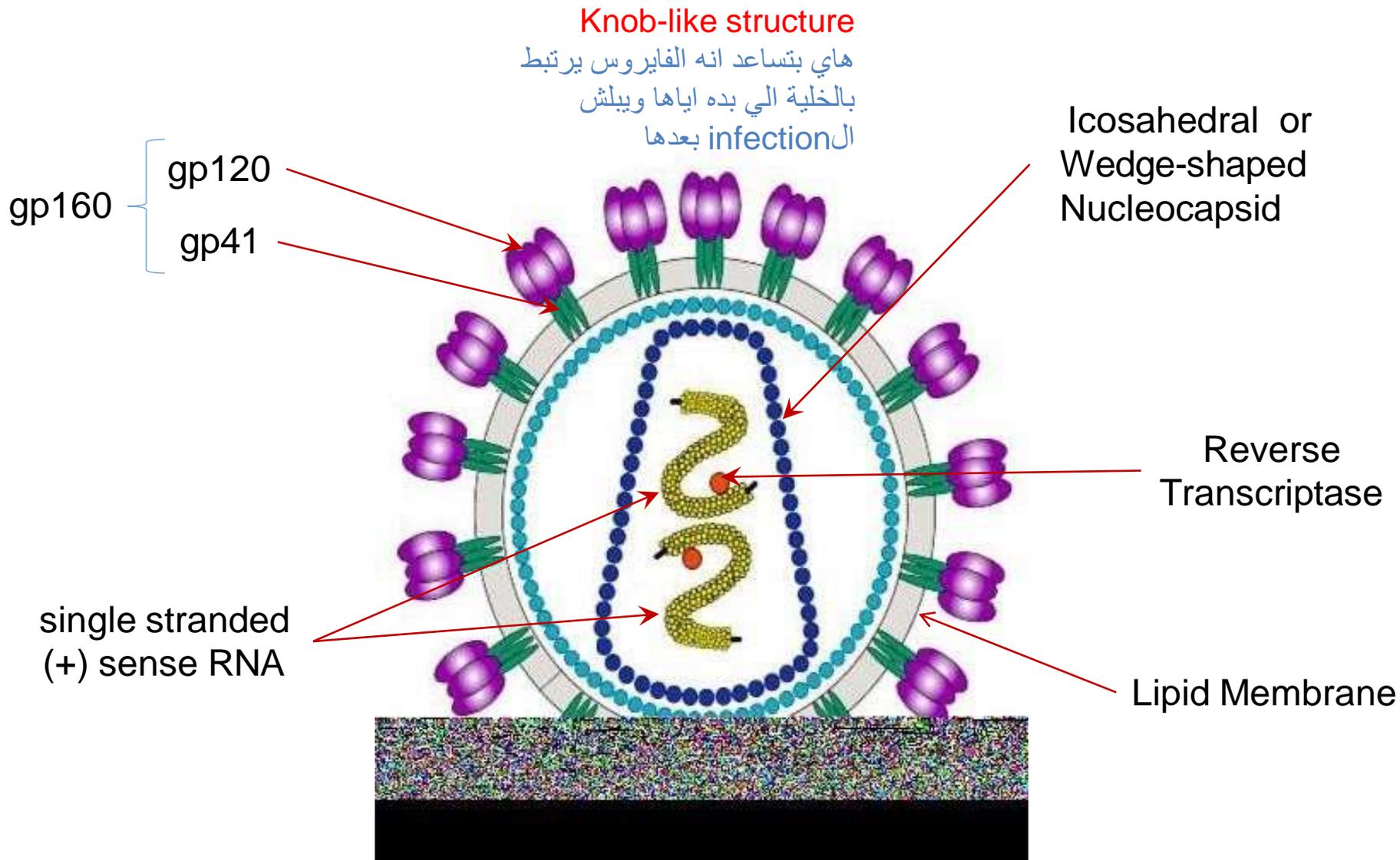
ممكن يوصل 10 سنين بعدين
بتبلش الاعراض تظهر

Morphology

متعدد الوجوه

- Icosahedral (20 sided)
- Retroviruses transcribe RNA to DNA
- Two viral strands of RNA found in core surrounded by protein outer coat.
- Enveloped virus
- Outer envelope contains a lipid matrix within which specific viral glycoproteins are imbedded.
- These knob-like structures responsible for binding to target cell.

برضو بكون في انزيم reverse transcriptase هاد الانزيم هو الي يمكن الفايروس يعمل transcription من ال RNA لل DNA بس يدخل لل Host cells بعد هيك هاي ال DNA بتدخل للنواة وبصير له integration بالكروموسوم بعد هيك بتبلش ال Host cell تصنع البروتينات الخاصة بالفايروس بصنع ال RNA وال capsid وال envelope بعد هيك الفايروس بطلع من الخلية وهاي منسميها shedding * عشان هيك بالكورونا كان يحتاج الفايروس 3 أيام ليظهر لانه كان يقعد 3 أيام لحتى يصير shedding لهاد الفايروس .



Types of HIV

❖ Two species of HIV infect humans:

1. HIV-1

- More virulent, relatively easy to transmit
- Majority of HIV infections globally
- 3 types of HIV-1: (based on alterations in *env* gene)

*لو سألت شو ال most common infect لل human من ال HIV ؟

HIV-1 هو عدائي وكتير سهل انتشاره

2. HIV-2

انتشاره قليل

- Less transmittable
- Largely confined to West Africa

Origins of HIV

*اول رواية بتحكي من وين اجى الايدز: هي انه الامريكيين الي كانوا يكتشفوا
الادغال في منهم مارسوا الجنس مع القرده فانتقل الايدز منهم
*في رواية تانية بتحكي : انه انتقل عن طريق انهم ذبحوا القرده واكلوهم فانتقل
عن طريق الاكل .

HIV-1 likely descended from

جاي من
ال chimpanzee

SIV_{cpz}

(Simian immunodeficiency virus)

HIV-2 likely descended from

SIV_{sm}



History

اكتر نسبة اصابة بالايديز او اكتر مسبب الها هو **sexuality between men**

- 1- 1926-1946 - Scientists believe HIV first spread from monkeys to humans
- 2- 1959 - First proven AIDS death
- 3- 1978 - Gay men in US and Sweden begin showing signs of what is now known as AIDS
- 4- 1981 - CDC notices increase in cases of **Kaposi's sarcoma** and **Pneumocystis carinii pneumonia**
- 5- 1982 - The term AIDS (acquired immune deficiency syndrome) is used for the 1st time
- 6- 1983 - Institute Pasteur ^{حذر من انتقاله بالدم} isolates HIV-1 CDC issues warning to blood banks about potential problem
- 7- 1984 - Dr. Robert Gallo claims discovery of HIV

Kaposi's sarcoma:

هي عبارة عن cancer بصير زي تقرحات بالجلد بكون لونها قريب من اللون النهدي واحيانا بتعمل كتل فهاي بتكون sign انه المرضى عندهم ايدز

Pneumocystis carinii pneumonia:

هي fungal infection بالعادة ما بتصيب الانسان لكن اذا ضعف جهاز المناعة بالانسان كتير بتقوى هاي الفطريات بتسبب pneumonia

*هدول مرتبطات ارتباط دقيق بمرض الايدز فمعظم الي عندهم ايدز بصيروا عندهم .

Epidemiology

- The virus was first successfully identified and classified in 1981.
- At end of 2003 in the U.S. 1,039,000 - 1,185,000 persons infected with HIV/AIDS
- Global (2006 statistics): 39.5 million infected with HIV/AIDS
- 4.3 million new infections in 2006; 2.8 million (65%) of these were in sub-Saharan Africa
- Increases in Eastern Europe and Central Asia, where there may have been a more than 50% rise in infection rates since 2004
- In 2006, 2.9 million deaths due to AIDS-related illnesses

Transmission

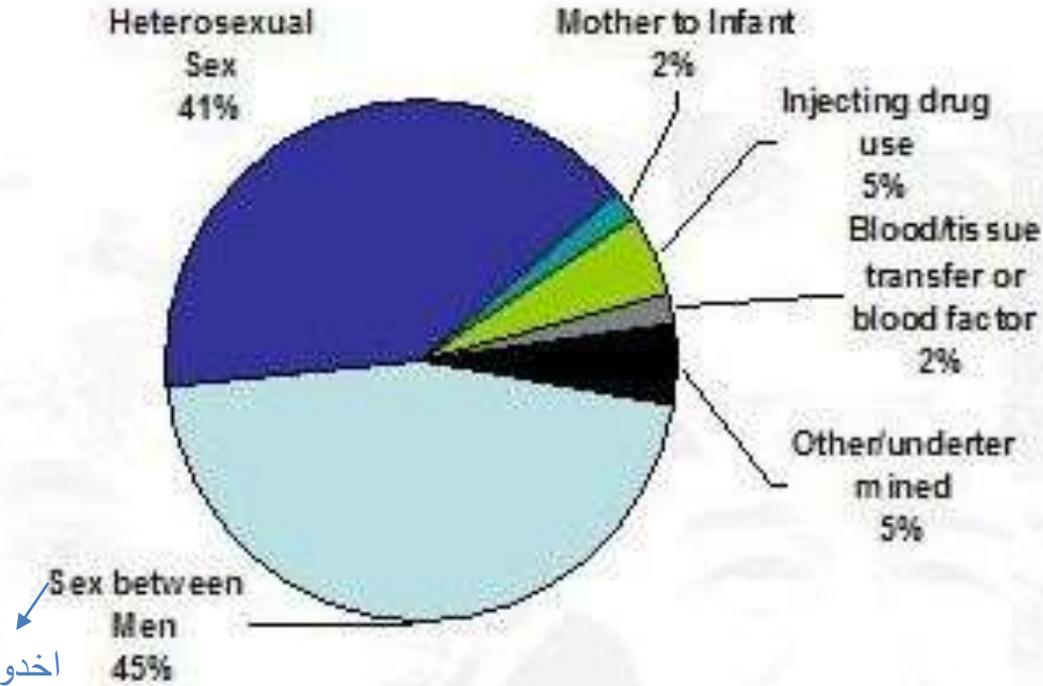
لازم نعرف انه مش اي شخص مصاب بالايذز يعني انتقله المرض عن طريق الجنس ممكن يكون ضحية للمرض

- Sharing of infected drug injection needles/syringes
- Accidental needle stick (healthcare professionals)
- Unprotected sex with infected individual
- Blood transfusions/Organ transplants
- Transmission from infected mother-to-fetus during pregnancy or delivery
- Transmission from breast milk of infected mother to her baby

هلا ال needle لها cap بشيلوها وبرجعوا بحطوها ممكن تنقل امراض هيك
فالطريقة الصحيحة : بجيب الغطاية بحطها على طرف الطاولة بعدين بجيب الابرة وبدخلها جوا
الغطاية بدون ما احط ايدي عالغطاي مجرد ما تدخل انا باجي وبسكرها منيح عالآخر
بهاي الطريقة بضمن انه الابرة ما لامست الجلد .

Route of Transmission of HIV Infection, infections before 2006

بين ذكر وانثى (اذا كان واحد فيهم infected)



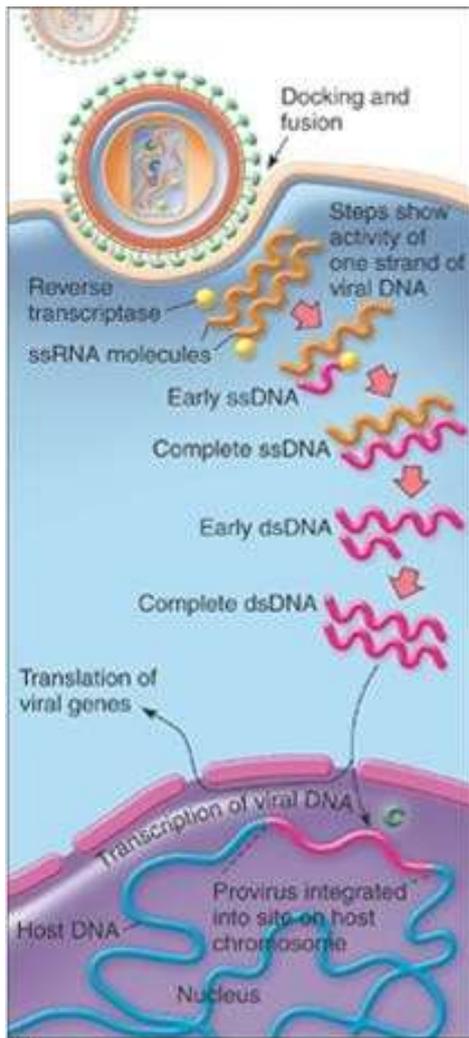
اخذوا نسبة 45% من اكثر نسبة انتشار للفايروس هاد بأكدنا ليش هاي العلاقات حرام شرعاً
"الحمد لله على نعمة الاسلام"

Pathogenesis and Virulence Factors

- 1- HIV enters through mucous membrane or skin and travels to dendritic phagocytes beneath the epithelium, multiplies and is shed.
- 2- Virus is taken up and amplified by macrophages in the skin, lymph organs, bone marrow, and blood.
- 3- HIV attaches to **CD4** and coreceptor; HIV fuses with cell membrane. الموجود عال Helper T cell
- 4- Reverse transcriptase makes a DNA copy of RNA.
- 5- Viral DNA is integrated into host chromosome
- 6- Can produce a **lytic infection** or **remain latent**

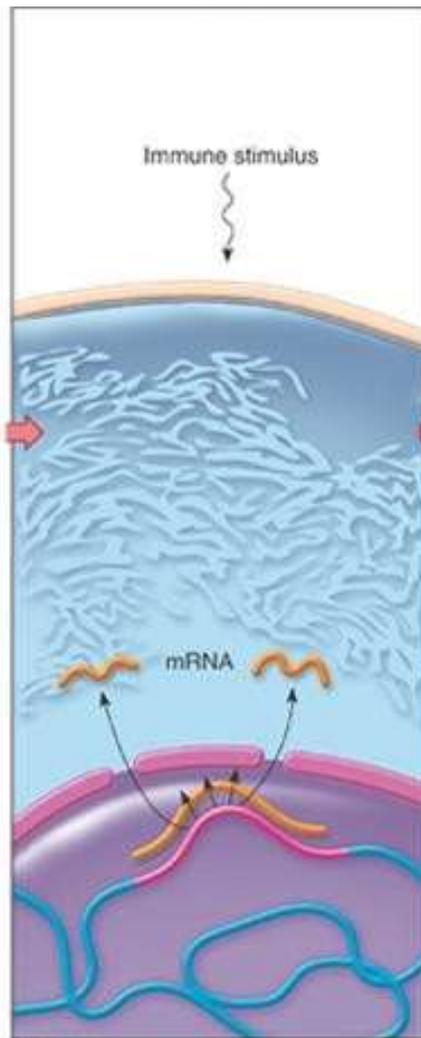
اما بعمل infection
وبصير shedding

او بضل ساكن بال incubation
period الي ممكن تضل 10
سنين وفجأة ممكن تظهر الاعراض



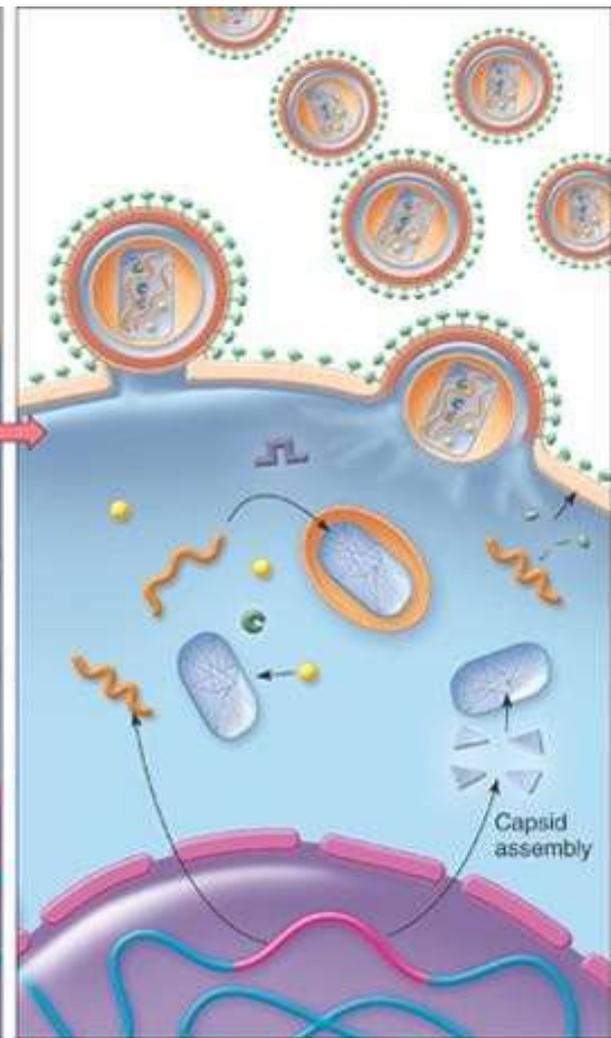
(a)

The virus is adsorbed and endocytosed, and the twin RNAs are uncoated. Reverse transcriptase catalyzes the synthesis of a single complementary strand of DNA (ssDNA). This single strand serves as a template for synthesis of a double strand (ds) of DNA. In latency, dsDNA is inserted into the host chromosome as a provirus.



(b)

After a latent period, various immune activators stimulate the infected cell, causing reactivation of the provirus genes and production of viral mRNA.



(c)

HIV mRNA is translated by the cell's synthetic machinery into virus components (capsid, reverse transcriptase, spikes), and the viruses are assembled. Budding of mature viruses lyses the infected cell.

Primary effects of HIV infection:

كريات الدم البيضاء عالية جدا
وبتكون ال T cell حجمها كثير كبير

- extreme leukopenia – lymphocytes in particular
- formation of giant T cells allowing the virus to spread directly from cell to cell
- Infected macrophages release the virus in central nervous system, with toxic effect, inflammation.

Secondary effects of HIV:

- Destruction on CD4 lymphocytes allows for ↑ opportunistic infections and malignancies.

Clinical Manifestations

- Human Immunodeficiency Virus (HIV) has an incubation period of about 10 years and eventually leads to Acquired Immunodeficiency Syndrome (AIDS), resulting in the impairment of the immune system.

- This can lead to death from infections, secondary diseases from opportunistic bacteria and/or viruses that are usually harmless to people, or many different types of cancers.

بسبب ضعف جهاز المناعة البكتيريا الي ما
بتسبب مرض عند الانسان الطبيعي بتصير
تعمل infection عند الانسان المصاب بالايذز
وبتصير تسبيله فطريات وطبيعة الفطريات
عندهم مش سهلة علاجها

- Common diseases associated with HIV infection:

- Kaposi's sarcoma (KS)
- Pneumocystis carinii pneumonia (PCP)
- Mycobacterium avium complex (MAC)

- **Early** Symptoms:

- Most don't exhibit symptoms when first infected
- However, may have flu-like symptoms (fever, headache, tired, enlarged lymph nodes) 1-2 months after exposure
- Very infectious during this period

- **Later** Symptoms:

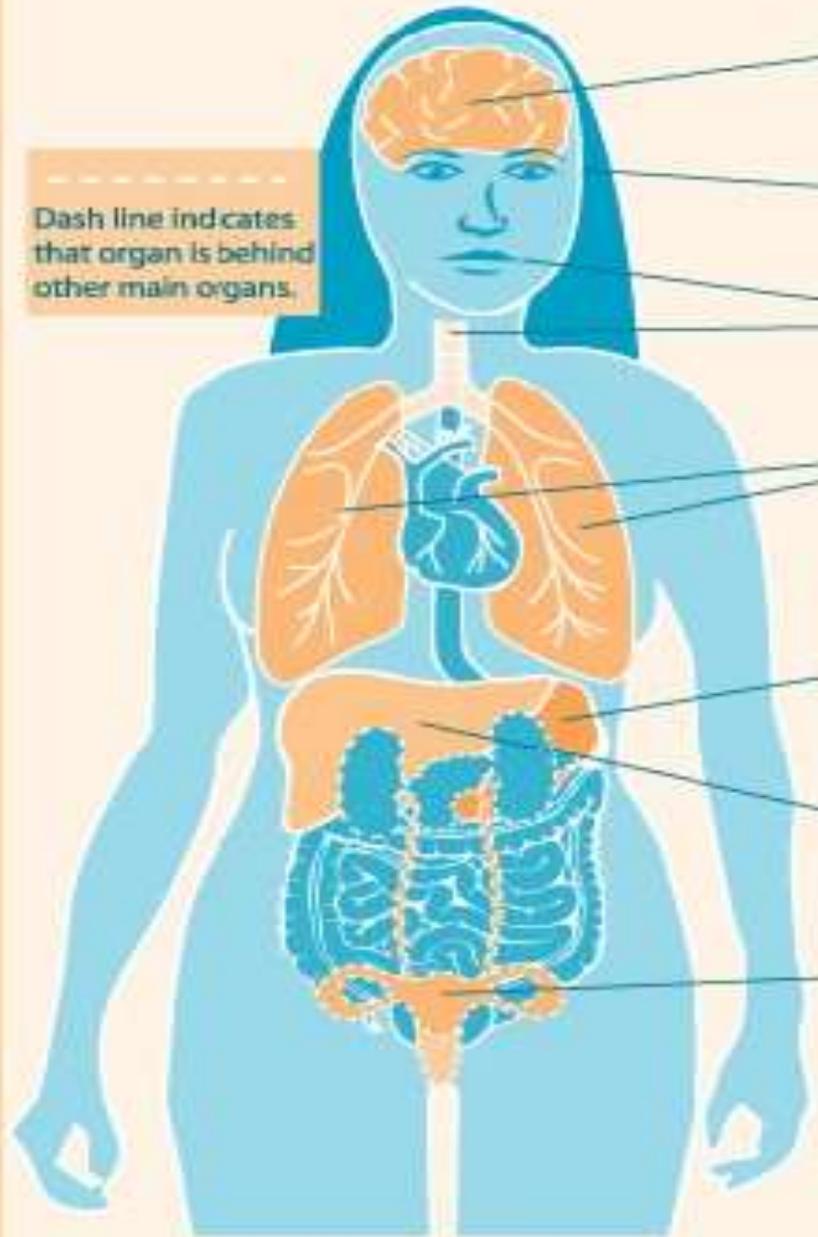
- More severe symptoms may not appear until after 10yrs, however this varies with each individual
- Decline in number of CD4 + T cells
- The most advanced stage of AIDS is classified as having < 200 CD4+ T cells/cubic millimeter of blood (in healthy adults CD4+ T-cell counts = 1,000+)

عند مرضى الايدز يتكون
200 فالمناعة كثير
ضعيفة عندهم حنكون

Opportunistic Infections

مطلوب داخل

Dash line indicates that organ is behind other main organs.



Brain

Toxo (toxoplasmosis)
Cryptococcal meningitis

Eyes

CMV (cytomegalovirus)

Mouth and Throat

Candidiasis (thrush) ★

فطريات بكميات كبيرة

Lungs

PCP (pneumocystis carinii pneumonia) ★
Histoplasmosis
TB (tuberculosis)

Stomach

MAC (mycobacterium avium complex)
Crypto (cryptosporidiosis)
CMV (cytomegalovirus)

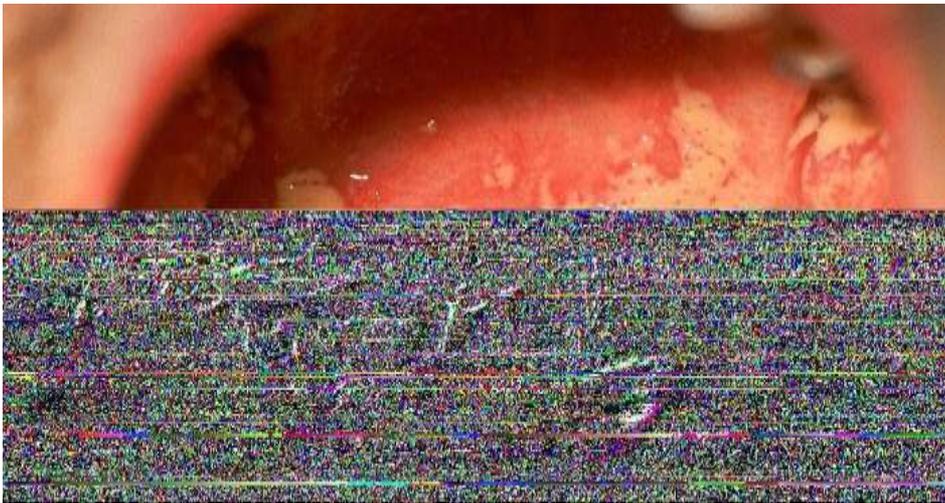
Liver

HCV (hepatitis C virus)

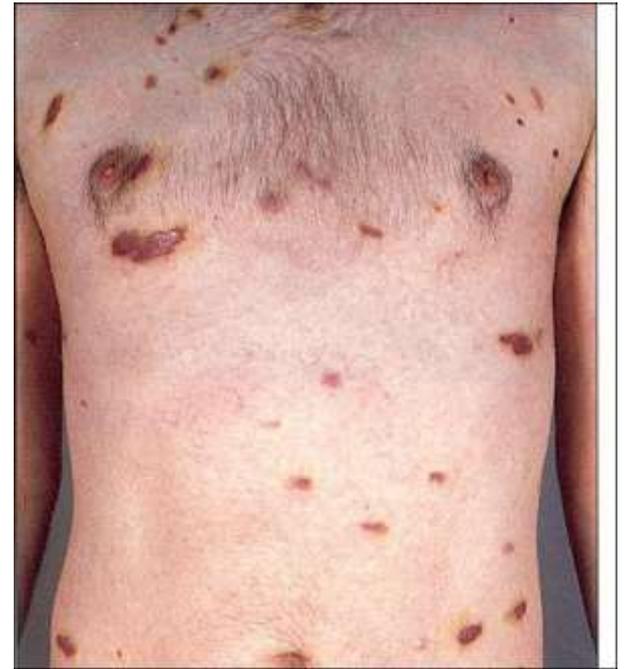
Reproductive System

HPV (human papillomavirus) and Cervical cancer
Menstrual problems
Vaginal candidiasis (yeast infection)
PID (pelvic inflammatory disease)
UTI (urinary tract infections)
Genital ulcers

Oral Candidiasis (thrush)



Kaposi's sarcoma (KS)



Laboratory Tests

- Methods utilized to detect:
 - Antibody
 - Antigen
 - Viral nucleic acid
 - Virus in culture

1

ELISA Testing

- First serological test developed to detect HIV infection.
- Antibodies detected in ELISA include those directed against: **p24, gp120, gp160 and gp41**, detected first in infection and appear in most individuals

هدول اذا كانوا موجودين مع الـ Ab رح

يعطينا الـ ELISA ← Positive result

- ELISA tests useful for:
 - Screening blood products.
 - Diagnosing and monitoring patients.
 - Determining prevalence of infection.
 - Research investigations.

دائما منفحص فيها

البروتينات

2

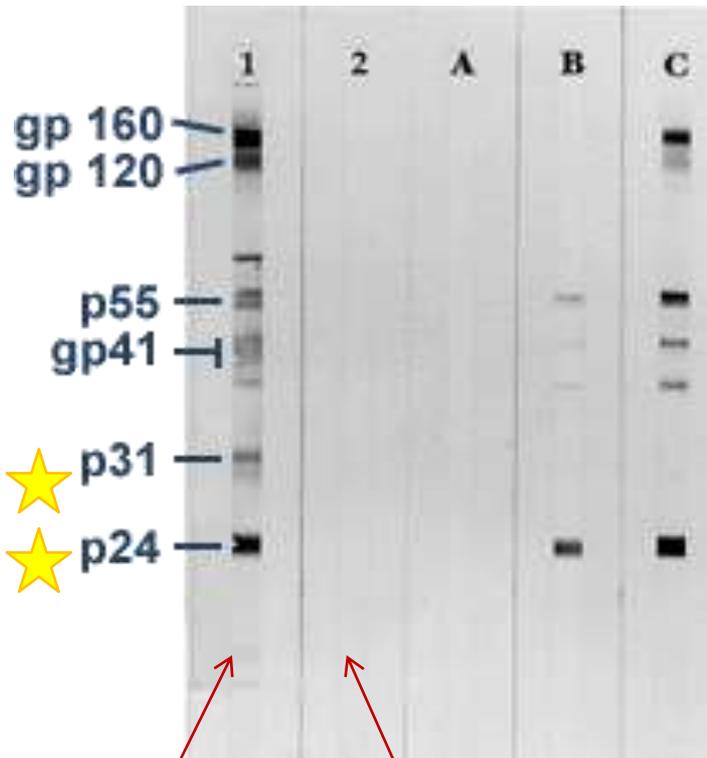
Western Blot

بتأكدلنا الاصابة

- **Most popular confirmatory test.**
- Utilizes a lysate prepared from HIV virus.
- The lysate is electrophoresed to separate out the HIV proteins (antigens).
- The paper is cut into strips and reacted with test sera.
- After incubation and washing anti-antibody tagged with radioisotope or enzyme is added.
- Specific bands form where antibody has reacted with different antigens.
- Most critical reagent of test is purest quality HIV antigen.

هاد الlysate اذا كان المريض مصاب المفترض
الantigen تكون فيه فمتمشي الlysate على
paper وعال electrophoresis المفروض لما
نحط الAb يرتبط بالantigen اذا كان موجود
وبعطينا P اذا اعطانا P الخاصة بالارقام بالاسلايد
الجاي بكون الشخص مصاب بالايديز 100% واذا ما
طلع ولا P اذن هاد الشخص مش مصاب

HIV – Western Blot Results



gp160 = viral envelope precursor

gp120 = viral envelope protein binds to CD4

p31 = reverse transcriptase

p24 = viral core protein

HIV (+) serum

HIV (-) serum

بجيبوا خلايا المريض وبثبتوها على slide وبعملوا Ab لل incubation فالمرريض اذا كانت خلاياه
بتحتوي على antigen الخاص بالايديز بصير fixing مع ال Ab فبتطلع

3 immunofluorescence بغض النظر شو اللون بطلع عنا بالصورة انه في positive result Indirect immunofluorescence .

- Can be used to detect both virus and antibody to it.
- Antibody detected by testing patient serum against antigen applied to a slide, incubated, washed and a fluorescent antibody added.
- Virus is detected by fixing patient cells to slide, incubating with antibody.

4

Detection of p24 HIV antigen

هاي الطريقة مش كثير دقيقة كونه ال p-24 antigen يكون متواجد لفترة قصيرة بعدين بروح فال ELISA بتكون دقيقة وافضل من هاي الطريقة

- The p24-antigen screening assay is an EIA performed on serum or plasma.
- P24 antigen only present for short time, disappears when antibody to p24 appears.
- Test not recommended for routine screening as appearance and rate of rise are unpredictable.
- Sensitivity lower than ELISA.

5 Polymerase Chain Reaction (PCR)

منبدأ بتركيز قليل يكون بال DNA
amplification بعد هيك بصيرله
عشان هيك اسمه PCR لانه بصير
كل DNA يعطي DNA 2 بعدين
منشئي العينة على
nitrocellulose paper

- Looks for HIV DNA in the WBCs of a person.
- PCR amplifies **tiny quantities of the HIV DNA present**, each cycle of PCR results in doubling of the DNA sequences present.
- The DNA is detected by using radioactive or biotinylated probes.
- Once DNA is amplified it is placed on nitrocellulose paper and allowed to react with a radiolabeled probe, a single stranded DNA fragment unique to HIV, which will hybridize with the patient's HIV DNA if present.
- Radioactivity is determined.

6

Virus isolation

- Virus isolation can be used to definitively diagnose HIV.
- **Best** sample is peripheral **blood**, but can use CSF, saliva, cervical secretions, semen, tears or material from organ biopsy.
للإناث females
للذكور men
كل هاي العينات ممكن تحتوي عاليدز فاذا بدى امنع الاصابة لازم ما يصير contact مع ولا وحدة من هذول ال secretions للشخص المصاب .
- Cell growth in culture is stimulated, amplifies number of cells releasing virus.
- Cultures incubated one month, infection confirmed by detecting **reverse transcriptase** or **p24 antigen** in supernatant.

إذا كان ال supernatant يحتوي على وحدة منهم يكون
الشخص مصاب ب HIV

بعد ما يعملوا isolation بحطوها ب culture ويزيد عددها ومنعملها incubation هاي الفيروسات
by detecting
reverse transcriptase or p24 antigen in supernatant

Prevention

كيف يمنع الإصابة؟

- Avoid sexual contact with infected individuals
 - Abstinence
 - Monogamous Relationship → يعني الاكتفاء بعلاقة واحدة
 - Protected Sex
- Avoid sharing needles/syringes that could be contaminated with HIV
- Avoid any type of contact with the bodily fluid of an infected individual

New Methods for Prevention

في طرق جديدة اذا كان واحد شريك حياته مصاب بالايديز ممكن ينضاف
Intravaginal lime او lemon juice بمنطقة ال vagina حتى تقتل ال HIV

- Intravaginal lime or lemon juice to kill the HIV virus before entry
- **Intravaginal oestrogen**: Karotinizing the vagina with estrogen
- **Male circumcision**^{الطهور}: Removal of the inner foreskin removes the main site of HIV entry into the penis, resulting in a sevenfold reduction in susceptibility to infection اله فائدة انه بحمي كثير من انتشار الامراض الجنسية
- **Post-coital penile hygiene**: Wiping the penis immediately after intercourse with lime or lemon juice or vinegar should kill the virus before it has had a chance to infect.

Treatment

- Anti-viral agents
- Nucleoside Reverse Transcriptase inhibitors
 - AZT (Zidovudine)
- Non-Nucleoside Transcriptase inhibitors
 - Viramune (Nevirapine)
- Protease inhibitors
 - Norvir (Ritonavir)

Vaccine

- Currently, no vaccines approved for use by the FDA

واحد بقوي جهاز المناعة وواحد بحمي من الاصابة لكن
التنين still under development

- **Two types** in development:

- Therapeutic Vaccine - intended to boost the immune systems of those already infected
- Preventive Vaccine – intended to generate an immune response in an uninfected person to prevent future infection

اللهم فرجاً عاجلاً للمستضعفين المظلومين في غزة..
اللهم انصرهم ومكّن لهم واكشف العذاب عنهم