



HIV Diagnosis

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Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Question #1

- A 26-year-old otherwise healthy gay white man has his first HIV test as part of a new health plan
- The fourth-generation test is antibody reactive and antigen non-reactive
- A supplemental third generation HIV-1/2 ELISA is non-reactive, and an HIV RNA test does not detect HIV RNA

What is the most likely explanation for these results?

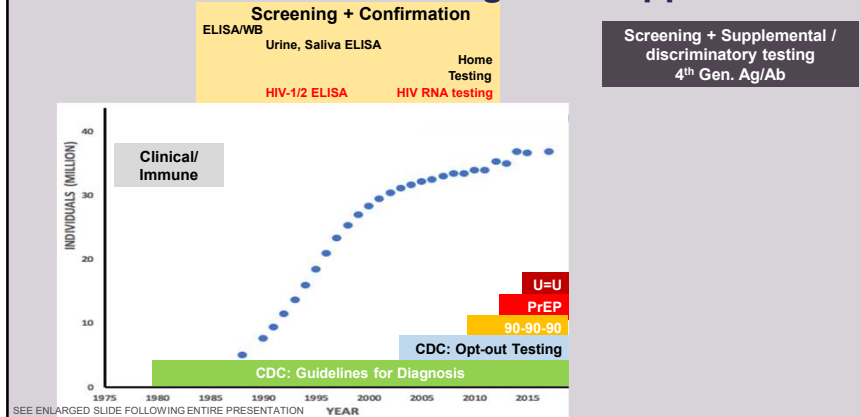
- A. This person HIV-infected and is an elite controller
- B. This person is HIV-infected but is in the window period for HIV infection
- C. This person is infected with an HIV variant that is not detected by the supplemental test
- D. This person is not HIV-infected

HIV Diagnosis:

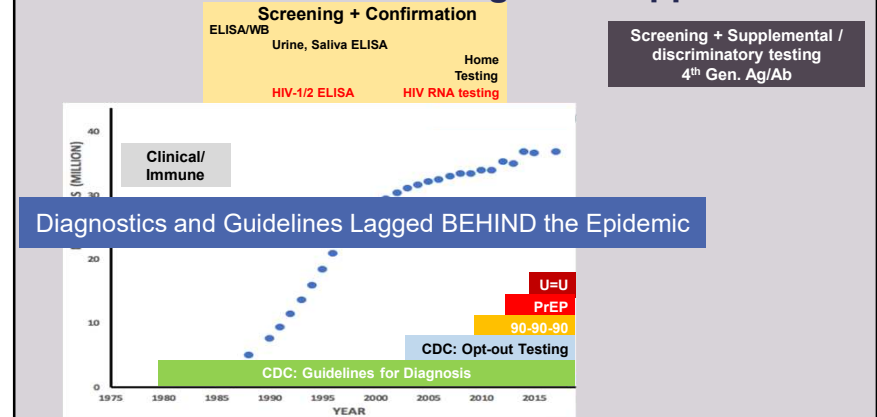
New Modalities and New Terminology Old Limitations Persist

- HIV Diagnosis
 - History
 - Physical
 - Laboratory testing
- Two Step Diagnostic Approach
- No Laboratory Test is Perfect
- False positive results require resolution
- PrEP places new stress on testing performance

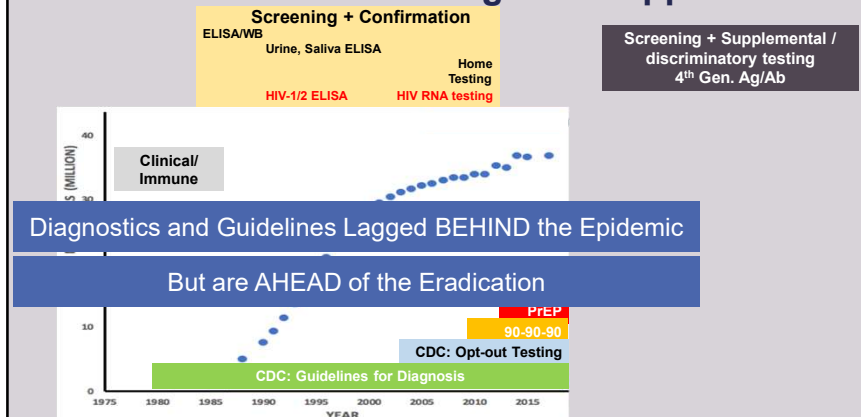
Evolution of the HIV Diagnostic Approach



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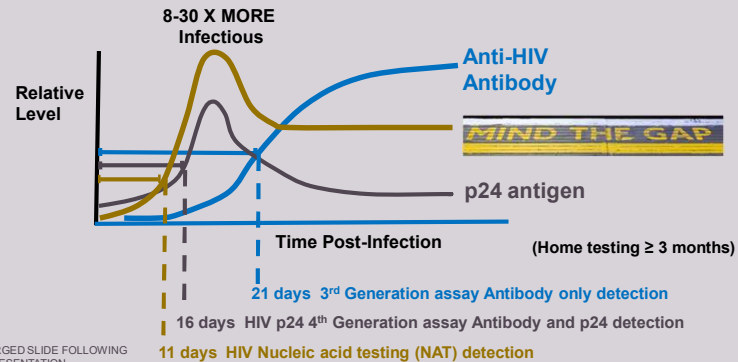
Question #2

- 27-year-old female commercial sex worker working in Washington DC visits your clinic and requests PrEP
- She shows you her home HIV test, which she took yesterday, and which is non-reactive
- She has normal laboratory results and a negative pregnancy test

Which of the following is most appropriate next step?

- She can immediately initiate PrEP with tenofovir-FTC with no additional testing
- She requires additional testing with fourth generation Ag/Ab HIV test to determine whether she is infected with a non-B subtype of HIV-1 that is not detected by the home HIV test
- She requires additional testing with fourth generation HIV test to determine whether she has early HIV infection not detected by the home HIV test
- She should not initiate PrEP because PrEP does not work well in women

HIV Detection: There is Always a Window Period



Detecting HIV Infection TWO STEPS

- Screening - Highest Sensitivity
 - 4th gen ELISA for HIV antibody + p24 antigen detection
 - Qualitative HIV RNA
- Supplemental/Discriminatory - Highest Specificity
 - GEENIUS
 - Confirms HIV-1 or HIV-2

Diagnosis of Early HIV Infection

History, Physical, Laboratory Testing

- Most sensitive Modalities
 - 4th Generation
 - HIV RNA: APTIMA
- Less Sensitive Modalities
 - Oral or urine testing
 - Home testing (3-month window)
 - GEENIUS is LESS sensitive for EARLY infection compared with 4th gen testing
- FOLLOW UP and REPEAT testing
- Antiretroviral therapy may blunt serologic immune response from maturing

Evaluation for HIV Infection During PrEP

- Every three months
- Includes detailed history and physical examination
- Ag/Ab (4th generation) testing preferred
- Viral RNA
 - Qualitative assay – FDA approved
 - Quantitative assay
 - >3000 copies/ml plasma cutoff
- DELAYED antibody emergence POSSIBLE in individuals infected during PrEP with extended-release cabotegravir

Question #3

- You are following a couple who have had a planned pregnancy
- The man is HIV positive and 100% adherent with first line therapy with Tenofovir+3TC+Dolutegravir
- The woman has had monthly fourth generation HIV testing, which has been non-reactive throughout the first two trimesters
- On the most recent visit the man has an HIV RNA was <20 c/ml, but the woman has shows HIV antigen negative and HIV antibody positive

What is the most appropriate next step?

- A. Obtain the HIV viral RNA test to find out how high the viral load is, and begin antiretroviral therapy immediately
- B. Consider laboratory error, repeat the same 4th generation test
- C. Perform supplemental testing with third generation discriminatory testing
- D. Reassure the couple that the woman is not infected and the test is just a false positive

HIV Serologic Testing Pregnancy

- False positive results with antibody testing are possible in pregnancy
- May be specific for individual's tests and persist during pregnancy
- Testing with viral RNA testing can resolve most issues
 - Qualitative tests (e.g., APTIMA) ARE FDA-APPROVED for testing
 - Expensive and generally longer turn around
 - Quantitative testing are NOT FDA-APPROVED for diagnosis
 - Rapid turnaround but low-level results are possible
- Rapid screening reactive during labor in previously untested
 - Initiate therapy
 - Do not wait for supplemental results

Question #4

- A 65-year-old American male has had unprotected sex with men for many years
- The HIV-1/2 ELISA is reactive, and supplemental testing is positive for HIV-1
- Viral RNA level is <50 copies/ml and CD4 count is 700 cells/ μ l.
- He has never been on antiretroviral therapy and has no history of travel outside the US

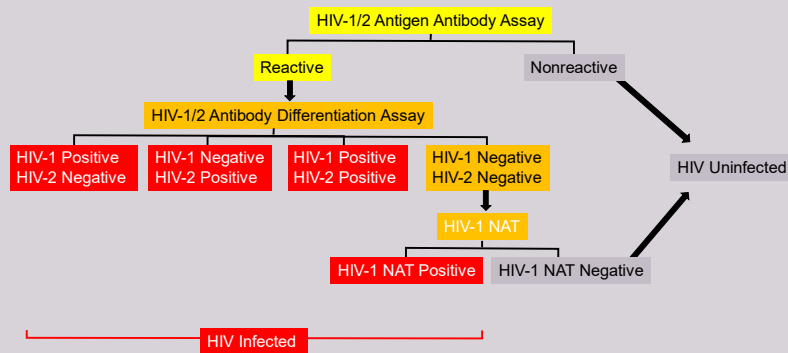
Which of the following is most likely?

- A. The patient is in the window period of HIV-1 infection
- B. The patient is chronically infected with HIV-1 and has a viral load too low to be detected because he is a long term non progressor
- C. The patient is not infected with HIV-1 or -2, all tests are false positive
- D. The patient is infected with non-B subtype of HIV-1

HIV-1 Long Term Non-Progressors

- Represents authentic HIV infection
- ELISA REACTIVE
- SUPPLEMENTAL POSITIVE
- HIV RNA may not be detectable
- Slow disease progression
- Associated with specific HLA subtypes

HIV Diagnostic Algorithm



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Question #5

- A 42-year-old woman has a reactive 4th generation test for HIV infection
- She is 7 months pregnant and had COVID-19 infection one month ago despite vaccination with Moderna COVID vaccine four months prior to testing
- She had a nonreactive 4th generation screen 7 months ago at the beginning of her pregnancy, she denies any HIV exposures
- Subsequent qualitative HIV RNA testing is negative

What is the most likely explanation for these results?

- False positive 4th generation test for HIV infection due to pregnancy
- False positive 4th generation test for HIV infection due to COVID vaccination
- False positive 4th generation test for HIV infection due to COVID infection
- False negative HIV RNA testing in the setting of recent HIV infection

MANY HIV Screening False Positives

Infections

- COVID
- African trypanosomiasis
- Babesiosis
- Schistosomiasis
- Malaria
- Dengue
- Mycobacterial
- Hepatitis A/C

Hematologic

- Polyclonal B cell responses
- Heterophile antibodies
- Workers in pork processing plant
- B cell lymphoma
- Autoimmune hemolytic anemia
- Angioblastic T cell lymphoma
- Hodgkin lymphoma

Rheumatologic Diseases

- Lupus
- Sjogren
- Rheumatoid

Iatrogenic

- Vaccines
- Rabies
- T-dap
- Hepatitis B
- SARS-CoV-2
- HIV vaccine trials
- Lentiviral therapy (e.g., CAR-T)

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

HIV Testing

- Opt-out testing is Recommended by IDSA and CDC
 - Patients are informed that an HIV test will be conducted unless they explicitly decline to be tested
 - Written consent in this setting is incorporated into intake
 - Counseling is available
- Opt-in: NOT Recommended by IDSA and CDC
 - Patients need to initiate the request for HIV infection
- Requirements for testing: FIVE C's:
 - Counseling
 - Consent
 - Confidentiality
 - Correct test results
 - Connection to prevention care and treatment

Pearls for Board Exam

HIV Testing is Comprehensive

- Non-B Subtypes are all detectable
- HIV-2 has an approved diagnosis
- Long term Non-Progressor
 - ELISA reactive / Supplemental Positive

Resources:

<https://www.cdc.gov/hiv/guidelines/testing.html>
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Reference slides follow

No Test is Perfect

- 4th Gen less sensitive
 - Acute
 - PEP/PrEP
 - Early Antiretroviral therapy
- False Positives
 - Pregnancy
- Mind the gap
 - Long gap for Home testing

Board exam isn't perfect either...so don't overthink it

