

Diagnosis and Staging of HIV

Objectives



- Describe the various diagnostic tests and how they work
- Interpret the results of the tests and make a diagnosis
- Discuss guidelines for testing in your local situation based on availability and cost of tests
- Establish the stage of the disease and exposure to other infectious diseases through a baseline laboratory evaluation of CD4+ cell count

Laboratory Testing: Overview



1. Introduction
2. Diagnostic tests in use
3. WHO testing strategy
4. Staging of disease

Introduction



- HIV antibody tests detect antibodies formed by the immune system against HIV
- In order to test positive, a patient would need to have been infected long enough to develop antibodies (usually 6 wks to 6 months)
- We will discuss testing strategies which Nigeria has adopted

LABORATORY TESTING : HIV/AIDS



Purposes

- **Laboratory diagnosis**
 - Adults
 - Children
 - <18 months
 - >18 months
- **Monitoring progression of HIV in ART naïve cases**
 - CD4 T-cell estimation
 - Viral load estimation
- **Monitoring response to ART**
 - CD4 T-cell estimation
 - Viral load assay

Basic Serologic Testing



- Rapid Tests
 - Various tests that provide results in ~10 minutes
 - Sensitivity approaches 100%; specificity is >99%
 - Negative tests can be reported as negative, assuming proper laboratory quality assurance system in place (such as use of controls)
 - Positive results should be confirmed, perhaps using a 2nd rapid test for antibodies to another part of the virus.
 - Useful in situations where immediate results are important to manage decisions

More Advanced Serologic Testing



- ELISA/EIA
 - Tests for a number of antibody proteins in combination
 - A *very sensitive* test, but not very *specific*
 - Positive result means sample needs to be tested by western blot or different ELISA test

More Advanced Serologic Testing, cont'd



- Western blot test (WB)
 - Used as a confirmatory test
 - Very specific for HIV
 - Antibodies to only a selection of viral proteins may yield an indeterminate Western blot
 - Bands corresponding to p24 and p55 are detected early in seroconversion followed by glycoprotein bands
 - Not routinely used in PEPFAR programs

Other HIV testing modalities



- DNA PCR
 - A qualitative test used to detect intracellular virus
 - Can detect 1-10 copies of HIV proviral DNA
 - Primarily used for viral detection with infant infection and with indeterminate serology
- RNA PCR
 - Measures “viral load” in copies/ml
 - Used more for monitoring than diagnosis
 - Can have an undetectable viral load (virus levels so low that the machine can't detect it) but still be HIV+
 - Rare, but possible even when not on therapy
 - May be used to diagnose infection in infants since viral load is usually very high

Voluntary Testing and Counseling (VCT)



- HIV testing for individual diagnosis should be performed according to the rules of voluntary counseling and testing (VCT) services.
- The rationale behind VCT is that people can make an educated decision about whether or not they want to test for HIV
 - may also reinforce preventive behavior in seronegative people
 - If people know they are seropositive, they can take preventive measures.

WHO Testing Strategy



- HIV infection is diagnosed by a positive HIV test.
- WHO has recommended testing strategies based on a combination of rapid tests that do not require expensive Western Blot confirmation assays.
 - Nigeria Ministry of Health has adopted these strategies
- HIV diagnosis based purely on clinical features is less common
- Use confirmatory assays to resolve indeterminate results for diagnostic purposes.

Testing Strategy Summary



- First rapid test
 - If positive, repeat with a second test
 - If negative, no need for 2nd test; patient is reported as negative
- Second rapid test
 - If positive, patient is reported as positive
 - If negative, this is an “indeterminate” result
 - * need 3rd test as tie breaker
- Third rapid test
 - “Tie Breaker”

Window period



- Window period = time in which a person may actually be infected with HIV but test negative
 - May take 6 weeks to 6 months (usually < 3 months) to develop antibodies in order to test positive
 - HIGHLY infectious during this time, as viral load is very high before there is an antibody response
- People who test HIV negative should be strongly counseled to return in three months for repeat testing
 - Should abstain from sex or practice safe sex while waiting for next test, or else they would need to test 3 months later from that repeat test

CD4 Counts



CD4 cell count

- Normal range: 500-1400/mm
- CD4 depletion is the most consistent and notable laboratory abnormality observed in HIV disease.
- This is the most useful test for assessing immune function.
- Knowing the baseline CD4 is of vital importance in assessing the patient.
- Staging of HIV infection, recommendations for ARV treatment, and prophylaxis against OIs are based on the degree of immunosuppression

The WHO Clinical Staging System



- A. The WHO staging system includes a clinical classification system and a laboratory classification to categorize the immunosuppression of adults by their *total* lymphocyte counts
- B. This staging system has been proven reliable for predicting morbidity and mortality in infected adults
- C. The WHO Clinical Staging System is based on clinical markers believed to have prognostic significance resulting in four categories. It is helpful to incorporate a patient performance scale into the system.

WHO Clinical Classification System



- Stage I:** Asymptomatic, generalized lymphadenopathy
- Stage II:** Weight loss <10%, prurigo, fungal nail infection, herpes zoster, recurrent URTIs
- Stage III:** Weight loss > 10%, chronic diarrhea or fever, oral candidiasis/HL, pulmonary TB, severe bacterial infections
- Stage IV:** AIDS-defining illnesses: e.g HIV wasting syndrome, PCP, brain toxoplasmosis, candida oesophagitis, extra-pulmonary TB, CMV retinitis, Kaposi's sarcoma, non-Hodgkins lymphoma and/or performance score 4: bedridden >50% of the day during the last month

Clinical and Immunologic Staging



Laboratory axis		Clinical Axis			
	CD4	Stage 1 Asymptomatic PGL	Stage 2 Early HIV	Stage 3 Intermediate	Stage 4 Late AIDS
A	>500	1A	2A	3A	4A
B	200-500	1B	2B	3B	4B
C	<200	1C	2C	3C	4C

- Hashed area represents those with case definition of AIDS
- Note, not everyone with HIV has AIDS