Updated HIV Testing Terminology and Technology

Michele Owen, Ph.D
Associate Director for Laboratory Science
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention

HIV Diagnostics Conference 101 Workshop
March 21, 2016

The findings and conclusions are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention. Tradenames are used for informational purposes and does not constitute an endorsement by CDC.
Alphabet Soup

- **Immunoassay (IA)** – a biochemical test that detects the presence of a substance in a biological specimen using the binding of an antibody to its antigen

- **Enzyme immunoassay (EIA or ELISA)** – an immunoassay that uses the catalyzing properties of an enzyme for detection of an immunological reaction

- **Chemiluminescent assay (CIA or CMIA)** – an immunoassay in which the signal is generated by a compound that emits light as the result of a chemical reaction

- **Nucleic acid test (NAT) (qualitative)** – molecular assays for detection of the presence of viral nucleic acids (DNA or RNA); NOTE: Sometimes referred to as nucleic acid amplification test (NAAT)

- **Nucleic acid test (NAT) (quantitative)** – molecular assays for quantification of viral nucleic acids (DNA or RNA); NOTE: Sometimes referred to as viral load assays

- **Initial or Screening test** - first test done in the field or in an algorithm

- **Supplemental test** - test used in an algorithm to "confirm" a previous result
SeroLogic Assays

Lysate indirect IgG

- Labeled anti-human IgG
- anti-HIV IgG
- HIV particle proteins

Peptide/recombinant protein indirect IgG

- Labeled anti-human IgG
- anti-HIV IgG
- HIV synthetic or recombinant proteins

Conjugated Synthetic Peptide IgG/IgM

- anti-HIV IgG
- anti-HIV IgM
- HIV synthetic or recombinant proteins

Antigen/Antibody Combo

- anti-HIV IgG
- anti-HIV IgM
- labeled p24 monoclonal
- HIV synthetic or recombinant proteins
- p24 monoclonal
Serology Technology

- Bio-Rad GS HIV Combo Ag/Ab
  ~ 3-4 hours

- Abbott Architect Ag/Ab Combo Assay**
  ~30 mins

- Alere Determine™ HIV-1/2 Ag/Ab #
  ~25 mins

- BioPlex® 2200 HIV Ag-Ab ** #
  ~ 1 hour

- ADVIA Centaur® HIV Ag/Ab Combo** #
  ~ 1 hour

• Need HIV algorithm data #
• Automated platforms – multiple pathogens **
Rapid Test Soup

• Characteristics
  – Individual sample
  – Produces result in 30 min or less
  – Currently 3 general platforms
    • Lateral Flow
      – Sample flows “up” test strip over antigen lines
      – Often CLIA waved
    • Dual Path Platform (DPP)
      – Sample and reagents flow from different directions
    • Flow Thru (Immuno-concentration)
      – Sample flows thru membrane containing antigens
      – Generally moderate complex
Immunochromatography
Lateral Flow

Key

- = Anti-HIV IgG
- = IgG (non-HIV)
- = Protein A colloidal gold
- = Antigen

Side View
- Wicking Pad
- IgG control antigen
- HIV Ag or Ab
- Conjugate pad with Protein A colloidal gold
- Sample addition port

Top View
- Sample addition port
- Sample
- Time (T)
- Conjugate pad with Protein A colloidal gold
- IgG control antigen
- HIV Ag or Ab
- Wicking Pad
Dual Path Platform (DPP)

After sample addition

Test Control

After reagent addition

Test Control

Sample 1st

Reagents 2nd

= HIV Ab

= Protein A colloidal gold
1. Wash

2. Anti-IgG enzyme conjugate

Sample

- Color reaction produced by enzyme substrate reaction

1. Wash

2. Protein A colloidal gold conjugate

3. Wash

Sample

- Color reaction produced by protein A colloidal gold binding to Ab

**Key**

- Green: Anti-HIV IgG
- Red: IgG (non-HIV) control
- Orange: Enzyme labeled anti-human IgG
- Yellow: Enzyme substrate
- Green: Protein A colloidal gold
- Red: HIV antigen
- Orange: non-HIV antigen
Moderate Complexity

Reveal G3
2003

Geenius™
2014

Multispot HIV-1/HIV-2
2004
Laboratory Markers of HIV Infection

Days since detectable RNA

HIV RNA (plasma)

HIV p24 Ag

HIV Infection?

Eclipse

IgM

IgG

Sequence of HIV Assay Reactivity During Early HIV Infection Relative to Western Blot*

*Assay sensitivity above is based on frozen plasma only. Whole-blood and oral fluid has not been characterized for early infection.

**Current data suggests that the Gen-Probe Aptima can detect HIV-1 RNA ~5-28 days after infection.

More Acronyms and Terminology 😊

- **PCR** – Polymerase chain reaction
  - Cyclic biochemical reaction that requires multiple temperatures
  - **RT-PCR**
    - Reverse Transcriptase PCR
      - RNA to cDNA (Viral Load)
    - Real-Time PCR
      - Allows real time monitoring of product

- **TMA** – Transcription mediated amplification
  - Uses gene transcription as the basis for amplification - isothermal
Both methods can be multiplexed qualitative or quantitative

Karan et al. Journal of the American Academy of Dermatology, 2005
Current NAT Technology

Hologic Aptima HIV-1 Qualitative NAT

Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1*

Abbott RealTime m2000*

Roche cobas® 6800*

* Not FDA approved for diagnosis
NATs on the Horizon

Hologic Panther

Cepheid GeneXpert® System

Diagnostics for the Real World

SAMBA

Alere™ Q System

Liat™ Analyzer Roche
Thanks!
Questions?

mowen@cdc.gov