ARCHITECT® HIV Ag/Ab Combo Assay: Correlation of HIV-1 p24 Antigen Sensitivity and RNA Viral Load Using Genetically Diverse Virus Isolates

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What is Acute Phase of HIV Infection?

Appearance of markers of HIV infection

- Absence of HIV specific antibodies
- Detect AHI by NAT or p24 antigen
- Rapid rise in plasma viremia
- Acute viral syndrome: fever, rash, diarrhea, fatigue, headache

Why is Detection of AHI Important?

- AHI makes a significant contribution to the ongoing epidemic
  - May account for 15-50% of new infections
  - Quebec study: 10% AHI accounted for 49% of transmissions

- During the acute phase, the risk of transmission is ~26-fold higher compared to asymptomatic chronic phase
  - Period of high viremia
  - Virus appears to be more infectious

- Individual unaware of infection status
  - Often test negative

Hollingsworth TD, et al, JID 2008; 198:687-693
Acute HIV Infection: Often Overlooked

- 40-90% of individuals develop symptoms with AHI
  - Symptoms typically begin 1-4 weeks following exposure
  - Duration of symptoms can be from days to several weeks

- 50-90% of individuals with symptoms seek medical care

- Missed Opportunities: many HIV-1 infected individuals access health care but are not tested
  - Generic symptoms: fever, rash, fatigue, …
  - Unrecognized risk

- Testing is part of the solution
  - More HIV testing – move away from risk-based testing
  - Use HIV assays that can detect acute, recent and chronic infections

Weintrob et al., *Arch Int Med* 2003;163:2907
Evolution of Test Reactivity:
Based on seroconversion panels

What is RNA Viral Load When HIV Combo Becomes Reactive?

- RNA detected
- HIV Combo reactive
- Total absence of antibodies to HIV
Study

- HIV-1 Group M Ag panel
  - 35 virus isolates derived from cell culture
  - Each diluted to 4 levels in HIV negative human plasma

- Test each sample:
  - ARCHITECT® HIV Ag/Ab Combo: S/CO value
  - RealTime® HIV-1: RNA copies/mL
  - Determine RNA copies/mL at HIV Combo assay cutoff (S/CO=1.0)

- Total absence of antibodies to HIV

- Impact of strain diversity
  - Subtypes A, B, C, D, F, and G
  - CRF01 and CRF02
  - URF_AB and URF_AG
ARCHITECT® HIV Ag/Ab Combo (HIV Combo)

- Chemiluminescent microparticle immunoassay for *in vitro* diagnostic use.

- Simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV-1 group M and group O and/or HIV-2 in human serum and plasma (EDTA and heparin).

- Intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary infection.

- HIV p24 Ag analytical sensitivity: 18.39 pg/mL (CE marked <2.0 IU/mL*).

RealTime® HIV-1 Assay

- Quantification range: $40 - 10^7$ RNA copies/mL
- Real-time detection using a partially double-stranded fluorescent probe design allows detection of diverse group M subtypes and group O isolates.
- Intended use is to aid in assessing viral response to antiretroviral treatment. Not intended for donor screening or as a diagnostic test to confirm HIV infection.

Package insert: 6L18, 51-602146/R2
Correlation of HIV Combo S/CO and RNA Copies/mL:

- 58,500 RNA copies/mL @ HIV Combo S/CO=1.0
  - N=2  RNA copies/mL > 58,500 and HIV Combo S/CO <1.0
    - 61,700 and 85,100
  - N=6  RNA copies/mL < 58,500 and HIV Combo S/CO >1.0
    - range 44,700 – 57,500
RNA Copies/mL at HIV Combo Assay Cutoff

- Range: 26,400 – 102,000 RNA copies/mL
- Median Value: 57,900 copies/mL
- Results consistent for different subtypes/CRFs
Acute HIV Infected Human Specimens: RNA+, Ab-

N=1

N=66

N=24

N=6

RNA copies/mL vs. HIV Combo S/CO


Put science on your side.
Survey of HIV Diversity In the US: ARUP Collaboration

- $n = 24,386$; 46 states
- 3.3% non-B strains ($n=798$; 37 states)
- 5 subtypes; 23 CRFs; 25 URFs

Pyne et al (Manuscript submitted)
Limit of p24 Ag Detection for HIV-1 Group M Isolates:
Ten CE marked Ag/Ab Combination Assays

- 79 unique isolates
- Ag concentration: Innotest p24 Ag assay w/ WHO standards
Conclusions

- ARCHITECT HIV Ag/Ab Combo Ag sensitivity at the assay cutoff correlates to approximately 58,000 copies/mL (range 26,000 – 102,000).
- This value is consistent with data reported for AHI in humans.
- This value is not impacted by HIV-1 strain genetic diversity.
- Results do not apply to other HIV Ag/Ab combination assays as assays vary widely in their limit of detection for Ag.

- ARCHITECT HIV Ag/Ab Combo assay with sensitive Ag detection reduces the window period relative to HIV antibody assays and detects a significant number of AHIs that are RNA+, Ab-.
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