Point of Care tests for HIV in Australia: update

NSW State Reference Laboratory for HIV
Centre for Applied Medical Research
St Vincent’s Hospital Sydney

Philip Cunningham
Presentation

• Situation in Australia
• PoCT and the HIV ‘window period’
• Test performance
• What’s available
• Considerations
Types of HIV tests

Screening test – *higher sensitivity*
Immunooassay (EIA, CEIA, rapid test)
Antibody (Ab) or Ab/Ag (4th generation)
**Purpose:** to identify the true negatives (without infection)

Confirmatory tests – *higher specificity*
Western Blot (Ab) ‘gold standard’
Second rapid test – different test principle, format, manufacturer
Supplementary tests – HIV-2 differentiation tests, nucleic acid (PCR) test, HIV Ag (p24), direct detection tests
**Purpose:** to identify the true positives (with infection) and false positives
Situation in Australia

Rapid tests have available in Australia for use in laboratories for over 10 years
Used in confirmatory testing strategies

First POC test was registered on the ARTG in December 2012 – Alere HIV ½ Ab/Ag combo
Several candidate HIV PoCT tests are in the regulatory pipeline including HCV
First Quality Assurance scheme rolled out 2 years ago (RCPA serology QAP)
3.4 Promote HIV testing, making HIV testing easier to have a test

- Increasing access and increase frequency
- Remove barriers to testing – returning for results, cost barriers, recommended frequency
- Introduce rapid testing
- Reduce late diagnosis of HIV
The Melbourne Declaration 2012

ACTION AREA 1: Substantially increase access to and uptake of voluntary HIV testing in Australia

Make rapid HIV testing widely available in clinical and community settings.

Expedite TGA licensing of reliable rapid HIV tests and funding arrangements with States/Territories (including through Medicare).

States and Territories to set up access programs for rapid HIV testing pending Commonwealth licensing and funding.

Investigate options to make rapid HIV tests available for home use, with appropriate linkages to STI screening.
# National HIV Testing Policy 2011

## Table 1: Categorisation of HIV IVDs for evaluation and use

<table>
<thead>
<tr>
<th>Purpose or uses of IVDs</th>
<th>Standard</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Donor Testing</strong> – screening of blood and tissue donations</td>
<td>Enzyme immunoassay</td>
<td>Enzyme immunoassay</td>
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<tr>
<td></td>
<td>Particle agglutination assay</td>
<td>Western Blot</td>
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<td></td>
<td>Machine-based immunoassay</td>
<td>Line assay</td>
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<tr>
<td></td>
<td>Nucleic Acid Amplification Test (NAAT) screening test</td>
<td>Rapid short incubation test (PoC)</td>
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<tr>
<td></td>
<td><strong>Class 4 IVD</strong></td>
<td><strong>Antigen enzyme immunoassay</strong></td>
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<tr>
<td></td>
<td></td>
<td>Discriminatory NAAT assay</td>
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<tr>
<td></td>
<td></td>
<td>Qualitative amplification assay</td>
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<tr>
<td></td>
<td></td>
<td>Quantitative amplification assay</td>
</tr>
<tr>
<td><strong>Diagnostic Testing</strong> – to determine the infection status of a sample for clinical and non-clinical purposes e.g. diagnosis, antenatal screening, viral insurance testing and supplemental and confirmatory purposes</td>
<td>Enzyme immunoassay</td>
<td><strong>Class 4 IVD</strong></td>
</tr>
<tr>
<td></td>
<td>Particle agglutination assay</td>
<td><strong>Class 4 IVD</strong></td>
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<td>Machine-based immunoassay</td>
<td><strong>Class 4 IVD</strong></td>
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<td><strong>Class 4 IVD</strong></td>
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<td>Assay used with alternative sample types</td>
<td><strong>Class 4 IVD</strong></td>
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<tr>
<td></td>
<td><strong>Class 4 IVD</strong></td>
<td><strong>Class 4 IVD</strong></td>
</tr>
<tr>
<td><strong>Point of Care testing</strong> – the use of rapid/short incubation test as a screening test for presumptive HIV infection. Not intended to replace conventional diagnostic testing or for home/self testing</td>
<td>Rapid short incubation test (PoC)</td>
<td><strong>Class 4 IVD</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Class 4 IVD</strong></td>
<td><strong>Class 4 IVD</strong></td>
</tr>
<tr>
<td><strong>Unlinked epidemiological surveillance</strong> – or definition of infection status of a population where no results are conveyed to individuals from whom samples are taken</td>
<td>HIV incidence assay</td>
<td><strong>Class 3 or Class 4 IVD</strong> depending on other intended purposes for the test; epidemiological surveillance is not a therapeutic use</td>
</tr>
<tr>
<td></td>
<td>Assays used with alternative sample types/sample collection devices</td>
<td><strong>Class 3 or Class 4 IVD</strong> depending on other intended purposes for the test; epidemiological surveillance is not a therapeutic use</td>
</tr>
<tr>
<td><strong>Monitoring and management</strong> – quantifies or characterises the virus for clinical management</td>
<td>Quantitative Nucleic Acid (viral load)</td>
<td><strong>Class 3 IVD</strong></td>
</tr>
<tr>
<td></td>
<td>Amplification assay</td>
<td><strong>Class 3 IVD</strong></td>
</tr>
<tr>
<td></td>
<td>Antigen enzyme immunoassay</td>
<td><strong>Class 3 IVD</strong></td>
</tr>
<tr>
<td></td>
<td>HIV genotypic drug resistance assay</td>
<td><strong>Class 3 IVD</strong></td>
</tr>
<tr>
<td></td>
<td>Pharmacogenomic assay for HIV drug susceptibility</td>
<td><strong>Class 3 IVD</strong></td>
</tr>
</tbody>
</table>
Rationale for Change

- HIV diagnoses increasing
- Study evidence that people (MSM) would test more regularly if more accessible (PASH)
- Widely used, developed & developing settings
- Rates and frequency of testing falling
- Testing precedes treatment
- Renewed enthusiasm for preventing HIV and talk of eradication or defeat of HIV
HIV and STI Testing

- 60.7% people never tested thought they were at low risk
- Incentives to increase frequency of HIV testing include able to obtain results in a few minutes (75.2%), home testing (65.5%), greater convenience (58.4%)
- Frequency of HIV testing among HIV-negative men (n=1738)

Pleasure and Sexual Health, the PASH study, Prestage G et al. NCHECR 2009
Out of the 12,500-15,000 people living with HIV in NSW,

- 10,178 know they are living with HIV
- 5,496 receive ART
- 5,166 have suppressed VL

Diagnosing HIV

Data source: David Wilson, Kirby Institute
Limit of detection for HIV Point of care tests

Adapted from McMichael AJ et al. Nature Rev Immunol 2010
Sensitivity of assay reactivity during early HIV-1 infections relative to number of days before first positive WB

- NAT
- 4th gen IA
- 3rd gen IA
- Rapid tests
- 2nd gen IA
- WB POSITIVE

Days before positive Western blot

-25 -20 -15 -10 -5 0

Aptima GenProbe(26) Architect Combo (20) BioRad combo (18) Determine Combo Ag+Ab (15.5) Advia 3rd (13) BioRad + O (12) Determine Combo Ab (11.5) Statpak & Complete (11) Multispot (7) Avioq (6) Inni (9) Oraquick (6) Unigold (2)
### Why no PoCT until now?:
Predictive values for rapid HIV tests

<table>
<thead>
<tr>
<th>HIV prevalence</th>
<th>0.1%</th>
<th>1%</th>
<th>5%</th>
<th>10%</th>
<th>30%</th>
</tr>
</thead>
<tbody>
<tr>
<td>NPV single test</td>
<td>100%</td>
<td>100%</td>
<td>99.9%</td>
<td>99.9%</td>
<td>99.6%</td>
</tr>
<tr>
<td>PPV single test</td>
<td>9%</td>
<td>50%</td>
<td>84%</td>
<td>92%</td>
<td>98%</td>
</tr>
<tr>
<td>PPV two tests</td>
<td>91%</td>
<td>99%</td>
<td>99.8%</td>
<td>99.9%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Assuming 99% sensitivity and 99% specificity

*WHO/CDC rapid testing guidelines 2004*
Australian HIV PoCT trials

- Victoria – Melbourne Sexual Health Centre
  Dr Tim Read

- Queensland - Brisbane Sexual Health Centre
  Dr Joe Debattista

- NSW – Sydney - Kirby Institute UNSW
  Dr Damian Conway

**Preliminary study results show:**

- Duration of time in the clinic was about the same
- Reports about PoCT acceptability was high
- Reports of likelihood of more frequent testing higher
- Reports of false positive results greater than conventional testing
- Some false negatives reported
- Field studies involving HIV(-) will not provide good data on test sensitivity
First test registered on ARTG December 2012
Alere Determine HIV-1/2 Ag/Ab combo

Easy to use point-of-care screening for HIV infection with results in just minutes.

Screen in just 3 Easy Steps

1. Prepare Test
   Tear one strip from the right and remove cover.

2. Add Sample
   Add sample of whole blood, wait 1 minute and add chase buffer.
   Also compatible with serum and plasma.
   Read full instructions prior to running test.

3. Read Results
   Read the results for both the HIV-1 p24 antigen (Ag) and HIV-1/2 antibodies (Ab) – in just 20 minutes.
   The control line should appear for all results. If it does not appear, the results are invalid.

Result Key

<table>
<thead>
<tr>
<th>Line</th>
<th>Positive</th>
<th>Negative</th>
<th>Invalid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ag</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ab</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
TGA conditions

A. Can be supplied to NATA accredited laboratories that participate in External Quality Assurance Program (EQAS)

B. Performed by Health Professionals working for an organisation that:
   • established relationship with NATA accredited laboratory
   • Participates in EQAS for PoCT
   • Training declaration every 12 months
   • Issues with NPAAC Supervision of Laboratories?
   • NATA accreditation issues?
   • Standardised Training?
Immunochromatography (ICT) (lateral flow)

- IgG Ab
- α-HIV Ab
- HIV-Ag
- α –hu-IgG
- label

Sample

HIV Ab

Hu-IgG
Oral fluid
OraQuick HIV-1/2
Identification of acute infection with HIV PoCT

Branson (CDC) reported 3 studies which failed to identify between 9% and 25% of participants found to have detectable HIV RNA testing.

FDA announcement indicated that 1 in 12 HIV(+) individuals could be missed by the OTC device (sensitivity 92%)

Urgently need more research on the contribution which acute HIV infection has on HIV numbers

July issue of PLoS looks at this issue and implications. But is not conclusive
Sensitivity Study – SVH

Acute HIV infection cases (n=58)
patients with serological evidence seroversion ie. 4th generation Ab/Ag combo +; p24 Ag detected; evolving WB, followup serum within 2 weeks; NAT detected

Newly diagnosed HIV cases – treatment naïve (n=100)
HIV positive – BED incidence CEIA classified incident (infected in last 6 months) (n=50)

HIV positive – BED incidence CEIA classified established >6 months) (n=50)

HIV seronegative (by 4th generation EIA) (n=50)
## Six (6) HIV rapid tests assessed

<table>
<thead>
<tr>
<th>Test</th>
<th>Sample</th>
<th>Time to result</th>
<th>Principle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alere HIV-1/2 Ag/Ab combo</td>
<td>Capillary blood</td>
<td>20-30 mins</td>
<td>ICT</td>
</tr>
<tr>
<td></td>
<td>50uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alere HIV-1/2 Ab</td>
<td>Capillary blood</td>
<td>15-25 mins</td>
<td>ICT</td>
</tr>
<tr>
<td></td>
<td>50uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trinity Uni-Gold HIV-1/2 Ab</td>
<td>Capillary blood</td>
<td>10-20 mins</td>
<td>ICT</td>
</tr>
<tr>
<td></td>
<td>60uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insti HIV-1/2 Ab</td>
<td>Capillary blood</td>
<td>2-5 mins</td>
<td>Immunoconcentration</td>
</tr>
<tr>
<td></td>
<td>50uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biorad Multispot HIV-1/2 Ab</td>
<td>Serum/plasma</td>
<td>10-12 mins</td>
<td>Immunoconcentration</td>
</tr>
<tr>
<td></td>
<td>50uL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orasure Oraquick HIV-1/2 Ab</td>
<td>Oral fluid or</td>
<td>20-30 mins</td>
<td>ICT</td>
</tr>
<tr>
<td></td>
<td>10uL ser/pla</td>
<td></td>
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</tr>
</tbody>
</table>
Quality issues relate to adequate sample collection and training.
Photographed results: 10 results/test x 4 tests

Participants:
Non-Laboratory (n=19), Laboratory (n=22) & Pathologists (n=34)

Sessions:
Before & After Training

6000 data entries

Source: Chiu, C etal NRL 2006
Correct interpretation (%)
Difficult results

- Non-Laboratory:
  - Before Training: 57.6%
  - After Training: 91.5%

- Laboratory:
  - Before Training: 58.0%
  - After Training: 96.5%

- Pathologist:
  - Before Training: 87.6%
  - After Training: 70.0%
Rapid testing strategy

Blood / Oral fluid Sample

PoCT

Negative
Result given

Reactive ‘presumptive’

Test 2

Negative
Result given

Positive result
Retest to confirm or Result given

Discordant
Retest after 6 weeks
Referral lab

Test 2 – may be conventional test performed in a laboratory

Adapted from: WHO/CDC rapid testing guidelines 2004
Importance of Quality Assurance

RCPA Serology QAP – HIV PoCT

- Program established 2011 – 4x distributions per year
- Approximately 30 laboratories enrolled
- Majority off-shore regional labs where HIV PoCT are widely used
- 1 Australian laboratory enrolled HIV -1/2 Ag/Ab combo test
- Overall high levels of concordance and performance among participants
- Issues relate to sample types (serum/plasma not reflecting intended use (oral fluid and whole blood fingerstick))
- Issues with participants using expired reagents and poor confirmatory testing strategies
- Other EQAS providers are likely to emerge (eg. NRL)
The way forward...

- Training program for operators - accreditation
- Quality Assurance is essential
- Targeted testing - high prevalence settings - sexual health settings, high case load GPs
- Formalise ‘relationship’ with NATA accredited labs
- Reactive PoCT tests are confirmed with conventional testing
- Develop protocols and testing strategies
- Innovative education for the community
- Clear understanding about any tests limitations eg. acute infection and false positive results