Recommendations for diagnosis and monitoring of HIV infection and treatment in infants and young children

HIV/AIDS Department
World Health Organization
Global tools and guidance required: diagnosis

Policy
Principles for HIV testing in children; informed consent, disclosure, confidentiality.
Need to provide services to children
Cost and equity of access

Programme level
Which platforms, testing strategies, test kits, algorithms, how to review and validate them
Definitions of HIV infection
Burden
M and E of testing
Lab elements and Quality assurance guidance for testing modalities
Models and programme approaches for service delivery
Regular periodic independent assessment of performance characteristics of the platform/test/algorithm
Access to bulk purchase and procurement agreements
Secure supplies

Facility level
Guidance on what service providers need to do, KSB required, counselling and associated package, how, who where
Training and tools to support this
Context - rapid evolution of HIV diagnostics

• Lab/equipment based technologies
  – Virological
  – Serological
  – Antigen detection
  – Common platforms
Context - flexibility required

*Individual*

- Mothers status known/unknown
- Mother on ART
- Baby ARV prophylaxis
- Age
- Clinical symptoms
- +/- Breastfeeding

*Programmatic*

+/- virologic tests (incl DBS)
+/- serologic tests (CD4 count)

Range of Follow up mechanisms & entry points
(e.g. FL HCW/IMCI)

Background pathologies
Context - clinical issues

- Lack of specificity of clinical signs & symptoms
- Rapid disease progression in younger children
- Ongoing HIV exposure through BF
- Few sensitive specific screening algorithms
- Little recognition of risk and referral for diagnostics if in place
- Poor linkages across ART/ PMTCT/HIV T & C and CH services
What is urgently required

- Simple programmatic orientated technical recommendations
- Projections & estimation of short & long term needs to allow planning and procurement
- Reduced prices
- 'Validation of performance' of platforms
So what is in place for early infant diagnosis?
Achievable immediately

• better use of what we have (antibody testing, VL technologies)
• ensure technical uncertainly doesn’t lead to programmatic paralysis
• Simple tiered programming approaches
• attention to registration & regulatory obstacles
• clear set of priority deliverables for WHO
WHO - Current steps towards recommendations
Universal reporting of HIV infection in children

- Regional consultations: all regions agree active case reporting of ped HIV required
- Common 'lab' based HIV case definitions
- Recognition of & commitment to monitoring HIV free survival
Major new technical recommendations

- Cotrimoxazole (start, stop, dosing)
- Diagnosis – algorithm & inclusion of presumptive diagnosis of severe HIV
- Revised clinical & immunological staging
- Age related thresholds for initiation ART
- Monitoring-clinical and immunological – promote greater use of CD4
Principles of the public health approach - diagnosis

• Regardless of HIV test used or age: IF baby is still BF & and mother HIV + baby remains at risk of HIV infection through BF (i.e. ongoing exposure to HIV)

• Where exposure HIV discontinued, testing for HIV infection by the best age appropriate test available is recommended, & can be undertaken at the earliest 6 weeks post-complete cessation of BF

• for public health purposes, one positive virological test 6 or more weeks of age in a young infant with documented HIV exposure (e.g., mother or child HIV ab+ve) if lab has QA deemed sufficient to diagnose HIV infection for purposes of clinical management and initiation of treatment (including ART)
Summary of recommendations on methods for establishing the presence of HIV infection in infants and children

<table>
<thead>
<tr>
<th>Method of diagnosis</th>
<th>Recommendations for use</th>
<th>Strength of recommendation/ level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virological methods (includes DNA, RNA, and ICD p24)</td>
<td>To diagnose infection in infants under age 18 months; initial testing is recommended at age 6-8 weeks</td>
<td>A (I)</td>
</tr>
<tr>
<td>HIV Antibody testing</td>
<td>To diagnose HIV infection in mother or identify HIV exposure of infant</td>
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<td></td>
<td>To diagnose HIV infection in children 18 months or older</td>
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<td></td>
<td>To identify HIV positive children under 18 months in whom HIV infection is likely(^a)</td>
<td>A (IV)</td>
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</tbody>
</table>

Notes:

\(^a\)Children less than 18 months of age who have reactive HIV antibody tests include children who are truly HIV-infected, as well as those who still have maternal antibody but are uninfected. By the age of 12 months most uninfected children will have lost maternal antibody and positive antibody testing at this time usually indicates probable HIV infection in the child (96% specificity).
Establishing presence of HIV infection in infants and children in resource-limited settings to enable ART and HIV care (NOT to be used for exclusion of HIV)
Presumptive diagnosis of severe HIV in HIV exposed infant

Seropositive Infant;
• Symptomatic with 2 or more of the following:
  – oral thrush;
  – severe pneumonia*
  – severe wasting/malnutrition*
  – severe sepsis*

• Other factors to support diagnosis of severe HIV include:
  – Recent HIV-related maternal death; or
  – Advanced HIV disease in the mother; or
  – Documented history of no maternal or infant ARV for MTCT

• Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

(*) As defined in IMCI
## Revised Staging & Classification

### Clinical classification

<table>
<thead>
<tr>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
<th>Stage 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Mild</td>
<td>Advanced</td>
<td>Severe</td>
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</table>

### Immunological classification

| Not significant | Mild    | Advanced      | Severe        |

### Clinical classification on treatment

<table>
<thead>
<tr>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
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<tbody>
<tr>
<td>WHO Paediatric Clinical Stage on ART</td>
<td>Availability of CD4 measurements</td>
<td>Management options</td>
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<tr>
<td>T1 and T2&lt;sup&gt;c&lt;/sup&gt;</td>
<td>No CD4</td>
<td>Do not switch regimen</td>
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</tbody>
</table>
|                                   | CD4                             | Consider switching regimen only if 2 or more values below age-related threshold for severe immunodeficiency<sup>d</sup> are available  
Increase clinical and CD4 follow up if CD4 approaches age-related threshold for severe immunodeficiency |
| T3<sup>c</sup>                    | No CD4                          | Consider switching regimen<sup>e</sup> |
|                                   | CD4                             | Switching regimen is recommended if CD4 at or below age-related threshold for severe immunodeficiency<sup>d</sup> and particularly if child initially had good immune response to ART |
| T4                                | No CD4                          | Switch regimen, regardless of CD4 |
|                                   | CD4                             |  |

<sup>a</sup> Based on availability of CD4 measurement

<sup>b</sup> WHO Paediatric Clinical Stage on ART

<sup>c</sup> For non-ambulatory children under 2 years of age

<sup>d</sup> Age-related threshold for severe immunodeficiency:

- 3 years or younger: ≤ 1.0
- 4 years: ≤ 1.0
- 5 years: ≤ 1.5
- 6 years: ≤ 2.0
- 7 years: ≤ 2.5
- 8 years: ≤ 3.0
- 9 years: ≤ 3.5
- 10 years: ≤ 4.0
- 11 years: ≤ 4.5
- 12 years and older: ≤ 5.0

<sup>e</sup> Consider switching if CD4 below age-related threshold for severe immunodeficiency and particularly if child initially had good immune response to ART.
<table>
<thead>
<tr>
<th>Laboratory parameters for monitoring infants and children at baseline, prior to ART and during ART</th>
<th>Baseline</th>
<th>Monthly at initiation of 1st or 2nd line regimen (weeks 4, 8, 12)</th>
<th>Every 6 months</th>
<th>As required (i.e., symptom-directed)</th>
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<tbody>
<tr>
<td><strong>Diagnosis and monitoring laboratory tests</strong></td>
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<td>HIV diagnostic testing: virological and Ab</td>
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<tr>
<td>Hemoglobin</td>
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<td>WBC and differential</td>
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<td>%CD4 or Absolute CD4 cell count</td>
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<td>Pregnancy testing in adolescent girls</td>
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<td>Full chemistry (including, but not restricted to, ALT, liver enzymes, renal function, glucose, lipids, amylase, lipase, and serum electrolytes)</td>
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<td>Screening for TB and malaria (basic microscopy; i.e. sputum smear test for TB and thick blood drop smear test for malaria diagnosis)</td>
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<td>Full cerebrospinal fluid (CSF) microscopy (including India ink for cryptococcal meningitis), in adolescents: syphilis and other STI diagnostic tests.</td>
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<tr>
<td>Diagnostic tests for treatable co-infections and major HIV/AIDS-related opportunistic diseases</td>
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<td>Diagnostic tests for hepatitis B, hepatitis C serology, bacterial microbiology, and cultures and diagnostic tests and procedures for PCP, <em>Cryptococcus</em>, toxoplasmosis and other major OIs)</td>
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<tr>
<td>HIV viral load measurement</td>
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</table>
Key Issues: diagnostics

Virological tests
HIV RNA or DNA (PCR ) or p24
which
timing
one or two needed to confirm HIV infection

Lab capacity & QA
DBS – standardise & operationalise systems for use distant from lab,
HIV subtypes

Antibody testing
Testing – how often, how soon
Window post BF
Use as screening tool

Counselling & consent, disclosure

Presumptive clinical diagnosis
Validation required
Simple algorithms for lower levels to recognise HIV exposed & infected
Improved specificity and sensitivity with simple add ons, Hb, CD4

Mechanisms for review and revision of recommendations
Learning by doing
Key WHO web resources

 crowleys@who.int
Web page: http://www.who.int


ARV toolkit on line
All integrated management tools: http://www.who.int/hiv/toolkit/arv/en/index.jsp

Diagnostics
http://www.who.int/diagnostics_laboratory/en/

HIV testing and counselling toolkit
http://who.arvkit.net/tc/en/index.jsp

Child health
http://www.who.int/child-adolescent-health/hiv.htm

Indicators

Revised Clinical Staging
Thank you