Global statistics and guidelines for pediatric HIV testing and treatment

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Outline

• Progress to date

• WHO 2015 Guidelines highlights: Innovations for infants and children
  – Timing of virological testing
  – Use of and progress towards bringing technologies closer to the point of care
  – Initiation of ART

• Conclusion
EID coverage remains LOW

Proportion of HIV-exposed infants receiving virological testing by their second month of age.

Source: 2015 Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS); Proportion of HIV-exposed infants receiving virological testing by their second month of age.

HIV-exposed Infants received a virological test in 21 African Global Plan countries in 2014
Paediatric coverage still lags behind

Source: Global AIDS Response Progress Reporting (WHO/UNICEF/UNAIDS); Proportion of HIV-exposed infants receiving virological testing by their second month of age.
2015 WHO ARV Consolidated Guidelines

Test earlier
Test closer
Treat earlier
Minimising mortality and maximizing programme outcomes with NAT at birth

Addition of nucleic acid testing (NAT) at birth to the existing EID testing approaches can be considered to identify HIV infection in HIV-exposed infants (conditional recommendation, low-quality evidence)

Adoption should ensure:

– collection of data on performance and feasibility of birth testing
– uptake and retention in the testing to treatment cascade
– active tracking of infants with negative NAT at birth to ensure they return at 6 weeks for retesting and co-trimoxazole initiation.
– re-testing of infants who test positive at birth with a second specimen as soon as possible (ART should be started immediately after the first positive test and can be stopped if second specimen is negative).
...BUT...Experience is very limited

- The **false-positive rate** is expected to double with birth testing; confirmatory test of a first positive NAT is critical

- A **higher number of tests** have to be conducted to identify positive infants

- Adding NAT at birth can be **cost-effective under the ideal scenario**; NAT at birth should happen with **improvement of the testing-to-treatment cascade**

- **Challenges**
  - tracing of negative babies at birth
  - need for active outreach to trace positives and indeterminate need repeat virological testing.

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...BUT...Experience is very limited

- Critical components needed to roll out NAT at birth:
  - Systematic process to determine maternal HIV status
  - Adequate numbers of trained staff
  - Registers and/or EMR to document testing activities and results
  - Protocols and systems to manage newly identified HIV+ moms/babies

WE NEED MORE EXPERIENCE AND OPERATIONAL RESEARCH

Nucleic acid testing (NAT) technologies that are developed and validated for use at or near to point of care can be used for early infant HIV testing. 

*(Conditional recommendation, low-quality evidence)*

- Complement and enhance conventional testing
- **Decentralization of ART** or strengthening of referral systems for ART initiation
- Targeted **operational research** is needed to address existing knowledge gaps resulting from the limited experience to date
CDC/WHO/NHLS collaboration for qualitative NAT, including EID

- Evaluation protocol agreed by all partners
  - Two products nearly finished evaluation at CDC and NHLS testing sites
  - Expecting results in Q4 2015
- Both products are eligible for abbreviated PQ assessment
  - Thus WHO will not require submission of product dossier
- PQ site inspections already conducted for both products
Rapid Diagnostic Tests

- **Performance** of the RDTs to assess HIV-exposure or HIV-infection differs based on age.
- In children **4-18 months** the sensitivity of RDTs is low.
- Use of RDT to test the **mother** should be prioritised.

- Rapid diagnostic tests (RDTs) for HIV serology **can be used to assess HIV exposure in infants less than 4 months of age**. HIV-exposure status in infants and children 4-18 months of age should therefore be ascertained by undertaking HIV serological testing in the mother (*Conditional, low-quality evidence*).

- Rapid diagnostic tests (RDTs) for HIV serology **can be used at 9 months to rule out HIV infection** in asymptomatic HIV-exposed infants. (*Conditional recommendation, low-quality evidence*).

- Rapid diagnostic tests (RDTs) for HIV serology **can be used to diagnose HIV infection in children older than 18 months following** the national testing strategy. (*Strong recommendation, moderate-quality evidence*).
Treat All at any CD4

ART should be initiated in all **children** infected with HIV, regardless of WHO clinical stage or CD4 cell count

- Infants diagnosed in the first year of life (*strong recommendation, moderate-quality evidence*)
- Children infected with HIV one year to less than 10 years of age (*conditional recommendation, low-quality evidence*)

<table>
<thead>
<tr>
<th>Age</th>
<th>When you start</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 years to less than 19 years</td>
<td>Treat all adolescents individuals with WHO clinical stage 3 or 4 and with CD4 count ≤ 350 cells/mm³ as a priority</td>
</tr>
<tr>
<td>1 year to less than 10 years</td>
<td>Treat all children (children ≤2 years or with WHO stage 3 or 4 or CD4 count ≤750 cells/mm³ or &lt;25% in younger than 5 years and CD4 count ≤350 cells/mm³ in 5 years and older as a priority)</td>
</tr>
<tr>
<td>Infants (&lt;1yr)</td>
<td>Treat all infants</td>
</tr>
</tbody>
</table>
Starting ART early is not easy

- Dealing with limited options for newborns
- Optimising options with the best formulation available
- Monitoring closely and adjusting dosing*
- Introduction of LPVr pellets (guidance for administration and procurement)

<table>
<thead>
<tr>
<th></th>
<th>0-2 weeks</th>
<th>2 weeks - 3 months</th>
<th>3 – 36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred</strong></td>
<td>AZT + 3TC + NVP</td>
<td>ABC or AZT + 3TC + LPV/r syrup</td>
<td>ABC or AZT + 3TC + LPV/r pellets</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td>AZT + 3TC + NVP</td>
<td></td>
<td>ABC or AZT + 3TC + LPV/r pellets</td>
</tr>
<tr>
<td><strong>Special circumstances</strong></td>
<td>AZT + 3TC + NVP</td>
<td></td>
<td>ABC or AZT + 3TC + RAL (from 4 weeks)</td>
</tr>
</tbody>
</table>
Starting ART in children

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Children &lt; 3 years</th>
<th>Children 3 years to &lt; 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC + 3TC + LPV/r or AZT + 3TC + LPV/r</td>
<td>ABC + 3TC + EFV</td>
<td></td>
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</tbody>
</table>

Alternative

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Children &lt; 3 years</th>
<th>Children 3 years to &lt; 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZT + 3TC + NVP</td>
<td>AZT + 3TC + EFV</td>
<td></td>
</tr>
<tr>
<td>TDF + 3TC (or FTC) + EFV</td>
<td>TDF + 3TC (or FTC) + NVP</td>
<td></td>
</tr>
</tbody>
</table>

In summary ...NO CHANGE

- Using the most potent regimen available for young children (LPVr)
- Simplifying where feasible (substitute LPVr with EFV)
- Using RAL-based regimen in special circumstances
- Keeping ABC + 3TC as preferred NRTIs
- Maintaining EFV-based regimen to harmonise with adults
To reach treatment targets...

But collect data as you do it, knowledge gaps remain and we need to inform the future!
Thank you!

Martina Penazzato  
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Nathan Ford  
Rachel Beanland  
Jessica Markby  
Divya Mallampati  
Lara Vojnov  
Jennifer Cohn  
Andrea Ciaranello

In 2014, only 50% of all HIV-exposed infants were tested by the second month of age. Innovative approaches such as use of assays at the point-of-care and adding virological testing at birth could speed up identification and ART initiation. Operational research to fully inform how to implement such innovations remains critical.

Mortality in the first year of life is very high among untreated infants infected with HIV, therefore early infant diagnosis (EID), prompt return of results and rapid initiation of treatment are essential.  

- HIV infection in infants is only definitively confirmed with virological testing using nucleic acid testing (DNA-PCR) NAT technologies due to the persistence of maternal HIV antibody up to 18 months of age.  
- Delays in obtaining results and further losses in the testing-to-treatment cascade still occur, so that only 30% of perinatally infected infants are effectively linked to services and started on ART in a timely manner.  
- Innovative approaches such as the use of assays at point-of-care and adding NAT at birth can speed up identification and ART initiation.

Diagnosing HIV earlier

- Due to recent cost reduction for NAT assays and the expansion of EID programmes, alternative testing approaches that maximize uptake, retention and timely treatment initiation can be considered.  
- There is insufficient evidence to recommend universal inclusion of NAT at birth, however, there are expected benefits to this approach which provides an additional opportunity for testing and enables earlier identification of infected infants.  
- The addition of NAT at birth can be considered where feasible, but only in parallel with efforts to strengthen and expand existing EID testing approaches (see Box 1).

Box 1 Adding NAT at birth to the existing EID strategy

As EID programmes are further scaled up, every effort should be made to improve uptake of NAT at 4–6 weeks, strengthen retention along the testing-to-treatment cascade, ensure confirmation of NAT positive results with a second sample and ensure that infants who test negative by NAT are retained in care until a final diagnosis is made. To add NAT at birth, effective linkage to maternal HIV screening at the time of delivery should be ensured and the following steps taken:

- collection of data on performance and feasibility of birth testing during implementation;  
- improvement of uptake and retention in the testing-to-treatment cascade;  
- active tracking of infants with negative NAT at birth to ensure that they return at six weeks for retesting and confirmatory initiation; and  
- retesting of infants who test positive at birth with collection of a second specimen as soon as possible. ART should be started immediately after the first positive test and can be stopped if the second specimen tests negative.

Testing closer to the point of care

RDTs for HIV serology

Rapid diagnostic tests (RDTs) with performance comparable to that of traditional laboratory-based serological assays are commercially available and widely used in clinic or community settings with minimal infrastructure.  

- WHO 2013 Consolidated guidelines on the use of antiretrovirals recommended the use of serological assays to diagnose HIV in children older than 18 months, to ascertain exposure in young infants and children below 18 months of age and to rule out established infection after 9 months in HIV-exposed infants who are well.
Alignment of recommendations on in-vitro diagnostics (IVDs)

- WHO PQ lists IVDs that meet PQ requirements to be procured by UN agencies, WHO Member States, etc.
- USAID issues recommendations on IVDs to be procured by SCMS and used in PEPFAR-supported countries
- Aim of alignment
  - to align WHO and USG assessments and create one common QA mechanism under a partnership agreement
- Goals of alignment
  - to reduce duplication of effort for each organization and for the manufacturers, leverage each others resources for laboratory evaluation, and to create one list of "approved" products
First product for common QA mechanism

- AQUIOS CL flow cytometer
  - Beckman Coulter Life Sciences, USA
- Dossier assessed by WHO
- Site inspection by WHO
- Laboratory evaluation conducted by
  - CDC (Atlanta) and
  - WHO (ITM, Antwerp)
- Product prequalified November 2015