CURRENT AND UPCOMING WHO GUIDANCE ON PAEDIATRIC HIV DIAGNOSTICS

Martina Penazzato
HIV Department -WHO, Geneva Switzerland
Outline

• Background
• Innovations for infant testing
  – Timing virological testing
  – Technologies
  – Service delivery
• VL monitoring and Genotyping: Any special considerations for children?
Addressing the first 90 for infants and children

New Initiatives on the Horizon:
1) Diagnostics Access Initiative (DAI)
2) Paediatrics – ACT, Double Dividend, PHTI, (IATT, PAWG, PAPWG)
3) Adolescents – All in!

Requires Treatment Optimization innovation:
1) Diagnostics – CD4/VL, Forecasting, HIV-ST
2) Drugs – CADO, PADO, IATT Formulary, PAWG
3) Service delivery – Tx2.0, Care packages, QA
WHO Innovations in HIV Testing

- Self testing
- Birth testing and integrated HIV testing for kids
- Targeted testing in low prevalence epidemics
- HTC within disease campaigns

50% of PLHWA have ever tested: to reach 90% must expand testing
Innovations in Diagnostics

• Increase options & platforms
• Maintain quality
All 22 Global plan priority countries have now adopted either B or B+

In 2014: 220 000 children newly infected
EID coverage in 2014

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

50%

HIV-exposed Infants received a virological test in 21 African Global Plan countries
WHO 2010-13 testing algorithm

Is this algorithm still appropriate?
Key considerations: 3 dimensions

**WHEN**
- Should we consider doing the first virological testing earlier? **At 4-6 weeks or earlier?**

**WHERE**
- Where do we need to test to identify the majority of infants that still get infected? **PMTCT setting AND beyond?**

**HOW**
- Are there operational innovations that will facilitate scale up?
- What are the **technologies** we could consider adopting?
Optimal timing

Context:

- **When** HIV transmission occurs
- **How** services are delivered

- 50% of children living with HIV die by 2 years of age
- HIV-related mortality peaks at 3–4 months of age
- Mortality and disease progression are greater among children infected in utero or intrapartum

- The available assays are optimally performed after 4–6 weeks
- There are concerns that exposure to ARV drugs (options B and B+) reduces the sensitivity of the test by reducing viral load
- As services to prevent mother-to-child transmission expand and HIV transmission declines, the positive predictive value of a single test will be lower

- In 2012, only 35% of infants born to women living with HIV were virologically tested by 2 months of age
- Even in well-functioning programmes to prevent mother-to-child transmission, only 70% of HIV-exposed infants receive early infant diagnosis
- 40% are successfully linked to care, and only 30% initiate ART
Continue to have theoretical concerns attached to the impact that ARVs may have on the test performance at 6 weeks

Lack of robust evidence to reassure us

Potential shift to enhanced prophylaxis may further complicate this scenario

D. Mallampati et al. 2015
Poster number: WEPED891
HIV Pediatrics International Workshop Vancouver- Canada (July 17-18 2015)
### Re-testing

<table>
<thead>
<tr>
<th>Prevalence in the population initially being tested (%)</th>
<th>1-test algorithm PPV (%)</th>
<th>1-test algorithm NPV (%)</th>
<th>2-test algorithm PPV (%)</th>
<th>2-test algorithm NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>33.3</td>
<td>100</td>
<td>96.1</td>
<td>99.5</td>
</tr>
<tr>
<td>2</td>
<td>50.3</td>
<td>100</td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>72.3</td>
<td>99.9</td>
<td>99.2</td>
<td>97.4</td>
</tr>
<tr>
<td>10</td>
<td>84.6</td>
<td>99.9</td>
<td>99.6</td>
<td>94.7</td>
</tr>
<tr>
<td>20</td>
<td>92.5</td>
<td>99.7</td>
<td>99.8</td>
<td>88.8</td>
</tr>
<tr>
<td>30</td>
<td>95.5</td>
<td>99.6</td>
<td>99.9</td>
<td>82.2</td>
</tr>
<tr>
<td>50</td>
<td>98</td>
<td>98</td>
<td>100</td>
<td>66.4</td>
</tr>
</tbody>
</table>

- After a first positive virological test, **re-testing** is recommended.
- Ab testing once ART is started can be difficult interpretation (high frequency of seroreversion with early ART).

**Included in country guidelines but very rarely done**
Negative Serology with early ART

~30% HIV Ab negative if start ART age <3 mos

We need to get the diagnosis right before ART is started

Payne H et al. CROI 2014

Tejiokem et al. CROI 2014

Kuhn L et al. 20th IAS Conference, 2014

Negative Ab test while on ART does NOT mean NO HIV infection!!!
Potential benefit of testing at birth

Is mortality the only benefit?
Early treatment reduce TB incidence, reduce morbidity and reduce viral reservoir..others?
Retention in the cascade

- Testing at birth: 100%
- Using POC: 70%
- Mother receives results: 40%
- Child initiates treatment: 30%

What does it take?

Critical components for an effective newborn diagnostic testing program:

• 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

This early experience suggests that additional staffing is required. For instance in a facility with about 200 HIV-exposed deliveries/month, 30/day the following were added:

• 4 full-time counsellors
• 2 full-time staff to obtain consent, blood drawing and specimen preparation
• 1 full-time nurse: supervise counsellors, draw blood
• data-capturers: reporting, results retrieval, patient tracking
• 3-4 professional nurses managing weekly clinic where moms obtain results

Some of the challenges reported were ensuring tracing of negative babies at birth and the need for active outreach to trace and engage all positives and indeterminate to repeat virological testing.

Technau Karl et al. CROI 2015
Rahima Moosa Hospital, Johannesburg, South Africa
## Exploring the impact of introducing Birth Testing

<table>
<thead>
<tr>
<th></th>
<th>6 wk PCR (current algorithm)</th>
<th>Birth PCR + 6 wk PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NO PMTCT</strong></td>
<td>HIV+ women: 5000</td>
<td>HIV+ women: 5000</td>
</tr>
<tr>
<td></td>
<td>HIV+ infants: 1500</td>
<td>HIV+ infants: 1500</td>
</tr>
<tr>
<td></td>
<td>Total tests: 6535 tests</td>
<td>Total tests: 11035 tests</td>
</tr>
<tr>
<td></td>
<td><em>Tests per positive child: 4.36</em></td>
<td><em>Tests per positive child: 7.36</em></td>
</tr>
<tr>
<td></td>
<td><em>Per 100 infants on ART: 2 FP</em></td>
<td><em>Per 100 infants on ART: 4 FP</em></td>
</tr>
<tr>
<td><strong>PMTCT</strong></td>
<td>HIV+ women: 5000</td>
<td>HIV+ women: 5000</td>
</tr>
<tr>
<td></td>
<td>HIV+ infants: 250</td>
<td>HIV+ infants: 250</td>
</tr>
<tr>
<td></td>
<td>Total tests: 5297 tests</td>
<td>Total tests: 10130 tests</td>
</tr>
<tr>
<td></td>
<td><em>Tests per positive child: 21.2</em></td>
<td>*Tests per positive child: 40.5</td>
</tr>
<tr>
<td></td>
<td><em>Per 100 children on ART: 16 FP</em></td>
<td><em>Per 100 infants on ART: 27 FP</em></td>
</tr>
</tbody>
</table>

- A higher number of tests have to be conducted to identify positive infants.
- The false-positive rate will nearly double.

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Cost implications

- Doubled programme costs
- $470 vs $838 per correct HIV+ diagnosis.
- Birth testing alone has limited impact in terms of averting pre-ART deaths due to leakage in cascade.

Collins et al. CROI 2014.

Investing in improving retention alongside birth testing would have greater impact

Finocchario-Kessler et al. AIDS 2014
Entry points to Testing

Going beyond the PMTCT: PITC and integration of infant testing into existing service delivery platforms for HIV and child survival

WHERE

- Malnutrition
- Paeds wards
- U5C 15-70%

HIV services
- PMTCT
- ART clinics 2.6-8%

Community based-programmes
- HIV
- Nutrition ?? %

Well baby services
- EPI
- PNC 2-5 %

1. Sick babies Services
2. HIV services
3. Community based-programmes
4. Well baby services

2.6-8% 15-70% ?? % 2-5 %
In generalized epidemics, provider-initiated testing and counselling should be recommended to everyone (adults, adolescents and children) attending all health facilities, including medical and surgical services; sexually transmitted infection, hepatitis and TB clinics; public and private facilities; inpatient and outpatient settings; mobile or outreach medical services; services for pregnant women (antenatal care, family planning and maternal and child health settings); services for key populations; services for infants and children; and reproductive health services.

In concentrated and low-level epidemics, provider-initiated testing and counselling should be recommended in all health facilities for:

- adults, adolescents or children who present in clinical settings with signs and symptoms or medical conditions that could indicate HIV infection, including TB; and
- HIV-exposed children, children born to women living with HIV and symptomatic infants and children.

Provider-initiated testing and counselling should be considered in sexually transmitted infection, hepatitis and TB services, antenatal care settings and services for key populations (notably men who have sex with men, transgender people, sex workers and people who inject drugs).
Universal testing of pediatric populations in key contexts offers high-yield opportunity to identify HIV-infected children

- Peds inpatient > Nutrition >> peds outpatient and EPI
- Triggered testing does not seem to have benefit over universal testing in peds inpatient
- Very high rates (compared to background population) in West and Central Africa
Total of 827 HIV-exposed infants were tested on both the qNAT and the Roche reference technology (65 +). 60% were tested between 1-2 months of age. Only 2 discordant samples were found. Sensitivity of the qNAT was 98.5%, specificity was 99.9% (Jani et al. JAIDS 2014)
Mean turnaround times for paper- and SMS-based results receipt excluding the largest study:

- 50.0 days, n=3,626
- 29.9 days, n=3,357

Courtesy of L Vojnov, CHAI
Results are currently received and clinical decisions made after the peak of mortality using paper-based systems.

DBS sample collected
Result returned to facility

Caregiver receives result

50 days

HIV/AIDS-related mortality counts

Age at death (months)

Bourne AIDS 2009
SMS printers can reduce the time to result receipt

- DBS sample collected
- Result returned to facility

Caregiver receives result

30 days

Bourne AIDS 2009
Moving Forward

- Moving towards a multi test algorithm
- Recognizing the potential value of adding virological testing at birth
- Emphasizing confirmatory test
- Optimizing the use of RDTs
- Opening the door to the use of POC which meet accuracy standards
- Emphasizing PITC at different points of entry
- Acknowledging the role of the community in creating demand
- Promoting tailored testing approaches to the epidemic setting and geographic focus (yield analysis)
WHO future directions for CD4 and viral load

ART initiation for all people living with HIV irrespective of CD4 count

In settings where viral load is routinely available, CD4 monitoring can be reduced or stopped in stable patients

CD4 cell count should be taken at baseline to support management decisions and determine risk of disease progression [and may be important for individuals failing therapy]
Acknowledgements

Divya Mallampati
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Lara Vojnov
Jennifer Cohn
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TESTING, NEW DIRECTIONS IN TREATMENT, AND MEASURING IMPACT: NEW WHO GUIDELINES
SATELLITE (SUSA06)

SUNDAY 19 JULY 12:30-14:30, Room 211-214 (Snacks will be served at this session)

In this satellite WHO will launch the new 2015 WHO consolidated guidelines on HIV testing services (HTS), share new directions and evidence that will shape the 2015 update to the Consolidated guidelines on the use of ARV drugs for treating and preventing HIV, and discuss the new 2015 Consolidated strategic information guidelines for HIV in the health sector.

The satellite features perspectives from WHO, members of the guideline development and systematic review groups and countries.

Moderator: Gottfried Hirnschall, Director HIV Department, WHO

Part one: Testing: New WHO guideline and new directions in self-testing (50 min)

Chairs:
Rusanne Barnabas, University of Washington, USA
Francois Venter, University of Witwatersrand, South Africa

Presentation:
Rachel Baggaley, Coordinator Key Populations and Innovative Prevention, and Cheryl Johnson, Consultant, HIV Department, WHO

Country Panel and Discussion:
HVST in Brazil, Fabrio Mesquita, Department of STIs, AIDS and Viral Hepatitis, Brazilian Ministry of Health
HVST in Rwanda, Sabine Nsanzimana, National HIV program and Institute of HIV Disease Prevention and Control-Rwanda Biomedical Center
HVST in Thailand, Prapchan Phanaphak, Thai Red Cross AIDS Research Centre

Part two: Treatment and Impact (70 min)

Chairs:
Elaine Abrams, Columbia University and International Center for AIDS Care and Treatment, USA
Serge Etienne, Treichville University, Côte d’Ivoire

Presentations:
New Directions in the 2015 Consolidated ARV Guidelines
Meg Doherty, Coordinator Treatment and Care, HIV Department, WHO

Priorities across the continuum of care: modelling the impact of interventions on mortality and HIV transmission
Tim Relman, Professor, Imperial College London, United Kingdom

Measuring impact across the continuum of care: The new consolidated SI Guidelines
Susan Low, Deputy Coordinator Strategic Information and Planning, Department of HIV, WHO

Country Panel and Discussion:
Sallim S. Abdi, Kenya, South Africa and Columbia University
Tutu Apollo, Zimbabwe Ministry of Health and Child Care
Fabrio Mesquita, Department of STIs, AIDS and Viral Hepatitis, Brazilian Ministry of Health
Prapchan Phanaphak, Thai Red Cross AIDS Research Centre
Anna Zaszkowicz, AIDS Healthcare Foundation, Ukraine

Disclosure: Gottfried Hirnschall, Director HIV Department, WHO, and Luiz Loures, Deputy Executive Director, UNAIDS