Diagnosis of HIV infection in children

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Basics of Paediatric HIV Prevention and Care,
18-19 April 2012, Upper Eastside Hotel, Woodstock
Outline

• Diagnosing HIV infection
• Goals of an HIV testing programme for children
• Terminology
• HIV testing beyond the PMTCT programme
• Different HIV tests & blood samples
• Algorithm for HIV testing process
• Case scenarios
Diagnosis of HIV infection in infants & young children

• Normal transfer of maternal antibodies across the placenta to the fetus during pregnancy (including antibodies to HIV if the mother is HIV-infected)

• Maternal antibodies slowly disappear from the child’s blood but may be present up to 18 months of age

• If the virus (HIV) itself passes to the baby (during pregnancy, birth or breastfeeding), the baby will produce its own antibodies

• HIV rapid test (ELISA) tests for antibodies to HIV but does not differentiate between maternal & child’s own antibody
Diagnosis of HIV infection in infants & young children

• A positive HIV ELISA or HIV rapid test result in an infant/young child <18 months of age does not mean the child has HIV infection. The correct term to use is “HIV-exposed”

• To diagnose HIV infection in an infant/child <18 months of age, a different test that tests for the virus itself is used (HIV PCR test)

• To diagnose HIV infection in a child ≥18 months of age, HIV antibody tests (HIV ELISA tests and/or HIV rapid tests)
Goals of an HIV testing programme for children

• Identifying HIV-exposed infants/young children

• Excluding HIV infection in infants/young children

• Confirming HIV infection in infants/young children

• Diagnosis of HIV infection in older children

• Action the HIV test results
Not all HIV-exposed infants are identified by our PMTCT programme

- Ideally,
  - PMTCT programmes would identify all HIV-exposed infants by identifying all HIV-infected pregnant women resulting in HIV PCR test on infants at 4-6 wks of age (and if breastfeeding, repeat PCR testing during and 6 weeks after completion of breastfeeding)

- But,
  - Antenatal HIV testing & PMTCT coverage is incomplete
  - New infections and seroconversions occur during pregnancy & breastfeeding
  - Infants may miss HIV testing at 4-6 weeks of age
  - Lack of integration between PMTCT & HIV/ART services for children results in late/missed diagnoses of HIV infection in children
Terminology:
HIV-exposed infant/child <18 months of age

What is “HIV-exposure”?

- An infant born to a mother with HIV infection and indicated by the presence of HIV antibodies in blood of infant/child <18 months of age

- Ingestion of breastmilk from a woman with HIV infection (HIV antibodies in blood of infant may be absent)

- Exposure to certain other body fluids of an HIV-infected person (e.g. following sexual abuse)
Terminology:
HIV-exposed infant/child <18 months of age

How do we determine HIV-exposure status?
► By testing for HIV antibodies (HIV ELISA or HIV rapid test)

HIV-exposed
– History of mother testing HIV-positive during pregnancy, at delivery or during breastfeeding or
– Current HIV antibody test on mother or infant/child <18 months of age is positive or
– Breastfeeding infant/child of HIV-infected mother and infant/child had previous negative HIV PCR test

HIV-unexposed
– Current HIV antibody test on infant is negative
– If mother is HIV-positive, infant/child may have been HIV-exposed and lost maternal HIV antibodies = “seroreversion”

HIV-exposure unknown
– Mother has not had current HIV test or result of previous HIV testing unavailable and
– Infant has not had current HIV antibody test and/or
– Unknown whether infant/child has been receiving breastmilk
Terminology

• Why don’t we just do an HIV PCR test on all infants/children <18 months of age with unknown HIV status?

▶ HIV antibody testing in these children:
  – Identifies HIV exposure within minutes
    • Can make decision to start co-trimoxazole prophylaxis and useful in management of infant/young child with acute illness e.g. pneumonia

  – Can exclude HIV infection in infant/young child (HIV-unexposed or seroreversion) within minutes & thereby avoid the need for PCR test: delay in getting result & cost
Terminology:
HIV-exposed uninfected (HEU) infant/child

- HIV-infected mother and
- Infant/child is HIV negative on the basis of
  - HIV antibody test is negative ("seroreversion") or
  - HIV PCR test is negative

Child may have ongoing HIV-exposure as a result of receiving breastmilk
Terminology:
HIV-infected infant/child <18 months of age

Confirmed HIV infection
- 2 x positive HIV PCR tests on 2 different blood samples
  ► HIV DNA PCR positive + HIV RNA PCR positive (baseline viral load >10,000 copies/ml)
  ► 2 x HIV DNA PCR positive on 2 different blood samples

Unconfirmed HIV infection
- HIV DNA PCR positive (x 1) and
- HIV RNA PCR (baseline viral load) not yet done/result pending
- Conflicting HIV antibody / HIV PCR / baseline viral load results
Terminology:
HIV-infected child ≥18 months of age

**Confirmed HIV infection**
- 2 x positive HIV antibody tests using 2 different tests
  - HIV rapid test followed by HIV ELISA
  - 2 x HIV rapid tests

**Unconfirmed HIV infection**
- 1 positive HIV antibody test
  - Conflicting HIV antibody / HIV PCR / baseline viral load results
Which children should be tested for HIV infection?

• All HIV-exposed infants

• Children with:
  – Clinical features suggestive of HIV infection
  – Acute illnesses, especially if severe

• All children with the following IMCI classifications: Suspected symptomatic HIV infection or possible HIV infection

• All children diagnosed with TB or who have a history of TB treatment

• Family and social history:
  – Parental request to test the child
  – Father or sibling with HIV infection
  – Death of mother, father or sibling
  – When the mother’s HIV status is unknown and her whereabouts are unknown

• When the child may have been wet-nursed or breastfed by a woman of unknown or positive HIV status

• When the child may have experienced or been at risk of sexual assault

• When it is in the best interest of the child where the child is being considered for foster or adoption placement
Suspect HIV infection in the presence of:

• Two or more of:
  – Generalised lymphadenopathy
  – Hepatomegaly
  – Splenomegaly
  – Dermatitis
  – Parotid enlargement
  – Persistent candidiasis
  – Recurrent or persistent upper respiratory infection or otitis media

• Other marker conditions include:
  – Repeated or chronic diarrhoea
  – Bacterial infection – single or multiple episodes
  – Tuberculosis
  – Persistent wasting
  – Chronic lung disease
  – Persistent anaemia, neutropenia or thrombocytopenia
  – Atypical infection incl. Pneumocystis jiroveci pneumonitis, salmonella septicaemia, severe or disseminated chickenpox, shingles, recurrent herpes stomatitis, neurodevelopmental delay, progressive encephalopathy, malignancy & low birth weight

Bottom line: HIV status of all infants and children should be established, testing should not just be on “clinical suspicion”
HIV testing of infants & children: beyond the PMTCT programme

• The HIV rapid test should be the first-line test for screening any child with unknown HIV status

• The Abbott Determine® HIV rapid test is the recommended test for all children (<15 years of age)

• Other HIV rapid tests have been used but there is less data and experience with their use in infants & young children
If the Determine test is negative, is the child HIV negative?

• Yes, but

  – **Breastfeeding children** will require repeat testing at least 6 weeks after stopping breastfeeding or if there are clinical features suggestive of HIV infection during the period of breastfeeding

  – If there is **strong clinical suspicion** of HIV infection and the rapid test is negative, a PCR test (if child <18 months old) or ELISA test (if child ≥18 months old) should be sent to the laboratory
If the Determine test is positive, what confirmatory test is to be used?

- If child is <18 months old
  - HIV PCR test

- If child is ≥18 months old
  - HIV ELISA test
  - Unfortunately, this requires sending venous blood to the laboratory and awaiting the result
  - There is limited data on the performance (sensitivity & specificity compared to HIV ELISA test) of various different HIV rapid tests in children as compared to adults. Research is ongoing.
Can HIV testing be done in infants <6 weeks of age?

• Yes

• HIV screening and testing is encouraged from as early as possible

• For infants who are known to be HIV-exposed (i.e. mother is HIV-positive), omit the Determine test and do the PCR test
  – A negative PCR test in an infant of <6 weeks of age must be repeated once the infant is ≥6 weeks of age

• For infants of unknown HIV status, the first test to do is the Determine test. If the Determine test is positive, then do a PCR test
What about consent for HIV testing in children?

- **Children’s Act (2005)**
  - **≥12 yrs of age**
    - Child can consent to testing & to disclosure of results
  - **<12 yrs of age**
    - Parent or primary caregiver unless child is of sufficient maturity to understand the benefits, risks & social implications of the test result themselves

- **Following may also provide consent:**
  - Superintendent or person in charge of a health establishment or hospital
  - A designated child protection organization arranging the placement of the child
  - Provincial Head of Social Development
  - The Children’s Court if consent from any of the persons listed above is withheld unreasonably or the child or their parent or caregiver is incapable of giving consent
Counselling guidelines (pre & post test)

• Review & build on mother or caregiver’s existing knowledge about HIV/AIDS & correct misconceptions

• Help mother to assess the impact that the test result (positive or negative) will have on her, her partner and her family
  – Coping mechanisms & support
  – Safe sexual practices & disclosure issues

• Emphasise the availability of follow-up, medical treatment & support for the mother and her child
Two kinds of blood test for HIV infection

• **Antibody test**
  - **Rapid tests**
    • Test done on-site with finger-prick blood sample or in laboratory
    • Colour change reading
    • 1 negative result = no infection
    • 1 positive result + repeat positive result with second sample & different rapid test = HIV infection
  - **ELISA** (Enzyme-linked immunosorbent assay)
    • Test done in laboratory

• **Screening test for children <18 months old; diagnostic test for children ≥18 months old**

• **Virus test**
  - **PCR** (Polymerase chain reaction)
    • Sophisticated test done in laboratory
    • Test used in PMTCT programme for infant diagnosis of HIV at 6 weeks of age
    • <1ml of blood in small purple-top tube from heel prick blood or dried blood spot sample

• **Diagnostic test for children <18 months old; not routinely used for HIV testing in children ≥18 months old or adults**
Blood samples for HIV testing:
EDTA tube (purple-top) or Dried Blood Spot (DBS)

Antibody tests (HIV ELISA or HIV rapid tests):
Capillary blood or venous blood used directly or collected into EDTA (purple-top) or clotted blood tubes (not heparinised tubes)

HIV PCR test:
Capillary blood or venous blood collected into EDTA (purple-top) tube or as dried blood spot sample

In infants, capillary blood may be obtained by finger/toe or heel-prick
Algorithm for HIV testing of children

• What’s an algorithm?
  – A flow diagram with boxes & arrows guiding the health care provider through the process of testing

• Why do we need it?
  – To simplify the process for health care providers
  – To ensure the same standard quality of care is provided to all children and their families undergoing testing
HIV Testing of Children, Western Cape (2008)

Child with unknown HIV status

<18 mths of age
- Pretest counsel caregiver & obtain consent for HIV testing
- Do Abbott Determine® rapid test on child
  - If mother is known to be HIV-infected & child is <9 mths of age, skip rapid test & proceed directly to PCR test

Rapid test is positive
- Do HIV DNA PCR test on child
  - Start co-trimoxazole prophylaxis if ≥6 wks of age
  - Arrange follow-up date for test results

PCR test is negative (≥6 wks of age)
Child is HIV-infected
- Post test counsel caregiver
- Manage further or refer to HIV clinic
- Encourage HIV testing for parents & siblings

Child is breastfeeding
- Continue co-trimoxazole
- Repeat HIV testing according to this algorithm: ≥6 wks after stopping breastfeeding or if child develops clinical features of HIV infection during period of breastfeeding

NO breastfeeding in last 6 weeks
Child is HIV-uninfected
- Post test counsel caregiver
- Stop co-trimoxazole

>18 mths of age
- Pretest counsel caregiver and/or child & obtain consent for HIV testing
- Children ≥12 yrs of age can consent for their own testing
- Do Abbott Determine® rapid test on child

Rapid test is negative
- Do confirmatory HIV ELISA test on child
  - Post test counsel caregiver &/or child
  - Manage further or refer to HIV clinic
  - Encourage HIV testing for parents & siblings

Positive rapid test & ELISA test
Child is HIV-infected

Child is breastfeeding
- Repeat HIV testing according to this algorithm: ≥6 wks after stopping breastfeeding or if child develops clinical features of HIV infection during period of breastfeeding

NO breastfeeding in last 6 weeks
Child is HIV-uninfected
- Post test counsel caregiver &/or child
NOTES:

1. When is it particularly important to perform an HIV test in a child?
   - All infants whose mothers were not tested for HIV during pregnancy or who were not enrolled on the PMTCT programme.
   - A negative HIV test in the mother during pregnancy does NOT exclude HIV infection in the child.
   - HIV screening of infants should take place at routine immunization visits from 6 weeks of age.
   - Children diagnosed with TB or suspected to have TB, because TB is often the sentinel disease with which an HIV-infected child presents to the health care worker (and because other conditions may mimic TB if child is HIV-infected)
   - Children with suspected symptomatic HIV infection (IMCI criteria)
   - Sexually-abused children

2. Consent for HIV testing in children (Children’s Act, 2005 Chapter 1.1 and Chapter 7 part 3)
   - Children <12 years of age (unless they are of sufficient maturity to understand the benefits, risks, and social implications of the test results themselves) require the consent of their parent or primary caregiver (i.e. does not have to be legal guardian, but the person who cares for the child) but all children should be provided with age-appropriate information prior to HIV testing.
   - Children >12 years of age can provide consent to be tested; they must also provide written consent if disclosure of their test result to anyone else is necessary.
   - Whoever consents must receive pre and post test counselling by an appropriately trained person.

3. At present, the only HIV rapid test that has been validated for use in these age groups is the Abbott Determine® HIV 1/2 test. If this test is not available at the clinic or hospital, blood should be sent to the laboratory for HIV ELISA test.

4. If HIV is suspected clinically and the rapid test is negative, an HIV DNA PCR test (<18 months) or HIV ELISA test (≥18 months) should be sent to the laboratory. (For PCR test, 0.5ml blood in purple-top tube via heel-prick in infants)

5. Co-trimoxazole prophylaxis dosing schedule for children

<table>
<thead>
<tr>
<th>Weight</th>
<th>Once daily dose (oral suspension or single-strength tablet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5kg</td>
<td>2.5mls</td>
</tr>
<tr>
<td>5-14kg</td>
<td>5mls or ½ tablet</td>
</tr>
<tr>
<td>14-&lt;30kg</td>
<td>10mls or 1 tablet</td>
</tr>
<tr>
<td>≥30kg</td>
<td>2 tablets</td>
</tr>
</tbody>
</table>

6. The HIV DNA PCR test is most accurate from ≥6 weeks of age. If the test is done at <6 weeks of age and is negative then it should be repeated when the child is ≥6 weeks of age. It is good practice to confirm the HIV status of HIV-exposed children with an HIV ELISA or Determine Rapid test at 18 months of age.

7. Further management includes treatment of opportunistic infections, clinical staging, CD4 count measurement and interpretation, and counselling to assess antiretroviral treatment readiness of child and caregiver. Depending on local capacity, children may need referral to an HIV/ART clinic for some or all of these steps. All children less than 12 months of age with confirmed HIV infection should be referred to an experienced clinician for assessment for antiretroviral therapy.
What is the purpose of the HIV testing algorithm?

• More infants and children being screened and tested for HIV infection
  – Aim is point-of-care screening and testing of any child with unknown HIV status

• Facilitate earlier initiation of co-trimoxazole prophylaxis and antiretroviral therapy when indicated, particularly for young infants

• Health care providers who are knowledgeable & confident with HIV testing of children
HIV Testing scenarios

• What would be your management of:

  – An 8-week old breastfed infant whose HIV PCR result comes back positive?
    – Post-test counselling of mother, stop dNVPp, urgent initiation of ART (within the next 1-2 weeks after further counselling), send blood for HIV viral load (RNA PCR) as confirmatory diagnostic test along with CD4 count, check that child is receiving co-trimoxazole prophylaxis, encourage mother to continue breastfeeding, check if mother had CD4 count/qualifies for ART & rest of family tested

  – A 10-week old infant whose Determine test is positive?
    – Send HIV PCR test, co-trimoxazole prophylaxis

  – A 10-week old formula-fed infant whose HIV PCR result comes back negative?
    – Post-test counselling: child is HIV uninfected, stop co-trimoxazole, check if mother had HIV test/CD4 count/qualifies for ART & rest of family tested
HIV testing scenarios

What is the appropriate testing process to follow in:

a. A well 1-year old child who has never breastfed and whose mother is HIV-positive?

✓ Determine test (child is ≥9 months of age)

• If Determine test is negative, child is HIV-uninfected (child has “sero-reverted” & delay in getting result/expense of PCR test has been avoided)

• If Determine test is positive, do PCR test
  If PCR test is negative, child is HIV-uninfected
  If PCR test is positive, child is HIV-infected & needs ART
HIV testing scenarios

What is the appropriate testing process to follow in:

b. A 3-month old infant whose mother is HIV-positive?

✓ HIV PCR test

– If HIV PCR test is positive, child is HIV-infected. Send confirmatory HIV viral load (RNA PCR) & plan to start ART within 1-2 weeks.

– If HIV PCR test is negative, is the child breastfeeding currently or within the last 6 weeks?

– If yes, infant will require, repeat HIV PCR test ≥6 weeks after last breastfeed or during period of breastfeeding if develops clinical features suggestive of HIV infection. Ensure mother of child is on ART or child is receiving daily nevirapine prophylaxis. Recommended duration of breastfeeding is 12 months.

– If no, child is HIV-uninfected
HIV testing scenarios

What is the appropriate testing process to follow in:

c. A 1-week old abandoned infant?

✓ Determine test

- If Determine test is negative, Determine test should be repeated at least 6 weeks later

- If Determine test is positive do PCR test on child
  if PCR test is positive, child is HIV-infected
  if PCR test is negative, PCR test should be repeated when the child is ≥6 weeks of age
HIV testing scenarios

• What is the appropriate testing process to follow in:

d. A 9-month old breastfeeding infant of HIV-infected mother and infant had negative PCR test at 6 weeks of age?

✓ PCR test

• Maternal antibodies may still be present in infant circulation or may have disappeared
HIV testing scenarios

Who could legally provide consent for HIV testing in the following situations?

a. A 3-year old child whose parents have died and who is cared for by the maternal grandmother?
   ✓ Maternal grandmother (‘caregiver’)

b. A 13-year old girl with a vaginal discharge?
   ✓ Patient

c. An 11-year old boy whose parents have died and who lives in foster care?
   ✓ Foster parent (caregiver) and/or possibly the patient (if of sufficient maturity to understand the benefits, risks & social implications of the test result himself)
Key messages

• Early identification of HIV status among children is essential to prevent rapid HIV progression and death

• Routine offering of HIV testing should be integrated into routine child health visits: Provider Initiated Counselling and Testing (PICT)

An example of a PICT approach is expanding where HIV testing takes place to include exam or immunisation rooms for a one-stop consultation service.
Discussion points

• What is the process for HIV testing of children at your clinic and what is your individual role as doctor/nurse/counsellor in this process?

• Can it be improved?
  – Is Provider Initiated Counselling & Testing (PICT) for HIV a routine for all children at any health care visit?
  – Is the Determine® HIV rapid test available and being used for HIV screening and testing of children?
  – What is the level of urgency with regard to HIV testing of infants & young children and are HIV test results being actioned?