

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 uncertainty 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

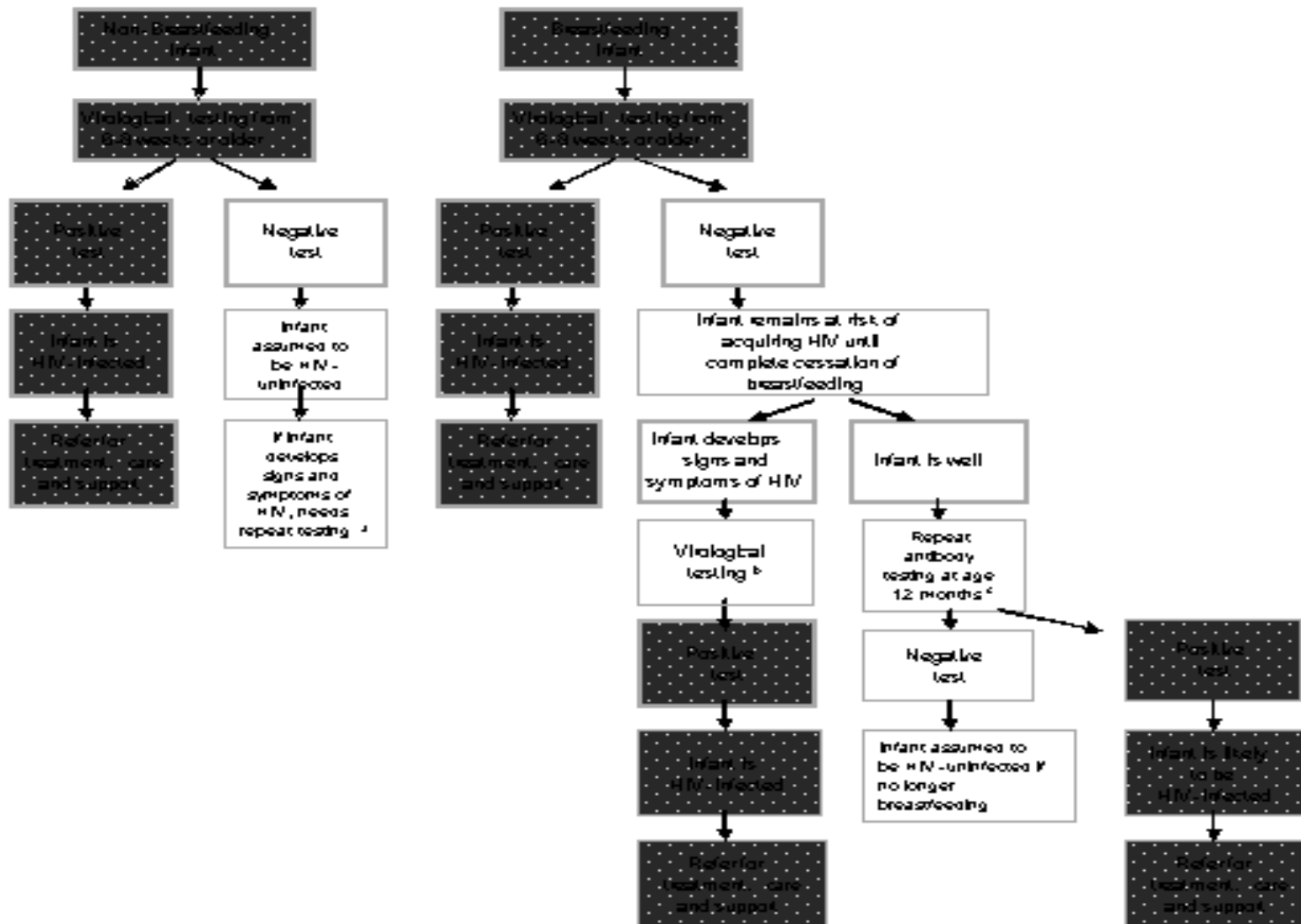
Principles of the public health approach - diagnosis

- 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

Method of diagnosis	Recommendations for use	Strength of recommendation/ level of evidence
Virological methods (includes DNA, RNA, and ICD p24)	To diagnose infection in infants under age 18 months; initial testing is recommended at age 6-8 weeks	A (I)
	HIV Antibody testing	
	To identify HIV positive children under 18 months in whom HIV infection is likely ^a	A (IV)
<p>Notes:</p> <p>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).</p>		

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			
Stage 1	Stage 2	Stage 3	Stage 4
No symptoms	Mild	Advanced	Severe

+

Immunological classification			
Not significant	Mild	Advanced	Severe

Clinical classification on treatment			
T1	T2	T3	T4

Decision -making regarding switching to second line therapy for treatment failure based on availability of CD4 measurement ^a

WHO Paediatric Clinical Stage on ART ^b	Availability of CD4 measurements	Management options
T1 and T2 ^c	No CD4	⊘ Do not switch regimen
	CD4	⊘ Consider switching regimen only if 2 or more values below age -related threshold for severe immunodeficiency ^d are available ⊘ Increase clinical and CD4 follow up if CD4 approaches age-related threshold for severe immunodeficiency
T3 ^c	No CD4	⊘ Consider switching regimen ^e
	CD4	⊘ Switching regimen is recommended if CD4 at or below age-related threshold for severe immunodeficiency ^d and particularly if child initially had good immune response to ART
T4	No CD4	⊘ Switch regimen, regardless of CD4
	CD4	

. Laboratory parameters for monitoring infants and children at baseline, prior to ART and during ART				
Diagnosis and monitoring laboratory tests	Baseline	Monthly at initiation of 1st or 2nd line regimen (weeks 4, 8, 12)	Every 6 months	As required (i.e., symptom - directed)
HIV diagnostic testing: virological and Ab testing	☒	-	-	-
Hemoglobin ^a	☒	☒	-	☒
WBC and differential	☒	☒	-	☒
%CD4 or Absolute CD4 cell count ^b	☒	-	☒	-
Pregnancy testing in adolescent girls ^c	☒	-	-	-
Full chemistry (including, but not restricted to, ALT ^d , liver enzymes, renal function, glucose, lipids, amylase, lipase, and serum electrolytes) ^e	-	-	-	☒
Diagnostic tests for treatable co - infections and major HIV/AIDS - related opportunistic diseases	Screening for TB and malaria (basic microscopy; i.e. sputum smear test for TB and thick blood drop smear test for malaria diagnosis) ^f	-	-	☒
	Full cerebrospinal fluid (CSF) microscopy (including India ink for cryptococcal meningitis), in adolescents: syphilis and other STI diagnostic tests.	-	-	☒
	Diagnostic tests for hepatitis B, hepatitis C serology, bacterial microbiology, and cultures and diagnostic tests and procedures for PCP, <i>Cryptococcus</i> , toxoplasmosis and other major OIs)	-	-	-
HIV viral load measurement ^g	-	-	-	☒

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>

'Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach' are available at: http://www.who.int/3by5/publications/documents/arv_guidelines/en/

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

<http://www.who.int/hiv/pub/me/youngchildren/en/index.html>

<http://www.who.int/hiv/pub/me/pubnapcs/en/index.html>

<http://www.who.int/hiv/pub/me/naparv/en/index.html>

Revised Clinical Staging

<http://www.who.int/hiv/pub/guidelines/casedefinitions/en/index.html>

Thank you

