HIV-disease in children: Diagnosis, staging and treatment

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Children acquire HIV-infection from adults

Timing of HIV transmission to children

- Vertical / Mother-to-child-transmission (MTCT):
  - In utero (transplacental)
  - At delivery
  - Breastfeeding

- Other:
  - Blood product transfusion
  - Sexual abuse

Diagnosis of HIV infection

- Antibody detection:
  - ELISA
    - Problem:
      - False positive in infants <18 mo
      - Due to maternal antibodies (IgG)
      - Ab's via placenta and breast milk
    - HIV-Dx more difficult in infants than in adults!

HIV IS A RETROVIRUS

DNA → RNA → PROTEIN

Reverse transcriptase

Diagnosis of HIV infection

- Viral detection tests:
  - p24 antigen
    - Poor sensitivity
  - DNA PCR
    - Test of choice for Dx in children < 18 mo
    - Viral RNA = incorporated into human DNA
    - Problems:
      - May give false positive results
      - If PCR positive (esp. if child asymptomatic):
        - Repeat PCR or VL
    - RNA PCR (=Viral load)
      - Confirmation of HIV Dx: VL>10,000
      - Monitoring of ART
Issues: HIV-testing in children

• Pre-test counselling
  – Proxy-consent from caregiver
  • Child’s HIV-test may reflect maternal HIV-status
  • New Child Care Act:
    – Parent can give consent
    – Caregiver may consent (not only parent or legal guardian)
    – Children ≥ 12y can give own consent
    – Consent may also be given by 2 Health care workers who
      agree that HIV testing is in best interest of child

• Post-test counselling

• Buddy:
  – To involve 2nd adult in Dx and Rx plan

• Disclosure of HIV-status to child

Issues: HIV-testing in children (cont)

• HIV-testing: PMTCT programme
  – At PHC visits (i.e. for immunizations):
    • Mother:
      – History HIV-testing & refusal to test
      – Offer HIV-testing (if not negative late in pregnancy;
        breastfeeding mothers)
    • All HIV-exposed children:
      – HIV DNA PCR at age 6 w (or earliest thereafter)
      – If BF: Redone 6w after weaning (or earlier if Sx)
      – Age 18mo: HIV rapid or ELISA (except if child on ART)
    – Consider child <18 mo HIV-infected only if
      • Positive HIV PCR (preferably 2 PCRs or 1PCR+VL)
      • Otherwise = HIV-exposed

IMCI guidelines for HIV-testing:
Diagnosing children with Sx

ASK, LOOK, FEEL

Classification:
2-3 features:
> Suspected symptomatic HIV
> Other HIV-testing
Mother HIV:
> HIV-exposed
> Other HIV-testing
1-2 features:
> Possible HIV-infection
> Other HIV-testing
No features:
> HIV-infection unlikely

NB: Testing of asymptomatic children is inappropriate of meaning

Maternal or infant HIV test done

Classification:
2-3 features:
Preanulosis now
Ear discharge over
Low weight for age
Inadequate weight gain
Persistant diarhoea now or past 2 mo
Enlarged lymph nodes at ≥ 2 sites
Oral thrush
Pedicel enlargement

>18 months
Test with an ANTIBODY TEST
ELISA or a rapid test

Natural progression
of HIV disease in children

• HIV progresses faster than in adults
  – By 12 months:
    • 38% AIDS or †
  – By 4 years:
    • 70% AIDS or †
  • High risk of disease progression in 1st year of life!!
    – CD4 count/% poor marker of disease severity
  • Little time to waste!!
Common clinical manifestations

- Rapid progressors
  - Failure to thrive
  - Recurrent severe infections
  - Pneumonia:
    - Bacterial, viral, PCP, TB
  - Encephalopathy
- Older children
  - Poor growth
  - Recurrent infections
  - TB
- Other issues to consider:
  - Social
    - Ill mother/parents
    - Poverty
    - Malnutrition

Clinical manifestations vary considerably

HIV affects growth & development

Nutrition

- Vital to pay attention to
- Many children from food-insecure households
- Malnutrition often multifactorial

HIV affects growth & development

- Growth
  - Use Road-to-Health-Card
  - Reasons for poor growth
    - HIV itself
    - Recurrent and chronic infections
      - Remember TB
    - Gastro-intestinal problems, e.g. diarrhoea
    - Developmental problems: Feeding difficulties
    - Early cessation of breastfeeding
    - Psychosocial reasons
      - Poverty, depression in mother, etc.

HIV affects growth & development (cont.)

- Neurodevelopment
  - HIV encephalopathy (NB!)
    - Poor brain growth (acquired microcephaly)
    - Regression of / failure to attain milestones
    - Tone disturbances/ UMN signs
  - Often not associated with low CD4

Staging of HIV disease

- Clinical staging more NB in children than CD4
- 2 Staging systems used:
  - CDC-classification
    - Combination of clinical features & CD4 count /%
    - Need for specialized laboratory facilities
    - First world countries
  - WHO-classification
    - Clinical staging
    - Used in SA National ART Programme
CDC staging

- Clinical staging:
  - N: Asymptomatic
  - A: Mild
  - B: Moderate
  - C: Severe

CDC staging

| IMMUNOLOGICAL CATEGORIES FOR CHILDREN WITH HIV INFECTION |
|-----------------|-------------------|-------------------|
| AGE OF CHILD    | 12 MONTHS         | 1-5 YEARS         | 6-12 YEARS        |
| CD4+/ml         | CD4+%             | CD4+/ml           | CD4+%             |
| Stage 1         | > 1 500           | ≥ 25              | > 1 000           | ≥ 25              |
| Stage 2         | 750 – 1 499       | 15 – 24           | 500 – 999         | 15 – 24           |
| Stage 3         | < 750             | < 15%             | < 500             | < 15%             |

These are easy! Also remember these!

4-stage WHO Staging:
Stage 1
- Asymptomatic
- Generalized lymphadenopathy

WHO Staging: Stage 2
- Hepatosplenomegaly
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Extensive human papilloma virus infection
- Extensive molluscum contagiosum
- Fungal nail infections
- Recurrent oral ulcerations (LGE)
- Angular cheilitis
- Parotomegaly
- Herpes Zoster
- Recurrent or chronic RTI's (OM, otorrhea, sinusitis)

WHO staging: Stage 3
- Moderate malnutrition
- Unexplained persistent diarrhoea
- Unexplained persistent fever
- Oral candidiasis
- Acute necrotizing ulcerative gingivitis / periodontitis
- Pulmonary TB
- Lymph node TB
- Symptomatic LIP
- Chronic HIV-associated lung disease
- Severe recurrent bacterial pneumonias
- Anaemia, thrombocytopenia, neutropenia

WHO staging: Stage 4
- Severe malnutrition
- PCP
- Recurrent severe bacterial infections
- Chronic herpetic infections
- Extrapulmonary TB, atypical TB
- Malignancies: Kaposi's sarcoma, lymphoma
- Oesophageal candidiasis
- Disseminated fungal infection: Cryptococcal meningitis
- Cryptosporidiosis, isosporiasis
- HIV encephalopathy
- CMV disease
- Cardiomyopathy, nephropathy
- Rectovaginal fistula
Early diagnosis and access to care
For HIV-infected children in the City of Tshwane
The Hide and Seek Project Team

Problem in Tshwane:
Children diagnosed & referred late
- HIV is major cause of childhood mortality
- Treated HIV in children has a good outcome

HIV-infected children in Tshwane:
- What problems do they face?
  - Medical
  - Diagnosis
  - Access to care
  - Life-long treatment (ART)
  - Social

Nr of undiagnosed HIV+ kids in Tshwane:
- HIV prevalence in children in SA: 2.5% - 3%

City of Tshwane:  
!! Estimated missing HIV+ children  
About 15,000 !!

HIV-infected children in Tshwane:
- Find children & test them – where?
  - Health care facilities
    - Primary health care
    - HCT sites*
    - ART sites*
    - Hospitals
  - In the community
    - Community organisations
    - Crèches, child care centres, schools

How can health care workers and students(!) be involved?
- Find & test children when they come for care
  - Even if required care is unrelated
- At ALL Health Care Facilities:
  - Routine testing (Babies from PMTCT)
  - Target children for HIV testing (HCT):
    - Children with Risk Factors
    - Children with early signs of HIV infection
  - Access to ART programme:
  - Testing & referral of family members/siblings
  - Referral for social interventions
We can do this for our children!

Lecture 2

The management of HIV-infected children

ART in children

Management of HIV-infected child

- Care is much more than just providing ART
- Goal: Maintaining health, growth & development
- Common infectious diseases = morbidity
- Well managed children = less hospital admissions
- Counselling and support

Management of HIV-infected child

- Access to early infant diagnosis
- Regular follow-up
  - Growth monitoring & dietary advice
  - Neurological development
  - Preventative measures
    - Hygiene
    - PCP: Bactrim® prophylaxis
    - Early Rx of infectious diseases
    - Education on oral rehydration solution
    - Immunizations
  - Referral for social intervention
  - Staging (clinical & CD4) >>> ART eligibility
- ART – once eligible
ART has changed health care in Africa – And we can play our part!

Why start ART earlier in younger children?

Differences in viral dynamics between adults and children

‘Train on tracks’

Viral Load  Speed

CD4 cells  Distance
**ART - Goals**
- To ↓ HIV-related morbidity & mortality
- To prevent opportunistic infections
- To improve growth
- To promote development
  - Physical, social & intellectual
- To preserve/ reconstitute immune system
  - Measured by CD4 count / % - which ↑
- To suppress HI-viral load
  - Aim for VL= undetectable

**ART: General principles**
- Holistic treatment programme:
  - Social intervention
    - See child in context of social environment
    - Child unable to take responsibility for own health & medication
  - Prophylactic management
  - Dietary intervention
  - Clinical care
  - Psychosocial support
  - Attention to adherence

**ART: General principles**
- Standard of care:
  - 3-drug combinations
    - ↑ Potency
    - ↓ Risk of viral resistance
  - Children have ↑ VL than adults
- Monitoring of response to Rx:
  - Clinical
  - Blood tests:
    - CD4+ counts/ %
    - HIV VL
- Monitoring for side effects

**Medical needs: Mother/caregiver**
- Enquire about health of caregiver
- Ensure access to medical care
  - ART, TB, contraception, other
- Enquire about siblings

**ART - Drug classes**
- Reverse transcriptase inhibitors (RTI)
  - NRTI (nucleoside RTI)
    - NNRTI (non-nucleoside RTI)
  - NRTI (nucleotide RTI)
- Protease inhibitors (PI)
- Other
We need to know the drugs we prescribe.

We need to empower our patients to take care of their health.

Reverse transcriptase

NRTI

NRTI

NNRTI

PI

- Medical criteria:

  - < 1 year: All children to be started on ART
  - 1 – 5 years:
    - Symptomatic (stage III, IV), or
    - CD4 ≤ 25%, or
    - CD4 abs count < 750 cells/μl
  - ≥6 years:
    - Symptomatic (stage III, IV), or
    - CD4 < 350 cells/μl

- Social criteria:
  - Reliable adult to administer medication
  - Treatment buddy (2nd adult)

First line ART: >3 yrs & >10 kg

- 2 NRTI + 1 NNRTI
  - ABC (abacavir)
  - 3TC (lamivudine)
    - Do not use NRTIs of same base (ie not AZT + d4T)
    - Combination of d4T & ddI: High risk of lactic acidosis
  - Efavirenz - Stocrin®

- Previously: d4T instead of ABC
  - Keep on this regimen if no problems
  - Change d4T to ABC if signs of lipodystrophy / SE

First line ART: < 3 yrs or <10kg

- 2 NRTI + 1 PI
  - ABC (abacavir)
  - 3TC (lamivudine)
  - Lopinavir/ritonavir - Kaletra®

- Previously: d4T instead of ABC
  - Keep on regimen if no problems
  - Change d4T to ABC if signs of lipodystrophy / SE

ART - Potential problems

- Need for combination therapy
- Potential toxic side effects
- Drug interactions (e.g. TB Rx)
- Lifelong therapy
  - Structured follow-up needed
  - Lack of adherence
    - Major risk factor for Rx failure
- Emergence of viral resistance
Adherence

- Adherence
  - Vital for good outcome
  - ↓ over time
- Every interaction
  - = Opportunity to reinforce adherence
- Ongoing support & monitoring essential
- Teenagers
  - Adherence needs special attention

VIRAL RESISTANCE

HIV IS A RETROVIRUS

DNA → RNA → PROTEIN

Reverse transcriptase

No proof-reading capacity

Second-line therapy

- Reason:
  - Virological failure
  - Immunological failure
  - Clinical progression (opportunistic infections)
- Never an emergency
- Assess adherence!!!!!!!!!
- ?Underlying chronic diseases like TB
- Patient / caregiver to understand that:
  - Moving to 2nd-line ART influences future Rx options

When to ask for help

- Previous exposure to ART
- Moving to 2nd-line therapy
  - NB: Previous PI = ritonavir only (previous guidelines)
- Concomitant drug therapy
  - Potential drug interactions
- Concomitant diseases
  - Severe conditions: BCG, MAC, MDR-TB, cancers, etc
  - Liver and kidney diseases
    - Metabolism & excretion changed
    - Adequate ART blood levels ➔ viral suppression
  - Serious side effects

Where to get information

- SA National Dept of Health
  - National ART guidelines
    - www.doh.gov.za
- SA HIV Clinicians Society
  - Paediatric ART guidelines
    - Tel 011 341 0162
    - www.sahivsoc.org
- Aid for AIDS (private practice)
  - AFA Clinical Guidelines
    - Tel 0800 227 700
    - www.aidforaids.co.za
- AIDS Helpline
  - Tel 0800 012 322
- Medicines Information Centre
  - Tel 021 406 6829
  - 0800 212 506
  - http://www.mic.uct.ac.za
- ART drug interactions:
  - www.hiv-druginteractions.org
- ART experts in the area
  - where you work 😊

Thank you!