Smear negative TB and HIV: urgent research priorities to inform a rolling global policy

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Smear negative TB in PLHIV

- Higher chance for smear negative disease
  - SN pulmonary = 24 – 61%
  - Extrapulmonary = 4 – 40%

- Autopsy studies = 14 – 54%

- Scale of problem is underestimated
  - Studies are institution based
  - Most TB services look for smear positives
  - Early death before diagnosis is established

Getahun H et al Lancet 2007 DOI:10.1016/S0140-6736(07)60284-0
The prevailing practice
(Analysis of national TB guidelines)

- Empiric antibiotics trial = up to 4 weeks
- AFB smears = up to 9
- CXR = very late after a number of visits
- Time before diagnosis = 13 – 44 days
- Number of consultations = 5 – 7 times
- Not included: HIV status, severity, culture

In the meantime patients die
Policy and practice need to change

– To expedite diagnosis and reduce mortality
– Special approach for HIV settings needed
– DOTS has evolved into Stop TB Strategy

The reality is..

• Technology vacuum of TB diagnosis
• Catastrophe posed by the dual epidemic
• Dire need to respond to an emergency
• Not enough evidence and experience
New policy (recommendations) issued

"In the absence of complete evidence, the recommendations were built on consensus and iterative global expert opinion."

"Careful evaluations by national authorities, research groups and interested parties are needed to assess the likely benefits and responsiveness of the recommendations"

Key changes in the new policy

- Case definitions revised for HIV settings
- Algorithms tailored to clinical condition (Ambulatory & seriously ill patients)
- HIV testing to TB suspects along with AFB
- Acceptable number of visits established
- CXR and Culture to be done earlier
Key changes in the new policy

- Vigilance and flexibility to start empiric treatment for suspected extrapulmonary TB in peripheral health facilities

- TB care should include HIV care
  - HIV staging (clinical, immunological)
  - PCP treatment
  - Co-trimoxazole preventive therapy

- Clinical management of extrapulmonary TB be included as TB control programme activity

- Recording and reporting of SN TB improved
FIGURE 1
Algorithm for the diagnosis of TB in ambulatory HIV positive patient

Ambulatory patient with cough 2–3 weeks and no danger signs

1st VISIT
AFB HIV test

HIV+ or status unknown

2nd VISIT
AFB positive

Treat for TB
CPT
HIV assessment

TB likely

AFB negative

CXR
Sputum AFB & cultures
Clinical assessments

TB unlikely

3rd VISIT
Treat for PCP
HIV assessment

Response

4th VISIT
No or partial response

Respond
Reassess for TB
Algorithm for the diagnosis of TB in seriously ill HIV positive patient

1. Seriously ill patient with cough 2–3 weeks and danger signs
   - Referral to higher level facility
     - Parenteral antibiotic treatment for bacterial infection
       - Sputum AFB and culture
       - HIV test
       - CXR
     - No TB
     - Treat TB
   - Immediate referral not possible
     - Parenteral antibiotics for bacterial infection
       - Consider treatment for PCP
       - Sputum AFB and culture
       - HIV test
       - HIV+ or unknown
         - AFB positive
           - Improvement after 3–5 days
           - Start TB treatment
             - Complete antibiotics
             - Refer for HIV and TB care
         - AFB negative
           - No improvement after 3–5 days
           - TB unlikely
           - Reassess for TB

   Reassess for other HIV-related disease

   - TB unlikely
   - Reassess for TB
Immediate implementation is crucial

• The recommendations are appropriate because
  – Latest available evidence considered
  – Developed through iterative global process
  – Give due emphasis for HIV
  – Maximise the use of existing tools

• Need to be implemented as a response to the emergency of the dual epidemic

• Need to be phased implementation
  – Infrastructure and human resources required
More evidence through implementation

- Evaluation (in collaboration with NTP/NAP) for:
  - Effectiveness (speed of diagnosis and mortality)
  - Feasibility (infrastructure and human resources)
  - Cost effectiveness

- Generic protocol developed

- Key parameters to be measured include:
  - Human resources and infrastructure cost
  - Satisfaction of patients and health workers with speed and quality of services
  - Patients receiving all available investigations and completing diagnostic evaluation
  - Death during evaluation and treatment
Discussion points

• Will you be able to piggy pack the evaluation of the new diagnostic algorithms into your research projects?

• Do you see any challenges in using these recommendations to improve the care for HIV infected TB patients in your research projects?

• Will you be interested to join an information and experience sharing network that will inform the rolling global policy as evidence evolves?