Diagnostic challenges of active childhood TB in Tanzania



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Diagnosis of Childhood Tuberculosis



Universal diagnostic challenges

Diagnostic challenges in a low-income, high TB burden setting

Estimated TB incidence 2010 Global TB control WHO 2011



	<u>Denmark</u>	South Africa
Total population	5,5 million	50 million
New cases	313	335974
Notification	6/100000	981/100000
Number of children	9	50474
Proportion of children	3%	15%

Pathogenesis in Adult vs Children/HIV pos



Risk of disease following primary infection Marais et al. Int J Tuberc Lung Dis. 2004.



Age-related manifestations of PTB



Age in years

Adapted from the age-related manifestations of pulmonary tuberculosis reported in immunecompetent children.(5)

- Complicated Ghon focus, Disseminated miliary disease and TB meningitis
- II Uncomplicated and complicated lymph node disease
- III Pleural effusion
- IV Adult-type disease

Childhood tuberculosis: epidemiology and natural history of disease. Marais BJ. Indian J Pediatr. 2011 Mar;78(3):321-7. Epub 2011 Jan 7. Review.



Diagnostic difficulties in children

- Signs and symptoms not specific. Marais et al. 2006
- TST false positives and negatives Guidance for NTP management childhood TB. WHO 2006
- Chest X-ray of limited value Koppaka R et al. WHO 2004
- Younger children cannot produce sputum.
- Microscopy and culture negative Zar 2005. Marais 2007
- Score charts not validated and low specificity

A Hessling 2006. P van Rheenen 2002.

Over- and Under-diagnosis





 Performance of Quantiferon-TB Gold In-Tube (QFT) for diagnosing active tuberculosis in children and adults in a high burden setting
 Rose MV, Kimaro G, Nissen TN, Kroidl I, Hoelscher M, Bygbjerg IC, Mfinanga SG, Ravn P.
 PLoS One. 2012;7(7):e37851. Epub 2012 Jul 12.

Primary health staff's perceptions of childhood tuberculosis: a qualitative study from Tanzania Bjerrum S, Rose M, Bygbjerg IC, Mfinanga SG, Tersboel BP, Ravn P <u>BMC Health Serv Res</u>. 2012 Jan 9;12:6.



Muheza District Report 2010

- 21% of population < 5 years old</p>
- <5 mortality: 208/1000</p>
- HIV incidence: 6-7%......40-50%
- TB notification rate 348/100.000
- Children: 75/761 new cases











Performance of QFT for diagnosing active childhood TB

Aim: Can QFT contribute to diagnosis of active TB in children?

- Adults in Japan. QFT Sensitivity: 89%. Mori T: Am J Respir Crit Care Med. 2004 Jul 1;170(1):59-64
- Children in South Africa. Elispot Sensitivity 81%. Liebeschuetz S et al, Lancet 2005, 18/252196-2203

Children in Germany. QFT sensitivity 93% *Detjen et al. CID 2007, 45*



Summary of results

	Children	Adults
Sensitivity QFT	19%	86%
Sensitivity of TST	6%	89%
Indeterminate rate	27%	6%

- Young age, HIV infection or malnutrition not adequately explain low sensitivity
- Median levels of IFN-gamma were lower in children, especially children < 2 years and HIV positive
- Indeterminate results associated with high mortality

Childhood mortality according to QFT result



TB management at primary level in Tanzania

Aim:

To explore perceptions, challenges and needs of primary health staff in regard to childhood tuberculosis











Summary of Results

Lack of awareness of burden of Childhood TB

 Missed opportunities for early detection as TB only considered in children unresponsive to treatment, severely ill and known exposure.

Obstacles identified:

 Lack of knowledge
 Lack of training
 Lack of appropriate tools and guidelines.

 Challenges of referral and stigma

Summary of challenges

Poor infrastructure



Thank you

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Principle of Quantiferon assay

M. Tuberculosis specific antigens M. Tuberculosis

Unaffected by BCG and most NTMs (non-tubeculous mycobacteria)
 TB infection (latent vs active?)

QuantiFERON[®]-TB Gold In-Tube

Assay Quick Reference Guide

Stage One - Blood Incubation and Harvesting



Stage Two - Human IFN-y ELISA

Tubes:	Results:
TB-antigen	Positive
Negative control (nil)	Negative
Positive control (mitogen)	Indeterminate

New diagnostics

- Apr 9;(62)
 Apr 9;(62)
 MTB/RIF. Bodmer T, Ströhle A. J Vis Exp. 2012
- MODS. Oberhelman RA et al, Lancet Infect Dis. 2010 Sep; 10(9):612-20.
- IP-10-new biomarkers. Ruhwald M et al, Expert Rev Mol Diagn. 2012 Mar;12(2):175-87. Review.
- Urine LAM. Peter J et al, Curr Opin Pulm Med. 2010 May; 16(3):262-70.
- Transrenal DNA. Green C et al, Lancet Infect Dis. 2009 Aug; 9(8):505-11.
- Urease breath test. Maiga M et al. Indian J Med Res. 2012 May;135(5):731-6.

TB in Tanzania

