

DFID Tuberculosis Knowledge Programme

**Project title: Evaluation of the role of new nucleic acid amplification tests in the routine diagnosis of tuberculosis in developing countries with a high prevalence of HIV infection.**

**Funding body:** Department for International Development, U.K.

**Principal Investigators:** Dr. Peter Godfrey-Faussett/Dr John Porter.

**Collaborating partners:**

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Ministry of Health, Chest Diseases Laboratory, Lusaka.

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Objectives of the research project

- To evaluate the role of the new, sensitive and rapid Nucleic Acid Amplification (NAA) technologies for the diagnosis of tuberculosis in the routine diagnostic setting of a developing country with a high incidence of HIV. This would include the logistics of implementation, expense, effects on patient management, potential effects on transmission and a cost benefit analysis.
- To evaluate these technologies at two different levels of the health care system: at the regional diagnostic laboratory level and at the district hospital/small hospital level.
- To publish guidelines and recommendations for the application of the new rapid and sensitive NAA technologies in the diagnostic setting which will enable health managers and health workers to make informed decisions about the benefits of the application of these techniques.

## Work undertaken

A low-cost 'in-house' polymerase chain reaction (PCR) and a commercial RNA amplification kit (AMTD, Gen-Probe Inc. San Diego) were compared to smear, culture and chest x-ray for the diagnosis of pulmonary tuberculosis in Lusaka on sputum specimens collected from suspected tuberculosis cases seeking diagnosis at the chest clinic. Clinical follow-up of suspects was undertaken.

The PCR was also tested in a rural district laboratory.

Economic studies were carried out at both sites.

The PCR used was a one tube nested, colorimetric assay based on the IS6110 insertion element. (*Wilson et al. 1993 J. Clin. Microbiol; 31:776-782*).

The Gen-Probe AMTD kit is based on the isothermal transcription mediated amplification of ribosomal RNA. (*Jonas et al 1993 J. Clin. Microbiol; 31:2410-2416*)

## Summary of major findings

- The sensitivity of microscopy for the diagnosis of pulmonary tuberculosis (PTB) was low and in Lusaka the majority of patients are diagnosed and treated on 'clinical suspicion' with some reference chest x-ray data.
- The 'in-house' PCR is not an appropriate technique for the routine diagnosis of PTB in Zambia. The PCR failed to identify all smear positive cases. The PCR was not sustainable for routine use at the rural site.
- The AMTD identified over 80% of PTB patients with results available within 3 days. It was the most sensitive of the laboratory techniques examined. However, the current high purchase cost of this test would prohibit its use for routine diagnosis in the public sector of such a low-income country.
- Possible false positive results for the AMTD were 3%. Contamination due to amplicon carry-over was not a significant problem in this study.
- In Lusaka a significant proportion (~20%) of patients placed on treatment for tuberculosis had no laboratory evidence of infection with *Mycobacterium tuberculosis*, their sputum being found smear, culture, PCR and AMTD negative.
- The incremental cost per case detected for performing a third smear at the rural site was US\$ 44.8. The use of three smears for initial screening of suspects should be reconsidered for low-income settings if further investigation of smear negative tuberculosis suspects is to be undertaken.
- The process of diagnosing tuberculosis has a significant economic impact on patients and guardians which may create barriers to prompt diagnosis. While seeking diagnosis in Lusaka patients incurred a mean total cost equivalent to 127% of their mean monthly income. Care-givers incurred costs equivalent to 31% of the mean monthly income.

## Related publications

Utility of nucleic acid amplification techniques for diagnosis of pulmonary tuberculosis in sub-Saharan Africa. Kambashi B, Mbulo G, McNerney R, Tembwe R, Kambashi A, Tihon V and Godfrey-Fausset P. *Int J Tuberc Lung Dis* 2001; 5 (4):364-369.

An incremental cost-effectiveness analysis of the first, second and third sputum examination in the diagnosis of pulmonary tuberculosis. Walker D, McNerney R, Kimankinda Mwembo M, Foster S, Tihon V, Godfrey-Faussett P. *Int. J Tuberc Lung Dis.* 2000; 4 (3) 246-251.

Barriers to tuberculosis case-finding in urban Zambia: the economic impact and burden on patients prior to diagnosis. Needham D.M., Godfrey-Faussett P., Foster S. *Intl. J. Tuberc. Lung Dis.* 1998; 2: 811-817.

Molecular diagnostics: a simple guide to diagnostic polymerase

chain reaction. McNerney R. 1997 Booklet published by LSHTM.  
(<http://www.lshtm.ac.uk/itd/units/pmbbu/mcnerney/introduction.html>)

Economic barriers to Tuberculosis control in Zambia Needham D.M.,  
Godfrey-Faussett P. *Lancet* 1996; 348: 134

Diagnosis: present difficulties and prospects for the future.  
McNerney R. *Africa Health* 1996;19 (1):22-23.

Microscopy negative but culture positive samples sent to the  
National Tuberculosis Reference Laboratory, Lusaka are not often  
due to false negative microscopy. (Abstract) Godfrey-Faussett P,  
Kahenya G, and Habeenzu C. *Tuberc. Lung Dis.* 1996; 77 suppl 2:  
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Utility of polymerase chain reaction for the diagnosis of pulmonary  
tuberculosis in a rural African laboratory. (Abstract) Kimankinda K.,  
Mee C., Mbulo G., Tihon V. and McNerney R. *Revista Portuguesa de  
Pneumologia* 1998 IV (3): 349

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