Diagnostics

Strategies for the management of multi-drug resistant tuberculosis in Kampala, Uganda

LSHTM investigators: Peter Smith, Alison Elliott, Ruth McNerney
Collaborators: University of Medicine and Dentistry of New Jersey, TB Treatment Centre of the Ugandan National TB and Leprosy Control Programme (NTLP), Mulago Hospital and Makerere Medical School, Kampala, Uganda.
Funding bodies: Wellcome Trust/Burroughs Wellcome Fund

This four-year study has three scientific aims:

To determine the prevalence of primary and secondary drug resistance in TB patients treated in the National TB and Leprosy Control Programme (NTLP) at Mulago Hospital.

To determine the extent of nosocomial transmission of drug resistant TB on the TB ward at Mulago Hospital and to identify host and microbial factors that predict transmission.

To evaluate new intervention applied on an individual basis to reduce nosocomial transmission of drug resistant TB:
- Rapid diagnostics
- Novel microbiologic and immunological approaches to monitor therapy.
- Modified lower cost third line treatment.

The surveys undertaken during this study will systematically determine the levels of mono-resistance and multi-drug resistance among re-treatment cases of pulmonary tuberculosis over a four-year period. These data will be useful to the NTLP for evaluating current and establishing future programs in Uganda, plus provide valuable information leading to interventions to reduce transmission and reduce MDR-TB. The TB Treatment Centre is an ideal unit to determine the scope of nosocomial transmission and to define host and bacterial factors influencing relapse. Because MDR-TB is difficult and expensive to treat, interventions shown to be cost-effective in Uganda could readily be adapted in many developing country settings. Thus, the proposed studies will allow the centre at Mulago Hospital to take the lead nationally and internationally in a comprehensive approach to assess and intervene in transmission of MDR-TB in a country with a high prevalence of HIV infected people.

Keywords: drug resistance, MDT-TB

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Risk factors for drug resistant tuberculosis in Zambia.

LSHTM investigators: Ruth McNerney, Peter Godfrey-Faussett.
Collaborators: ZAMBART Project, MOH Chest Diseases Laboratory, Lusaka, Zambia

This two year project aims to identify biological and demographic risk factors for the emergence of drug resistant tuberculosis in Zambia. This study will be performed in conjunction with a national survey of susceptibility to anti-tuberculosis drugs.

Keywords: Drug resistance, MDR-TB, molecular epidemiology

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Evaluation of new tests for drug resistance

LSHTM investigators: Ruth McNerney, Kim Mallard
Collaborators: Centre for Infectious Diseases and International Health, University College London (CID&IH)
Infectious and Other Diseases Research Department,
Ethiopian Health and Nutrition Research Institute, Addis Ababa, Ethiopia
Funding bodies: DFID

Development of a simple bacteriophage based test for screening TB isolates for resistance to anti-tuberculosis drugs. A low-cost phage based method has been adapted to a colorimetric end point which may reduce both reagent and labour costs. The accuracy of this novel technology will be assessed by testing a panel of 100 clinical isolates.

Keywords: Drug resistance, MDR-TB

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Olfactory sensing for diagnosis of tuberculosis

LSHTM investigators: Ruth McNerney, Kim Mallard, Peter Godfrey-Faussett.
Collaborators: Inscentinel Ltd, Harpenden, UK.
Funding bodies: DFID

Honeybees show a remarkable sensitivity to detect trace odours. This project aims to investigate use of honeybees held in small, portable sensing units to detect tuberculosis.

Keywords: Diagnosis

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Trace odour detection for diagnosis of tuberculosis using the zNose.

LSHTM investigators: Ruth McNerney
Collaborators: Graf International, UK, University of Birmingham.
Funding bodies: DFID and Graf International

Screening clinical specimens for trace odours characteristic for tuberculosis infection has the potential to provide simple, low cost 'point of care' diagnosis. Previous studies have demonstrated that headspace vapours associated with *M. tuberculosis* are detectable in clinical materials. However, the development of a robust diagnostic test will require defined vapour analysis to enable calibration and standardisation of the technology.

Recent technological advances have led to the development of cheaper, highly sensitive platforms for vapour analysis, where prior chemical manipulation of samples is not necessary. First amongst these is zNose which incorporates capillary GC with a novel solid state detection system. The use of a temperature regulated surface acoustic wave (SAW) sensor provides enhanced detection capacity and high sensitivity. The zNose has been shown to distinguish bacteria by sampling headspace gases. When coupled with a pre-concentrating device detection is in the range of parts per trillion. The ability to separate compounds prior to detection and quantification with a piezoelectric SAW sensor offers analytical robustness not available to other electronic nose technologies.

We will investigate the application of this technology for diagnosis of tuberculosis.

Keywords: Diagnosis

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A novel target antigen for diagnosis of tuberculosis.

LSHTM investigators: Ruth McNerney
Collaborators:
Funding bodies: Heptagon Fund

The group has previously produced antibodies against a novel antigen that is secreted by complex *M. tuberculosis* bacilli. This project will examine clinical specimens for the presence of this marker of TB infection using an antibody-based test. Evidence that the antigen is detectable in specimens from TB patients, but not in specimens from healthy donors, will permit development of a diagnostic test.

Keywords: Diagnosis

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Confirmation culture isolates of Mycobacterium tuberculosis using MPB64-A simple and rapid test

LSHTM investigators: Peter Godfrey-Faussett, Helen Ayles, Joseph Banda, Ruth McNerney, Dirk Muller, Ab Schaap
Collaborators: Zambia: Monde Muyuyeta, ZAMBART Project; Ministry of Health; Chest Diseases Laboratory
Funding bodies: FIND Diagnostics

There has previously been no rapid and simple test available to test clinical isolates of mycobacterial to differentiate the *M. tuberculosis* complex from MOTT. The technologies that have been available include the use of molecular probes, gas liquid chromatography, and high liquid chromatography and Niacin strip test, but these tests are technically complex, cumbersome and expensive. In countries with limited resources such tests are not practical for routine use. A new immnochromatographic test (TAUNS) has been developed where results are available within 15minutes.

Objectives:

Primary objectives

1. To compare the use of MPB64 (TAUNS), Niacin and spoligotyping for the identification of MTB from culture isolates
2. To compare the time to identification of culture isolates using Niacin test and MPB64 test.
3. To determine the sensitivity of and specificity of MPB64 test and Niacin Test compared to spoligotyping.

Secondary objectives

1. To measure the costs of using MPB64 test as compared to Niacin test and spoligo typing when used in a high through put laboratory in a resource limited setting.

Keywords: Diagnosis

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Demonstration project: BACTEC MGIT for diagnosis of *M. tuberculosis*

LSHTM investigators: Peter Godfrey-Faussett, Helen Ayles, Joseph Banda, Ruth McNerney, Dirk Muller, Ab Schaap
Collaborators: Zambia: Monde Muyoyeta, ZAMBART Project; Ministry of Health; Chest Diseases Laboratory
Funding bodies: FIND Diagnostics

Traditional methods of isolating *M. tuberculosis* from clinical specimens using solid media (LJ) are slow. Using liquid culture, the time to detection of positive cultures is shortened. The mycobacterium Growth Indicator Tube (MGIT), a non-radiometric system liquid culture system will be evaluated for the diagnosis of tuberculosis. Its performance and associated costs will be assessed.

Keywords: Diagnosis

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Demonstration project: Quantiferon Gold In Tube for diagnosis of M. tuberculosis infection

LSHTM investigators: Peter Godfrey-Faussett, Helen Ayles, Joseph Banda, Ruth McNerney
Collaborators: Zambia: Kwame Shaunabe, Grace Mbulo, ZAMBART Project; Ministry of Health; Chest Diseases Laboratory
Funding bodies: FIND Diagnostics

The traditional method of detecting infection with M. tuberculosis using the tuberculin skin test has some disadvantages, despite being widely used and much studied. Interferon gamma release assays may be more sensitive and should be more specific, but the predictive value of such tests in a high prevalence setting has not been documented. We will follow up members of the SOCS studies (part of the ZAMSTAR studies) to determine whether qualitative or quantitative responses to tuberculosis specific antigens can be used to predict the development of tuberculosis in household contacts.

Keywords: Diagnosis

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