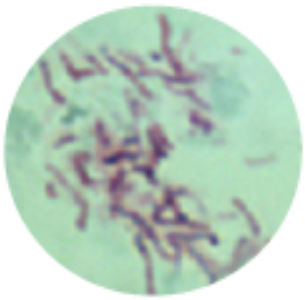
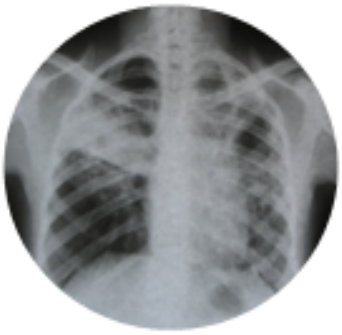
Research Report: Drug Resistant TB

A report of research undertaken in Kampala, Uganda with the support of the Burroughs Wellcome Trust Fund Infectious Disease Initiative 2002-2007.



Mycobacterium tuberculosis kills more adults than any other single pathogen. It is a slow-growing bacteria with a lipid rich cell wall that is naturally resistant to many drugs. Resistance to anti-TB drugs emerges through the selection of naturally occurring mutations by inadequate treatment.



TB is infectious by the respiratory route. It is spread via aerosols created during coughing sneezing, or even speaking. Effective treatment quickly renders patients non-infectious. However, if strains are resistant to anti-TB drugs then patients may remain infectious. TB that is resistant to the two major drugs rifampicin and isoniazid is termed multidrug resistant (MDR-TB).

MDR-TB has been observed in many countries and is a serious threat to TB control Little is known about MDR-TB in Africa where 2nd line treatment is rarely available.

Strategies for the management of multi-drug resistant tuberculosis in Kampala, Uganda.
From 2002 to 2007 a consortium of international partners undertook a programme of research to investigate the emergence and control of MDR-TB in Mulago Clinic, the referral TB clinic for the Ugandan National TB and Leprosy Control Programme.

Project Review Meeting Kampala 2006

UMDNJ
University of Medicine & Dentistry of New Jersey

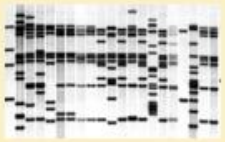
TBRU

MRC Medical Research Council

Strategies for the management of multi-drug resistant tuberculosis in Kampala, Uganda was approved by the HIV/AIDS Committee of the Ugandan National Council for Science & Technology, University of Medicine and Dentistry of New Jersey Institutional Review Board and the Research Ethics Committee of the London School of Hygiene & Tropical Medicine.

Through the study we implemented enhanced clinical care at the TB ward through regular inpatient clinical rounds and weekly educational conferences with students, residents and nurses.
We developed a nutritional program (funded by the World Food Program) for hospitalized patients and their families. This program has improved the outcome of patients, both directly through better nutrition and indirectly by increasing compliance with TB treatment.

We developed a sustainable, evidence-based 'infection control' policy in the TB ward including air-sealed isolation rooms, segregation of infectious patients, respiratory masks and improved ventilation with extraction fans where required.

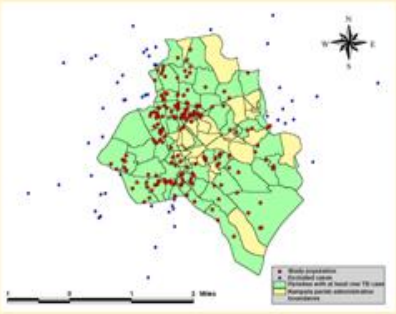


We used molecular epidemiology to monitor nosocomial transmission of TB. Preliminary data suggest there has been relatively little patient-to-patient transmission of MDR-TB in this tropical medical facility with open air ventilation and the simple infection control measures instituted.

The capacity of the TB laboratory at JCRC was increased and testing for resistance to 2nd line TB drugs was introduced.
We evaluated a novel low-cost method for screening TB isolates for resistance to rifampicin and a number of methods for detecting drug resistance directly from clinical specimens were compared for accuracy, turn around time and cost. Direct testing of sputum for resistance to rifampicin and isoniazid was implemented using a liquid culture system (MGIT960, Becton Dickinson).

We measured resistance to anti-tuberculosis drugs. Resistance was high in re-treatment cases with a quarter (24.5%) having resistance to isoniazid and 12.7% (52/409) having MDR-TB. The prevalence of resistance to second-line drugs was low. Factors associated with MDR-TB at enrolment included a history of treatment failure, the presence of cavities on chest x-ray and an increasing number of previous TB episodes. HIV was not associated with resistance.

Kampala residents attending the clinic were invited to join the study. TB cases were seen to cluster in areas associated and high density housing and low incomes, reaffirming the link between TB and poverty. No significant clustering was observed for MDR-TB.



Expertise in clinical management of MDR-TB has been developed at Mulago Hospital. Community health workers were trained to provide the necessary care (DOTS-Plus). Treatment regimens may continue for two years and use drugs of heightened toxicity.

We obtained assistance from the WHO Green Light Committee for procurement of second-line drugs to treat MDR-TB.

We established an 'International MDR-TB Case TeleConference' between Kampala and the Lattimore TB Clinic-Global Tuberculosis Institute at UMDNJ New Jersey Medical School which supports on-going education at both sites.

We have developed and field-tested effective and affordable tools to assist control of drug resistant tuberculosis.

We suggest this model DOTS-plus program could be replicated in other countries in sub-Saharan Africa.

The MDR-TB program described here has solidly placed Uganda, a country widely recognized for its early leadership and vision in addressing the HIV/AIDS epidemic, as a leader in research on the emerging problem of TB drug resistance in sub-Saharan Africa.

Acknowledgments: people, places and funding.

The success of this project is due to the enthusiasm and professionalism of the doctors, drivers, laboratory scientists, home visitors, nurses and statisticians who made up the Project Team.

The principle investigators were

Prof. Roy Mugerwa, Dept. of Medicine, Makerere University Medical School, Kampala, Uganda.
Prof. Jerrold Ellner, Dept. of Medicine, New Jersey Medical School-UMDNJ, USA.
Prof. Peter Smith, Dept. of Tropical and Infectious Diseases, London School of Hygiene & Tropical Medicine, UK.

The Project was co-ordinated by Dr Edward Jones-López, New Jersey Medical School-UMDNJ, USA and administrated by Ms Annette Mugenyi, Makerere University – UMDNJ Research Collaboration. The clinical team was led by Dr Alphonse Okwera at Mulago Hospital TB Clinic, who also co-ordinated with the National TB and Leprosy Control Programme.

Data analysis was performed by staff of the Medical Research Council/Uganda Virus Research Institute Uganda Research Unit on AIDS and Prof. Kathleen Eisenach of the University of Arkansas for Medical Sciences, Little Rock, USA provided expert support to the laboratory.

Institutional support was received from Old Mulago Hospital, Makerere University, Joint Clinical Research Center (JCRC), Case Western Reserve University, New Jersey Medical School-UMDNJ and London School of Hygiene & Tropical Medicine.

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We dedicate this report to the patients who generously consented to partake in the study.

Dissemination

A workshop was held in Kampala 22nd October 2007
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for further details

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