**UNFINISHED BUSINESS**

**Stopping transmission**
- Better understanding transmission
- Early diagnostic tests
- Prevention of transmission
- Epidemiology and mapping
- Improving service provision
- Effective awareness strategies
- Innovative approaches to leprosy control

**Preventing disability**
- Clinical management of leprosy complications
- Economic effects of leprosy-related disability
- Improving early diagnosis
- Effective CBR programmes
- Cross NTD and disability studies
- Innovative approach to prosthetics and orthotics

**Promoting inclusion**
- Stigma and discrimination – its measure and interventions
- Effective approaches to support the mobilisation and empowerment of leprosy people’s organisations
- Leprosy and human rights
- Inclusive employment
- Inner wellbeing (mental health)
Who we are

The Leprosy Mission (TLM) is a Global Fellowship of 32 member countries. We are active in more than 40 countries around the world. We work hand-in-hand with governments and local communities, UN bodies, local non-governmental organisations, local churches, and many others to achieve our vision of: ‘Leprosy defeated, lives transformed’

Why research with TLM?

- TLM has been involved in research for more than 50 years, from the testing of anti-leprosy drugs such as Clofazimine in the 1960s and 1970s to the innovative surgical procedures pioneered by Dr Paul Brand.

More recently, we have been involved in studies investigating the effectiveness of community-based rehabilitation as well as increasing our social studies research portfolio looking at topics such as stigma and discrimination, empowerment and life-course research.

We have experience in both quantitative and qualitative research and where we lack the capacity ourselves, our partnerships with other researchers allow us to tap into their capacity.

- TLM owns internationally recognised laboratories in India and Nepal.

The Stanley Browne Research Laboratory (SBL) in New Delhi, India, has a significant publication record for molecular and drug resistance studies including leprosy viability investigations (nasal and environment sampling).

The Mycobacterial Research Laboratory (MRL) at Anandaban Hospital in Kathmandu, Nepal, has a history of clinical, molecular and immunological international collaborative partnerships, currently including: Leiden University Medical Centre (The Netherlands); London School of Hygiene and Tropical Medicine (UK); and the Department of Health and Human Services National Hansen’s Disease Programs (USA).

Both SBL and MRL participate as sentinel sites nationally and within the World Health Organisation (WHO) Global Surveillance Programme for Leprosy Drug Resistance.

- Cutting edge biomedical research is conducted in collaboration with universities and research groups in Asia, America, Australia and Europe, focused mainly on transmission, diagnosis, leprosy reactions and drug resistance monitoring.

- TLM has a strong field presence as a direct programme implementer, employing around 2,000 staff.

Our programmes include referral hospitals, leprosy control initiatives and community-based health and rehabilitation projects. Together they provide a platform for clinical, social, epidemiological and operational research.

Our clinical work in endemic countries keeps us in daily contact with people affected by leprosy.

- We are involved in international, multidisciplinary networks which enable us to further the research agenda and to bring the results of research to practical application.

This involvement is growing and is a strategic priority to increase our impact.

- Current global research collaboration is taking place in Bangladesh, DR Congo, Ethiopia, India, Mozambique, Myanmar, Nepal and Nigeria.
Where we work

We are a global network active in around 45 countries across the world. We work hand-in-hand with governments and with local communities, with partner health organisations, WHO, local non-governmental organisations (NGOs), local churches, Christian partners and many others to achieve our vision of: leprosy defeated, lives transformed.

Members of The Leprosy Mission Fellowship are in bold text. In the remaining countries, closely connected partners either share the same Leprosy Mission heritage or are implementing significant programmes with Leprosy Mission support.
The following pages outline some current research projects we are involved in...

**Stopping transmission**

The combined effect of chemoprophylaxis with Single Dose Rifampicin (SDR) and immune-prophylaxis with Bacille Calmette Guerin (BCG) to prevent leprosy in contacts of newly diagnosed leprosy cases: a cluster randomized controlled trial (MALTALEP study).

**Lead researcher:** Prof Jan Hendrik Richardson, Erasmus University. Co-investigators: Renate A. Richardus; Khorsshed Alam; David Pahan; Sabiena G. Feenstra; Annemieke Geluk

**Partnered with:** Department of Public Health, Erasmus MC, University Medical Center Rotterdam; The Leprosy Mission International Bangladesh; Department of Infectious Diseases, Leiden University Medical Center, The Netherlands

Combined chemoprophylaxis and immunoprophylaxis is potentially a very powerful and innovative tool aimed at contacts of leprosy patients that could reduce the transmission of M. leprae substantially.

The trial intends to substantiate this potential preventive effect, building on work conducted in the same leprosy control project in 2003-2007 (“CoLEP trial”) which demonstrated efficacy of single dose rifampicin (SDR) given to contacts. This reduced incidence of leprosy to 57% over a two-year period.

The study aims to examine the effect of chemoprophylaxis with single dose rifampicin and immune-prophylaxis with BCG on the clinical outcome as well as on host immune and gene profiles in contacts of new cases of leprosy.

We hypothesise that the effects of both interventions may be complementary, causing the combined preventive effect to be significant and long-lasting.

Through a cluster randomised controlled trial we compare immunisation with BCG alone and with BCG plus SDR in contacts of new leprosy cases.

Contact groups of around 15 persons will be formed for each of the 1,300 leprosy patients included in the trial, resulting in a total of around 20,000 contacts. The intervention group will be given BCG immunisation followed by SDR, two months later. The control group will receive BCG only. In total, 10,000 contacts will be included in each intervention arm over a two-year period. The primary outcome is the occurrence of clinical leprosy within two years.

The index cases and contacts are identified, enrolled, and followed up by The Leprosy Mission (TLM) field staff through the leprosy clinics which function as part of a national leprosy elimination programme.

**Progress to date:**

Study enrolment began in 2012 and will be completed by the end of 2016. Early finding of 21 new cases presenting soon after BCG vaccination, was published in Vaccine® journal in 2015.

*http://dare.uva.nl/document/2/70723*

**Developing diagnostics and understanding pathology**

**Opening a can of worms: M. leprae outcomes and complicit neglected tropical diseases**

**Lead researcher:** Deanna A. Hagge, Director of Research and Laboratories, Mycobacterial Research Laboratories (MRL), Anandaban Hospital, Nepal

**Co-investigators:** Annemieke Geluk, Linda B. Adams, Indra B. Napit, Mahesh Shah, Peter G. Nicholls

**Partnered with:** The Leprosy Mission Nepal; Department of Infectious Diseases, Leiden University Medical Centre, The Netherlands; Department of Health and Human Services, Health Resources and Services Administration, Health Systems Bureau, National Hansen’s Disease Programs (DHHS/HRSA/H5B/NHDP), Baton Rouge, Louisiana, USA; School of Health Sciences, University of Southampton, United Kingdom

**Agencies include:** The Leprosy Mission England and Wales, Vittori Charitable Foundation, Leprosy Research Initiative (LRI) and the Order of Malta-Grants-for-Leprosy-Research (MalTALEP)

More than 94% of all annual new leprosy cases originate from areas co-endemic for both leprosy and soil-transmitted helminths (STH).

Research has demonstrated that chronic STH co-infection can profoundly divert host responses from Th1 or cellular immunity towards Th2 or humoral immunity, thereby impacting disease outcomes across a variety of immunopathologies, including: tuberculosis, HIV, malaria and allergy.

Previous studies have indicated that leprosy patients with chronic STH co-infection more often had higher M. leprae loads and tendency towards development of more severe disease (multibacillary or lepromatous leprosy).

Our laboratory has been investigating STH co-infection relevance to leprosy reactions, unpredictable and debilitating immunological complications that can afflict up to 30-50% of all leprosy patients at some point.

Leprosy reactions are dynamic shifts in Th1-Th2 response that are also the primary factor for development of neuropathy and disability development in leprosy patients.

We hypothesise that chronic STH co-infection is related to leprosy reactions and immune biomarker detection within co-endemic populations.

Cutting edge methods in microscopy, molecular and immunological assays are employed to screen and follow patient outcomes within services of a national leprosy referral centre (Anandaban Hospital, The Leprosy Mission Nepal).

Findings are in process for publication.

Impact is expected in areas of clinical management and diagnostics as well as current understanding for leprosy transmission, susceptibility and control activities alongside other neglected tropical disease (NTD) programmes.
Preventing disability

Integrated mapping and basic support of patients with disabilities caused by lymphatic filariasis and leprosy in selected co-endemic districts of the province of Cabo Delgado, Mozambique.

Lead Researchers: Professor Charles Mackenzie and Dr Arie de Kruijff
Partnered with: Filarial Programme Support Unit, Liverpool School of Tropical Medicine; The Leprosy Mission Mozambique and Cabo Delgado Health Department, Mozambique

Mozambique started the implementation of Disease Management and Disability Inclusion (DMDI) activities for lymphatic filariasis in 2015, which include the burden assessment of patients suffering from hydrocele and lymphedema.

With regards to leprosy, the country declared elimination in 2008, but the number of cases since then has increased, with an elevated number of visible impairments in undiagnosed cases.

Following the guidelines on the integration of Neglected Tropical Diseases (NTDs) control and elimination activities, both The Leprosy Mission Mozambique and the Filarial Programme Support Unit at the Liverpool School of Tropical Medicine, are implementing a collaborative project with the aim of conducting an integrated mapping for leprosy and lymphatic filariasis patients in the co-endemic districts of Cabo Delgado province.

The project is based on the training of volunteers in the recognition of both leprosy and lymphatic filariasis in their communities and the construction of a preliminary database to assess the burden of both diseases. In a second phase, the clinical confirmation and registration of identified patients will be carried out by electronic means to be able to provide them with adequate access to health care.

The effectiveness of a five-month prophylactic prednisolone course on the prevention of clinical neuropathy in leprosy patients with subclinical neuropathy

Lead researchers: Erik Post, Wim Brandsma, Inge Wagenaar, Peter Nicholls. Co-investigators: Dr. Sajid Husain, Dr. Krishna Lama, Md. Khorshed Alam; Dr. Varaja Shetty. Partnered with: Central JALMA Institute for Leprosy, Agra, India; Lalghadh Hospital, Nepal; The Leprosy Mission International Bangladesh; Foundation for Medical Research, Mumbai, India

Leprosy is an infectious mycobacterial disease that may result in neuropathy with subsequent nerve function loss, which in turn may lead to disabilities.

It is assumed that when nerve function loss is clinically detectable, quite some damage has already been done to the nerves, the so-called subclinical neuropathy.

The INFIR (ILEP Nerve Function Impairment and Reaction) study shows that of the leprosy patients having subclinical neuropathy, 16% will eventually develop clinical nerve function loss.

Preventing this development may be a very important step in the prevention of disabilities. So far, however, few studies looked into the prophylactic treatment of subclinical neuropathy.

The objective was to study the effectiveness of prednisolone in the prevention of nerve function loss in patients with subclinical neuropathy.

In a randomised triple blind placebo controlled trial, 363 newly-diagnosed leprosy patients with subclinical nerve function impairment were enrolled.

Four centres participated in this research: The Foundation for Medical Research, Mumbai and JALMA, Agra in India, The Leprosy Mission, Nilphamari in Bangladesh, and Lalghadh Hospital in Nepal.

Patients received five months of prednisolone or a placebo. Subjects were first assessed with Voluntary Muscle Testing (VMT) and monofilament testing (MFT) to exclude clinical neuropathy, and were subsequently tested with Nerve Conduction Studies (NCS) and for Warm Detection Thresholds (WDT), to determine the degree and extent of subclinical neuropathy.

Primary outcome was defined as the proportion of patients developing clinical nerve function loss during 78 weeks of follow-up.

An important secondary outcome was occurrence of adverse events.

The analyses have not been completed, but the preliminary results show that prednisolone is not effective in preventing clinical nerve function impairment in newly-diagnosed leprosy patient with subclinical neuropathy.
Promoting inclusion

Civil Society Organisations, Resource mobilisation, Empowerment, Advocacy, Training and Employment of people affected by leprosy (Create) in India – Research into stigma and discrimination


CREATE project will be working across four Indian Districts from 2016 – 2018.
A core component of the project is operational research – related stigma and the effectiveness of measures to combat this stigma and promote inclusive development for people affected by leprosy and disabilities.
Field research is being conducted by the project team who are also training people affected by leprosy to gather their own data in order to provide an evidence-base for their advocacy efforts.

Mixed method data collection will be used by the researcher to analyse stigma and discrimination reported through data sources.
This will eventually lead to the development of a stigma toolkit, which will help civil society organisations representing people affected by leprosy and disabilities to identify stigma and develop effective approaches to combating it.

Case study

Angels in blue work to defeat leprosy

Research is important but can only have an impact if its results are used to improve programme implementation.

Findings from The Leprosy Mission’s study in Bangladesh have shown that Rifampicin can be used as a post-exposure prophylaxis (PEP), helping to prevent leprosy in the contacts of index cases.

This is now being rolled out in numerous countries, including Nepal.

Numkala Nuwani is one of 12 angels in blue, all Female Health Volunteers in a village in Kapilvastu district who are involved in both diagnosing and preventing leprosy.

Married with three children, Numkala has been a volunteer for 23 years and has encouraged many others to join the team. Educated at school up to grade 10, she understands the importance of health care.

She became a health volunteer because she wanted to help women in the community.
Many women were not allowed to leave the home, and their husbands prevented any access to health clinics.

By becoming a health volunteer, she has been able to educate women about many health issues and support them and their children to access treatment.
Training from The Leprosy Mission has enabled her and her fellow volunteers to identify the signs and symptoms of leprosy and ensure people access treatment.

More recently, the volunteers not only identified new cases but are now also involved in ensuring their contacts receive the single tablet that can help prevent the disease.

Numkala says: “As a volunteer we regularly undertake house-to-house visits informing people about the disease and screening people.

“If it turns out to be leprosy, we screen all the people who have been in close contact, be it relatives, friends and work colleagues or, in the case of children, their classmates.

“Through the programme all contacts of every new person diagnosed will be given a single dose of Rifampicin to help stop leprosy.”

Numkala Nuwani
The objective for this piece of research is to assess improvements in social acceptance and dignity of people disabled by leprosy after adult literacy in four districts of North West Bangladesh.

There are about 4,000 disabled people living in these districts who have completed anti-leprosy treatment under The Leprosy Mission International-Bangladesh and are followed up annually. Seven hundred Self-Help Groups (SHG) have been formed as part of a Community Based Rehabilitation (CBR) Project amongst people disabled by leprosy.

To facilitate participation in SHGs, 30 adult literacy classes were established and participants completed a 10-month course.

Of the 300 participants in the literacy classes, 10 were selected for an interview to enquire more about their social acceptance and dignity.

The subjects were asked questions on the following areas of their life:

1. Experience of leprosy disability and destitution.
2. Social relationships, acceptance and support by family and community.
3. Economic development and mental satisfaction

Almost all 10 interviewees spoke of their life history being affected by leprosy and disability, family and society. Because of leprosy they lost their limbs, dignity and quality of life. After being involved in a SHG their life experiences were improved.

They participated in adult literacy classes for 10 months. After completion of the literacy course they were able to read the Bengali newspaper, posters, signboards, and leaflets as well as write minutes of group meetings and maintain all other registers. In addition, they were able to monitor their personal income and expenditure, write letters, and use a mobile phone. Some of them have become leaders of SHGs and support other SHG groups.

Participants report that the community where they live now respects them and in some cases they are taking on the role of community advisor.
Our research partners include ...