Dear Friends,

At TLMTI we have entered into a new era!

This has been a very intense year so far, and I believe when we look back we will see it as one of significant progress. While there is not much time for celebration, real progress is being made, and the facts speak for themselves.

The innovations that are transforming our work and the people we work for, our organisation events, internal and external and the new initiatives are reflecting the paradigm shift and transformation within the organisation.

This year the National Consultation on Rehabilitation of people affected by leprosy organised jointly by Pandit Deen Dayal Institute of Physically Handicapped, Mo SJ&E and TLMTI, brought in many policy makers, organisations working for people affected by leprosy, bureaucrats, people affected by leprosy and we hope that this step will bring about a real difference in the life of people affected by leprosy.

We have also sought to advocate more effectively for change. Alongside our work on the ground, we launched the HEAL India campaign in 2013 and plan to scale it further this year. The campaign is steadily creating an impact, and our reach is increasing. Thanks to research, we are adapting to a rapidly changing world: we are expanding our work and campaign design to match the changes we see in the world.

Research is crucial in achieving lasting change. From policy research to base line research, surveys tracking, and impact assessment to research in new areas, it plays a very important role in bringing about the change we want to see. We have been working at our greater involvement in research as it will strengthen us to make a positive contribution towards bringing about a change.

Together let us change the way the world thinks and acts to ensure not just lasting change, but lasting happiness for generations to come.

Change begins with you. Take action. Ensure that research becomes a policy priority.

Best wishes,

Nikita Sarah
Head - Advocacy & Communication

Greetings from TLM India!

2014 is already more than 3 months old and we at the Research Domain have been having a busy, challenging and exciting time!

As you will see in the Research Events section, we have been busy with meetings, workshops and conferences, all of which needed a great deal of hard work and Team spirit, to be fruitful. A 20 strong contingent attended the 29th. LEPCON (Indian Association of Leprologists Conference) at Chandigarh, presenting a number of posters and papers. We won two awards – Dr. Jerry Joshua for the Best Poster and Sundeep Chaitanya for the Ackworth Memorial Lecture. We congratulate them and wish them the best for their future projects.

As TLMIndia engages with newer areas such as advocacy, inclusion and Rights based approach, our staff are eager to learn as we progress. A Social Science Research workshop was held to build the capacity of staff in this area so that research becomes an integral part of the new projects and facilitates learning at all stages and levels of the organisation.

The concern regarding the ongoing transmission of leprosy, as evidenced by the New Case Detection rate which does not show any indication of decreasing, is growing. There were a number of presentations at the LEPCON on this issue and the leprosy world is looking for new strategies to address it. Various Contact centred strategies are being discussed and some tested such as chemoprophylaxis, active search in high endemic areas and involving the community. The ICMR has also issued a new set of Research Priorities in response to the present situation.

All in all these are exciting times for research in leprosy and many opportunities to make a difference!

We welcome your suggestions, questions and feedback. Please write to the address given.

Wishing all our readers a Blessed Easter!

Annamma S. John
Editor
The LEPCON 2014, 29th Biennial conference of Indian Association of Leprologists, was held during 28-30 March 2014, by the Department of Dermatology, Venereology & Leprology, at the Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh.

Leprologists from all over India and many scientists from abroad attended and there was good representation from every field of leprosy. Special features such as Leprosy Workshops, the invited and award paper sessions and Leprosy Quiz for PG students from different universities, were the highlights of the conference.

The Leprosy Mission Trust India (TLMTI), participating actively in the conference with about 20 delegates sponsored by TLMTI from different centres, who presented scientific papers on specialized areas such as Social sciences, Immunology, Operational issues, Media and communication, Physiotherapy, Reconstructive Surgery etc.

An oral presentation of a paper entitled “A report of Rifampicin Resistant Leprosy from Northern and Eastern India: Identification and in-silico analysis of molecular interactions” by the staff of Stanley Browne Research Laboratory, won the “Acworth Leprosy Hospital Society Award for Research, Rehabilitation and Education in leprosy for Best Scientific Paper Presentation on Leprosy “ award meant for young scientists.

Dr. Jerry Joshua, received a prize for his Poster entitled “Changes in plantar pressures on heel following medial plantar artery flap cover in leprosy affected patients with heel ulcers ” which was selected as the best paper presented in the conference, which also shows TLMTI’s achievements in the field of research.

Prize winning Abstracts

Changes in plantar pressures on heel following medial plantar artery flap cover in leprosy affected patients with heel ulcers

Jerry Joshua, Mrinmoy Karmakar

Background: Plantar ulcers are one of the most common sequelae of leprosy with almost 10% of ulceration occurring in heel. Flap cover along with calcaneal paring is commonly done to prevent recurrence of ulcers. Extensive literature search was done and to date no studies have quantified the changes in heel pressures following such surgery. The objective of the study was to validate the assumption that the surgery redistributed body weight over a larger portion of the heel by quantification of the proportion of body weight.

Methods: Leprosy affected patients complaining of heel ulcer, who underwent flap cover and calcaneal paring were included in the study. 22 patients (9 female and 13 male). (Average age 48.8 years) were assessed on GAIT scan preoperatively and post operatively after the completion of healing of the wound to find the changes in heel pressures following surgery. The GAIT scan assesses pressures on the medial and the lateral heel, mid foot, 1st to 5th Metatarsal heads and toes. Static and dynamic measures were taken. 18 out of 22 patients had follow up of more than 6 months.

Results: Preoperative and post-operative data for the medial and lateral heel were collected and analysed. Results show that there is a significant change in the medial and lateral heel pressures between the preoperative and post-operative data in all the 22 patients. The changes were stable in the 18 patients followed up. The mean percentage pressures preoperatively for the lateral heel was 87% of body weight and the mean postoperative pressure for the lateral heel was 62%. The mean preoperative percentage pressure for the medial heel was 62% which came down to 53% post operatively. The average duration of weight bearing on the heel was 60% of the gait cycle preoperatively and this reduced to 45% of the gait cycle post operatively.

Conclusions: Flap cover and calcaneal paring decreases the pressure over the medial and the lateral heel and also the duration of concentrated weight bearing. The changes in the pressure may be attributed to the calcaneal paring which increases the heel surface area and the flap which replaces the area of weight concentrating scar tissue.

A report of Rifampicin Resistant Leprosy from Northern and Eastern India: Identification and in-silico analysis of molecular interactions.

Chaitanya VS, Lavania M, Kumar M, Punit Kaur, Turankar RP, Singh I, Nigam A & Sengupta U

Aim: Emergence of drug resistant Mycobacterium leprae (M.leprae) poses a threat to the treatment and control strategies for combating leprosy. Presence of point mutations within the drug resistance determining regions of the M. leprae genome confer molecular basis of drug resistance to Dapsone, Rifampicin & Ofloxacin which are further confirmed with conventional mouse foot pad methods. This study focused on the identification of mutations within the rpoB gene region that are specific for rifampicin interaction and further in-silico analysis was carried out to determine the variations in the interactions.

Materials and Methods: DNA and RNA were isolated from slit skin scrapings of 60 relapsed leprosy patients from The Leprosy Mission Hospitals in India. PCR targeting rpoB gene region and ampiclon
sequencing was performed to determine point mutations. mRNA expression levels of rpoB and High Resolution Melt Analysis of mutants was performed using Rotor Gene Q Realtime PCR. In-silico docking experiments were performed using Ligand fit Molecular Docking Program.

Results and Conclusion: 10 cases having point mutations within the rpoB gene region were identified and were clinically suspected to be resistant to rifampicin. Along with the known mutations, a novel mutation at codon position Gln442His has been identified. There is a 9.4 fold up-regulation in the mRNA expression of rpoB gene in mutant/resistant samples when compared with the wild/sensitive samples. In-silico docking analysis of rifampicin with wild and Gln442His mutant RpoB proteins revealed a variation in the hydrogen bonding pattern leading to a difference in the total interaction energy (-73.98 kcal/mol in wild protein Vs -71.54 kcal/mol in mutant RpoB) and conformational change at position Asp441. The high resolution melting curves revealed a variation in difference relative fluorescence units of greater than 5 units in mutant samples when normalized with wild samples. The inhibition constants (Ki) increased significantly in mutant samples in comparison to wild (614.14 µM Vs 142.72 µM). These preliminary downstream functional observations revealed that the presence of point mutations within the rifampicin resistance determining regions of rpoB gene play a vital role in conferring genetic and molecular basis of resistance to rifampicin in leprosy.

BRIEF REPORT ON THE WHO MEETING ON SENTINEL SURVEILLANCE OF DRUG RESISTANCE IN LEPROSY
Feb 5-6th 2014, Cebu – Philippines

As a part of the WHO program on sentinel surveillance of drug resistance in leprosy initiated by WHO Global Leprosy Program (GLP) in 2008, a meeting to discuss the program level, clinical and laboratory findings on the status of drug resistance in leprosy was conducted by WHO and hosted by Leonard Wood Memorial Leprosy Hospital in Cebu, Philippines from Feb 5-6th 2014.

This surveillance network comprises 14 sentinel sites and 11 reference laboratories from different leprosy endemic countries, which report the status of drug resistance in leprosy to WHO- GLP. Stanley Browne Laboratory (SBL) is one of the reference laboratories and TLMTI Hospitals in India comprise one sentinel site. The meeting was conducted for two days and included a clinical and national program level representation from the 14 sentinel sites. Presentations were made by experts on clinical and technical aspects: Global Leprosy Situation – Dr. Sumana Barua, Whole Genome Sequencing – Prof. Stewart Cole and Management of drug resistant cases of leprosy – Prof. Emmanuelle Cambau. Dr. Mallika Lavana and Mr. Sundeeq Chaitanya from SBL are the focal persons for WHO GLP to represent the TLMTI India sentinel site and are involved in identifying the burden of drug resistance in leprosy at the TLMTI hospitals in India.

82 relapsed leprosy cases (clinically and histopathologically determined) were reported by 14 TLMTI hospitals across India in 2013. Out of these, 53 slit skin scraping samples were collected and sent to SBL for determination of molecular basis of drug resistance in leprosy. Laboratory methods involved Polymerase chain reaction (PCR) based amplification of Dapsone, rifampicin and fluoroquinolones targeting genes in Mycobacterium leprae genome followed by DNA sequencing to determine mutations that confer drug resistance.

From 2009 - 2013, 9 cases with Dapsone resistance, 9 cases with fluoroquinolones resistance and 7 cases with rifampicin resistance were identified at the TLMTI Hospitals across India. Additionally 26 relapse leprosy cases were identified at TLMTI Hospital in Purulia in West Bengal from samples collected from the field area (patients' houses). 3 of these 26 patients were identified to be resistant to rifampicin bringing rifampicin resistant cases to a total of 10. Rifampicin resistance was identified for the first time at TLMTI hospitals in India.

The molecular basis of drug resistance is determined through presence of point mutations within the drug resistance determining regions of M.leprae genome. SBL has identified a novel mutation causing amino acid substitution at position 442 in RNA polymerase protein which is responsible for rifampicin resistance. The functional effects of this mutation in conferring rifampicin resistance has been studied using bio-informatics tools and in collaboration with Department of Biophysics, All India Institute of Medical Sciences. The observations were presented at the above meeting and were appreciated by various scientists involved in the similar work.

Discussions were initiated by SBL staff with scientific experts to seek collaborations on developing studies on functional aspects of drug resistance in leprosy. The novel mutation was accepted for further validation and West Bengal was included as WHO priority area to intensively screen for drug resistant leprosy with the help of National Leprosy Eradication Program (NLEP) in India. Minocycline was recommended as a second line of treatment for Rifampicin resistant cases and impetus was given for screening of primary drug resistance within the leprosy endemic pockets of India.
Research Priorities in TLMTI

Research in TLMTI aims to be relevant and applicable in the field, answering problems that face us as we struggle to overcome leprosy.

Till recently most of the research being done in TLMTI was either in basic sciences such as immunology and molecular biology or in clinical aspects. As our programmes move from a purely technical/medical service delivery mode to more participatory, development and rights based programmes, the research we conduct should contribute to the work being done and facilitate reaching our goals. This includes field research to improve services and develop newer, more effective models, participatory models to involve our stakeholders as well as continuing to address important issue such as the emergence of resistance to Anti leprosy drugs.

With this perspective we have aligned our priorities to the Short Term Goals of the TLMTI Country Strategy. So our research is being focused on the issues in the tagline – Healing, Inclusion and Dignity. We hope to build the capacity of our staff to engage in research around Stigma, Inclusion and Advocacy issues. The projects that are taken up will be in the following priority areas.

- **Healing**: Leprosy services (New Drugs, Access, Early diagnosis, Disability, Reactions, Psychological support), Transmission, Drug Resistance etc.
- **Inclusion**: Advocacy Research - generating evidence on social exclusion, denial of rights / entitlements, measurement of and interventions to reduce stigma, integration within communities and education and livelihood issues.
- **Dignity**: Issues of human rights, facilitating participation of leprosy affected people in society.

Research Events

2014 has been a very busy year for the Research Domain, so far. The SBL and all field research were officially brought together as the Research Domain. What was previously known as the RRC, shifted from Media Centre at NOIDA to premises at TLMTI Community Hospital Shadara.

A mini workshop was held at TLMTI Naini from 4th. to 7th. February at which a few papers were written up and submitted.

**The Scientific Advisory Committee** for Stanley Browne Laboratory met on 12th. February at Shahdara. It was a fruitful meeting, where experienced scientists gave their inputs on the work of SBL.

**A Social Science research Workshop** was held from 11th. to 14th. March. 17 participants from TLMTI projects and hospitals attended the workshop. Dr. Pim Cuipers from Griffiths University, Australia, Dr. M. S. Raju, Ms. Tina Mendis and Dr. Shyamala Anand were the resource persons. The workshop, which had a practical orientation helped the participants to develop their skills in development of proposals for field based projects and also learn something of the methods employed for qualitative research.

**The TLM India Research Committee** was held on 22nd March at ICMR. The Director General of ICMR, Dr. V M Katoh, chaired the meeting and provided strong support, especially regarding the way forward in view of the emerging Drug resistance situation.

**The TLM International Research Committee** on the 26th. March was held through Skype, and as many of the members were present in Delhi, they participated in it together from CNI Bhavan.

**The Indian Association of Leprologists Conference**, LEPCON, was held from 28th. to 30th. March at Chandigarh. TLM deputed 20 staff members, who presented 7 papers and 32 posters, and won two awards.