Editorial

Dear Friends,

As the year 2017 races past, we at the Research & Training Domain of The Leprosy Mission Trust India, bring you this issue of our Newsletter to share the progress, challenges and interesting events that have kept us busy over the last few months.

Mr Babu Govindan has joined us recently as Training Coordinator; he is a Physiotherapist who has been involved with The Leprosy Mission Training Unit and TLM Naini for many years, and we are happy to have him with us to expand and strengthen our training activities.

In this issue, there is a brief article on advancements and usefulness of serological tests in leprosy. Dr Beenu Joshi is Scientist F in JALMA (ICMR) Institute, Agra and has vast experience in this field and explains the relevance of these tests.

Dr Ruth Butlin has contributed an article that is very helpful for those writing proposals or papers for publication and need references. She gives details about the facilities offered by Infolep.

Apart from this, there is a report of a conference ‘Microbial Pathogenesis, Infectious Disease, Antimicrobials and Drug resistance’ which was attended by Dr Mallika Lavania and Mr Vinay Pathak. Dr Mallika Lavania also visited the head office, effect:hope, The Leprosy Mission Canada, and presented the work of the Stanley Browne Laboratory. This issue also contains some Abstracts of interesting publications on leprosy. We hope you enjoy reading it and would welcome any comments, suggestions and article you may like to contribute.

Happy Reading!

Annamma S. John
Editor & Head (Research & Training)

What have other people found out?

Whenever we try to write a grant application or research protocol, as well as when we reach the stage of “writing up” for a peer-reviewed journal at the end of our piece of practical research, we need to find out what is already known on the topic. What studies have others done in this area of knowledge? What have they found out which may throw light on the research question before us?

How do you find out what else has been published on the topic? Ideally, in addition to consulting a textbook, you will be looking at least one relevant journal regularly, and for many of us it is Leprosy Review* we like to read because it has papers from many different countries and covers a broad range of leprosy-related topics from which we can select those of most interest to our own work; it is more accessible than some other good quality journals since it is an ‘open access journal’ (which means no-one has to pay to read it). But most of us do not have time to regularly read several journals to keep fully up to date. After reading a paper in one journal we can consult the list of references at the end to find other related papers in a variety of journals and set off on a journey from one paper to another! Done easily enough if one is studying in a big library, for example, like at a university.

However, when working in a hospital or other leprosy centre, away from any academic institution, one may have difficulty obtaining copies of the papers one wants to consult. With the internet now available to most of us, the problem is less than it used to be! Many journals (including Leprosy Review) are now published both as printed copies and on a website. Some are only published on the internet (for example, PLOS NTDs). However, on the internet one often finds only the abstract is available, not the whole paper, and often older papers cannot be found on the journal website (e.g. for Indian Journal of Leprosy and its predecessor Leprosy in India see www.ijl.org.in). International Journal of Leprosy used to be an excellent publication from the International Leprosy Association, but
unfortunately, the journal closed a few years ago. All old copies are available on the internet, but they are very difficult to find. The address is in Leprosy Review June 2015, vol 86 (2) p 141 in Dr Paul Saunderson’s Editor’s Choice (http://www.leprosy-ila.org/leprosyjournal/gn1/edicoses_anteriores.php)

When we are writing a paper to submit to a journal for publication we must include the ‘references’ to other people’s published work to support statements which we make, and a responsible author will read the original paper before he/she quotes it.

How many staff of TLM know about the wonderful service provided by Infolep (www.leprosy-information.org)? I want to recommend it all of you. This service is supported by several ILEP members so that it can be offered free of charge to anyone who needs to consult the literature on leprosy. At its office in Netherlands, INFOLEP has a large library, and its staff have access to other libraries to obtain papers from any journal not in its own collection. The staff look through many journals as they are published and select papers on leprosy-related topics. There are three ways you might like to use the service yourself:

1. Go to the website and do a “search” to obtain a list of relevant papers, then “click on” the ones you want to read, and download to your computer anything you might need for future reference.

2. “Sign up” to receive regular email alerts which will carry lists of many recently published papers of interest to those working in leprosy – there are in built “links” to make it easy to read any of these you choose.

3. Make a request to the librarian if you need a copy of a paper for which you have the reference, when you cannot obtain it directly from the Infolep website or the journal’s own website.

I have recently made many email requests to the librarian, and she cheerfully sends me the papers, in most cases, within a couple of days. This is such a great help when one is trying to write a paper or a book chapter! The address to use is infolep@leprastichting.nl

On the Infolep website, I see they are also offering other services which I have not tried: for example, arranging training sessions to help people utilise Information Resources such as Pub Med and “reference manager” software. Have a look at the website home page for a description of what Infolep can do for people like you. If you are reading this newsletter as a “soft copy” you can probably click on the address and to be taken directly to the right website.

* Leprosy Review, which is published by LEPRA and subsidised by other ILEP members, can be read on the internet (go to www.lepra.org.uk for back copies, or sign up for emails alerting you when the current issue becomes available). If you want to receive a paper copy for you project library, write to the assistant editor, Irene Allen (who has discretion to give free subscriptions to people working in leprosy in endemic countries), and reconfirm each year that you wish to continue receiving the journal. The address is in every issue of Leprosy Review.

INFOLEP | Leprosy Information Services
www.leprosy-information.org

Infolep is the international knowledge centre for leprosy and related subjects. It facilitates access to information for anyone involved in leprosy: from researchers and students to programme managers and field workers. Infolep provides information both on demand and on a pro-active basis. Services include:

Leprosy Information Portal: It is the place to search for articles, (e-) books, book chapters, (e-journals), films, cd-roms and more on leprosy and related subjects.

Literature Searches: Infolep conducts bibliographical searches using a variety of databases as well as the Internet. These searches generate a list of journal citations, available with or without abstracts. Customers review the lists and then may request relevant full-text articles.

Document Delivery Services: Requests for articles or books are filled using the following process:
- The Infolep collection is consulted first.
- If not available in house, inter-library loan services are used.

Quick Reference Service: Infolep answers reference questions using in-house materials such as dictionaries, handbooks, textbooks, encyclopedias, and resources on the Internet. In addition, information referral services are provided, granting Infolep customers access to experts within the leprosy field.

Advice and Support: Infolep provides advice and support to leprosy information centres.

Training Sessions: Infolep organizes training sessions, at Infolep or on location on:
- Infolep collections and services;
- How to stay up-to-date with leprosy information;
- How to use information resources like the Internet, databases, PubMed, reference manager;
- How to evaluate and use information found.

Infolep Library Collection, Amsterdam: The Infolep library collection consists of reference works on leprosy: (e-)books, journals, articles, training- and audiovisual material. The Infolep library can be visited during office hours. An Information Specialist is available for all onsite enquiries and any research assistance you may need.

Loan Service and Inter-Library Loan: All documents except for reference materials may be borrowed. Infolep also takes part in the national and international inter-library loan service, which makes it possible to obtain materials from other libraries. infolep@leprastichting.nl

Dr C Ruth Butlin
**Serological advancements in leprosy**

Diagnosis of leprosy is mainly done by clinician based on three cardinal signs: i) characteristic patch (skin lesion) with impaired sensation, ii) thickened and/or tender cutaneous or peripheral nerve of the area where sensation is impaired, iii) skin smear examination showing acid fast bacilli (AFB). However, in the field setting, AFB examination is often not possible. Further, patients with neuritic leprosy (without skin lesion) and around 30% of patients (including MB patients) do not exhibit skin lesion with sensory loss.

Serological tests are simple, easy to perform, and cost effective tests which can be performed in field settings. Serological diagnosis has been tried for leprosy in the 1980’s using crude *M. Leprae* sonicated antigens. Further, *M. leprae* specific antigens were identified and purified. Antibodies were detected against 35kD antigen by competitive radioimmunoassay using monoclonal antibody against 35kD protein. Later the test was modified using enzyme linked antibody detection assay. Almost 100% positivity was observed in active LL/BL although only 40% of TT/BT patients were found to be positive. Recombinant 35 kD was developed later and was used in indirect ELISA and gave similar result as competitive ELISA using MLO4. The antibody level also decreased gradually after treatment. Phenolic glycolipid-1 (PGL-1), a *Mycobacterium leprae* specific lipid antigen, has been used extensively for developing various types of serological tests. The test using IgM antibody present in PGL-1 was found to be responsible for the reactivity of antibody in patient’s sera. These sugars were conjugated with bovine serum albumin ND-O-BSA/NT-O-BSA and found to have higher specificity than PGL-1. Later, using PGL-1 antigen a rapid lateral flow assay, ML Flow test was developed for the detection of antibody. By this assay 92% of multibacillary and 32% of PB patients were positive.

Though serological assay cannot be used as an adjunct to clinical diagnosis, it can be used as a surrogate marker for bacterial load in leprosy. Hence, these tests could be used as supplementary tools for determining the operational classification, in addition to identifying infected individuals and as a strategy for surveillance of household contacts. Antibody tests can also be used to help clinicians in confirming doubtful cases of leprosy.

**Author Biosketch**

Dr Beenu Joshi works as Scientist F in the Immunology Division in National JALMA Institute for Leprosy & Other Mycobacterial Diseases (ICMR), Agra. She has more than 23 years of experience in Leprosy and Tuberculosis; and has more than 40 publications in reputed National and International journals to her name. Her specialized area is Mechanism of T cell function in tuberculosis and leprosy.

Two proteins of *M. Leprae*, ML0405 and ML2331, were tested for serodiagnosis of leprosy and only LL/BL patients were found to be showing antibody reactivity to these antigens. These two proteins were together designated Leprosy IDRI diagnostic1 (LID-1), and follow up study of household contacts using LID-1 and ND-O-BSA both showed rise in antibody levels before clinical manifestation of leprosy. Apart from extensive use of these antigens, LSR antigen was found to be having antibody reactivity in reactional patients such as ENL cases. *M. leprae* specific culture filtrate protein-10 (CFP-10) was also tried in ELISA and it was found to be highly specific and equally efficient as PGL-1 ELISA. Recently, we have tried *M. tuberculosis* specific Ag85c antigen based ELISA in paediatric leprosy cases. We observed higher positivity in leprosy cases with Ag85c (76.6%) than PGL-1 (46.6) whereas specificity with both the antigens was 90%. Using *M. leprae* Ag85c could possibly be able to give higher specificity, making the test more useful. Use of multiple antigens based serological assay needs to be evaluated and this may help in enhancing the performance of antibody based assay.

**Dr Beenu Joshi**

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Dr Mallika Lavania (Research Scientist) and Mr Vinay Kumar Pathak (Senior Research Fellow) at Stanley Browne Laboratory, Shahdara, Delhi, attended the annual conference on Microbial Pathogenesis, Infectious Disease, Antimicrobials and Drug resistance held during August 23 – 24, 2017 in Toronto, Canada. The organizing committee, Microbial Pathogenesis 2017, hosted the programme in collaboration with Allied Academies as ‘Antimicrobial and Drug Resistance 2017’, to increase the scope for networking by creating an opportunity for all speakers and delegates to interact with various other dignitaries. The main theme of the conference was “Innovations in Microbial Pathogenesis”.

The opening remark was by moderator Dr Terry Ann Else, Touro University, Nevada, USA, followed by welcome notes, and keynote speakers who started the major sessions and talked about their work. Some of the major talks delivered are in brief here. Dr John J. S. Cadwell (FiberCell System Inc., USA) discussed the topic “The hollow fiber infection model: Principles and practice”. He discussed two-compartment in-vitro pharmacokinetic model utilizing hollow fiber bioreactors (HFIM) and utility of the system to studies related to antibiotics and other drugs. Dr P R Raghavan’s (Nonorx Inc., USA) topic was “Metadichol a novel nano lipid: A solution for the post-antibiotic era”. He explained that Metadichol acts as inverse/protean agonist on nuclear vitamin D receptors (VDR) and it has potential to serve as a novel, broad-spectrum treatment against viruses, bacteria and parasites that confront public health today without eliciting a resistance. There were other talks mainly focused on Antibiotics and Drug resistance. Dr Mallika Lavania (Stanley Browne Laboratory, Delhi) talked about her study entitled “Molecular patterns of multidrug resistance of *Mycobacterium leprae* in India”. She showed the occurrence of MDR strains of *M. leprae* in MDT treated leprosy patients from endemic regions of India. The chairperson appreciated her talk. Mr Vinay Kumar Pathak (Stanley Browne Laboratory, Delhi), presented his study in the poster presentation session. He showed utility of multiplex PCR for early detection of leprosy, and got the best poster presentation award for his study.

Dr Mallika Lavania visited the head office of effect:hope, The Leprosy Mission Canada. After a warm welcome by the staff members, a presentation session was organized. Dr. Mallika Lavania presented a progress report of all ongoing projects and discussed the grants received for the concerned projects. Her supervision for research module and financial as well as technical management of Stanley Browne Laboratory was highly appreciated by Dr Deborah Mensah (Interim Director of International Programs) and other staff members.

### Abstracts

**Early Detection of Neuropathy in Leprosy: A comparison of five tests for field settings**

Wagenaar, Post E, Brandsma W, Ziegler D, Rahman M, Alam K, Richardus JH.


**Background:** Early detection and treatment of neuropathy in leprosy is important to prevent disabilities. A recent study showed that the Nerve Conduction Studies (NCS) and Warm Detection Thresholds (WDT) tests can detect leprosy neuropathy the earliest. These two tests are not practical under field conditions, however, because they require climate-controlled rooms and highly trained staff and are expensive. We assessed the usefulness of alternative test methods and their sensitivity and specificity to detect neuropathy at an early stage.

**Methods:** Through a literature search we identified five alternative devices that appeared user-friendly, more affordable, portable and/or battery-operated: the Neuropad®, Vibratip™, NC-Stat®DPNCheck™, NeuroQuick and the Thermal Sensibility Tester (TST), assessing respectively sweat function, vibration thresholds...
sensation, nerve conduction, cold sensation and warm sensation. In leprosy patients in Bangladesh, the posterior tibial and sural nerves that tested normal for the monofilament test and voluntary muscle test were assessed with the NCS and WDT as reference standard tests. The alternative devices were then tested on 94 nerves with abnormal WDT and/or NCS results and on 94 unaffected nerves. Sensitivity and specificity were the main outcomes.

**Results:** The NeuroQuick and the TST showed very good sensitivity and specificity. On the sural nerve, the NeuroQuick had both a sensitivity and a specificity of 86%. The TST had a sensitivity of 83% and a specificity of 82%. Both the NC-Stat®DPNCheck™ and Vibratip™ had a high specificity (88% and 100%), but a low sensitivity (16% and 0%). On the posterior tibial nerve, the NeuroQuick and the TST also showed good sensitivity, but the sensitivity was lower than for the sural nerve. The Neuropad® had a sensitivity of 56% and a specificity of 61%.

**Conclusion:** The NeuroQuick and TST are good candidates for further field-testing for reliability and reproducibility. The feasibility of production on a larger scale should be examined.

**Keywords:** Detection; Field use; Leprosy; Neuropathy; Subclinical

**Enhanced Worldwide Dermatology-Pathology Interaction via Facebook, Twitter, and Other Social Media Platforms**

Madke B, Gardner JM.


The practice of dermatopathology requires close interaction between dermatologists and dermatopathologists. Yet, in many areas of the developing world, dermatologists lack easy access to pathologists with expertise in skin disease. Twitter, Facebook, and other social media provide free powerful tools that enhance interaction between dermatology and pathology regardless of geographic barriers. Although there are some limitations, the immense potential benefits that social media unlocks for patient care, education, research, and networking cannot be overstated.

**Dermatopathology and Social Media: A Survey of 131 Medical Professionals From 29 Countries**

Carlquist E, Lee NE, Shalin SC, Goodman M, Gardner JM.


**Context:** Use of social media in the medical profession is an increasingly prevalent and sometimes controversial practice. Many doctors believe social media is the future and embrace it as an educational and collaborative tool. Others maintain reservations concerning issues such as patient confidentiality, legal and ethical risks.

**Objectives:** To explore the utility of social media as an educational and collaborative tool in dermatopathology.

**Design:** We constructed 2 identical surveys containing questions pertaining to the responders’ demographics and opinions regarding the use of social media for
dermatopathology. The surveys were available on Twitter and Facebook for a period of 10 days.

**Results:** The survey was completed by 131 medical professionals from 29 different countries: the majority (81%, 106 of 131) were 25 to 45 years of age. Most replied that they access Facebook or Twitter several times a day (68%, 89% of 131) for both professional and social purposes (77%, 101 of 131). The majority agreed that social media provides useful and relevant information, but stated limitations they would like addressed.

**Conclusion:** Social media is a powerful tool with the ability to instantaneously share dermatopathology with medical professionals across the world. This study reveals the opinions and characteristics of the population of medical professionals currently using social media for education and collaboration in dermatopathology.

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**Short-term Leprosy Forecasting From an Expert Opinion Survey**

Deiner MS, Worden L, Rittel A, Ackley SF, Liu F, Blum L, Scott JC, Lietman TM, Porco TC.


We conducted an expert survey of leprosy (Hansen’s Disease) and neglected tropical disease experts in February 2016. Experts were asked to forecast the next year of reported cases for the world, for the top three countries, and for selected states and territories of India. A total of 103 respondents answered at least one forecasting question. We elicited lower and upper confidence bounds. Comparing these results to regression and exponential smoothing, we found no evidence that any forecasting method outperformed the others. We found evidence that experts who believed it was more likely to achieve global interruption of transmission goals and disability reduction goals had higher error scores for India and Indonesia, but lower for Brazil. Even for a disease whose epidemiology changes on a slow time scale, forecasting exercises such as we conducted are simple and practical. We believe they can be used on a routine basis in public health.

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**Understanding Genomics during emerging resistance in Mycobacterium leprae by Whole Genome Sequencing**

Leprosy is a poverty related disease with multidimensional consequences. Emergence of drug resistance and genetic mutation in *M. leprae* is a serious threat at a time when a dramatic decline in prevalence and new case detection have been achieved by concerted chemotherapy interventions by the National Leprosy Program and its global partners. Multi Drug Therapy is the mainstay of leprosy control programs. If the emergence of mutation is not controlled with alternative drug regimens, control measures with chemotherapy will be completely defeated. A surveillance mechanism should function as a watchdog for the appearance of drug resistance in-country; rapid detection and control of drug-resistant strains is essential for countries approaching leprosy elimination levels. To monitor the transmission dynamics of drug resistant leprosy, genome-wide sequencing and comparison of *M. leprae* strains by whole genome sequencing (WGS) of strains from drug resistant patients can reveal specific polymorphisms associated with resistance. WGS can detect specific signatures of disease presentation and progression among relapsed cases. This will aid in understanding transmission and the possibility of compensatory mutations related to resistance between the strain and the endemicity. Rapid testing for drug resistance in patients on treatment can monitor emergence of resistance and enable early intervention to avoid its onward transmission.

SB Lab has been working in the areas of drug resistance for the past 8 years as a part of the WHO Sentinel Surveillance Study on Drug Resistance in Leprosy and have already recorded the emergence of resistance against DDS, Rifampicin and Ofloxacin from our hospitals. We have performed mouse foot experimentation to check whether novel mutations in rifampicin drug are conferring resistance or not. We have screened all these resistant cases for further analysis.

This study will aid in developing rapid and affordable assay testing for drug resistant strains of *M. leprae* in leprosy patients on treatment. Early testing of resistant strains will also help us to monitor emergence of resistance and enable early intervention to avoid its onward transmission.
May the Festival of Lights bring radiance to your home and your heart always

Happy Diwali