Dear Readers

It’s once again that time of the year when there is a nip in the air and we begin to feel festive. The year has come to end, and we have much to be thankful about. There have been a lot of happenings in the research arena of leprosy. Early detection tools, contact tracing and prophylaxis are raging topics of research.

We as team could submit some exciting proposals. The evaluation of the research domain was completed, and we got some glowing compliments for our work. A whopping 12 papers were published in peer reviewed journals. An operational research workshop was conducted where staff from TLM India, Nepal, Bangladesh and Myanmar participated. This was a time of capacity building for the participants as well as the facilitators.

Our senior scientist Dr Mallika recounts her training experience at the NHDP, Louisiana. It was an opportunity of a lifetime.

This newsletter has a write up on Pure Neuritic leprosy. This presentation is quite common in India and with dwindling expertise in leprosy diagnosis and management, this article comes at a pertinent time to refresh our understanding. Dr Bhushan Kumar, eminent dermatologist and leprologist has penned this article. The case study to go with it is young Pintu who developed a nerve abscess due to leprosy but was misdiagnosed as tuberculosis. The clinician came very close to diagnosing a caseating abscess but forgot leprosy as differential diagnosis. Why? Because, he just looked at the abscess! Little Pintu developed a claw hand and no one noticed, not even he himself. What happened to holistic care that we were taught in medical school. Who will look at the person! Researchers consider p value of great significance. But lives like Pintu’s matter however low that p value be.

The NNN conference this year had discussions on many topics and themes, but one that touched me was on compassion! If we are compassionate enough, we will SEE the needs of people affected by leprosy and act upon them.

Christmas is around the corner, celebrating the birth of Jesus. Jesus became human to bring justice to mankind. Let us celebrate Christmas with the mandate that we will advocate for the cause of those to whom justice is denied.

Merry Christmas and a Blessed New year 2019.

Joydeepa Darlong

Pure Neuritic Leprosy

Leprosy is primarily a disease involving the nerves, because M.leprae have a special affinity for the Schwann cells that surround the nerve fibers and axons. The disease sometimes presents with only nerve involvement, only skin lesions and sometimes with both. In about 4-8% of the cases there is exclusive nerve involvement with nerve thickening, related nerve deficit and deformities and no skin lesions, and negative skin slit smears. This is called Pure Neuritic Leprosy (PNL).

It is more common in Indian subcontinent and its incidence in India varies from 5.5 to 17.5% of all leprosy cases, and patients from India, contribute to more than half of global leprosy numbers1-3. Only the Indian Association of Leprologists classification recognizes ‘Pure Neuritic Leprosy’ as a distinct sub group of leprosy, cases nonetheless are reported from various countries of Asia, Africa, South America and Europe, indicating its global relevance.

Clinical presentation: The most common presentation is mononeuritis i.e. single nerve involvement 4-5 followed by mononeuritis multiplex-asymmetric involvement of more than one nerve and least common being polyneuropathy or symmetrical polyneuritis as the name explains. Temperature and pain sensation are the first to be affected, but there can also be sensory and or motor impairment, numbness, paresthesia and neural pain 4-7.

Incidence Wade had mentioned about the recognition of neuritic leprosy in the International Symposium on Leprosy held in
1952. Incidence of the disease has varied from 8.2% (Indian study on 8000 patients) to 5.5% (another Indian study on 11,581 patients). In a Brazilian study PNL was diagnosed in 34 of the 162 nerve biopsies studied.

An assessment of 20,000 patients from 6 continents over 28 years revealed that pure neurological symptoms are common and may precede the skin lesions by many months.

**Diagnosis**

Most of the patients present with nerve function impairment (NFI) of sensory, motor or both and it requires a high degree of clinical suspicion for diagnosis of PNL. As there are no absolute diagnostic clinical features for PNL, a wide range of differentials have to be considered. Nerve thickening is only a soft pointer, other causes of neuropathy which should be excluded are diabetes mellitus, amyloidosis, toxic, nutritional, syphils and HIV associated.

Lyme disease, sarcoidosis and rare conditions like congenital or hereditary neuropathy, traumatic and compressive are other disorders causing neuropathy.

A complete skin examination and slit skin smear should be done in all cases. Tests including blood glucose, ANA, ANCA, HIV, HBs Ag, and anti HCV are done (or as the situation requires) to exclude other causes of peripheral neuropathy.

Nerve biopsy preferably from a purely sensory nerve is the gold standard for demonstration of AFB and diagnosis of PNL. However, there is risk of nerve damage and poor sampling and low sensitivity. AFBs are found in only half of the nerve biopsy specimens. In the absence of molecular diagnostic facilities, presence of epithelioid granuloma, endoneurial infiltrate, endoneurial and perineurial thickening/fibrosis and a reduction in the number of myelinated nerve fibers helps. Immunolabeling with lipoarabinomannan (LAM) or phenolic glycolipid 1 (PGL-1) can also be added. Fine needle aspiration cytology (FNAC) of the nerve is a simple and minimally traumatic procedure and preferred before a nerve biopsy. Polymerase chain reaction (PCR) on tissue from nerves can help in the diagnosis of AFB negative material.

Serology can be of some help in follow up. Electrophysiological studies nerve conduction, sensory nerve action potentials, and compound motor action potential can be used for diagnostic and monitoring purposes. Currently high resolution ultrasonography (HRUS) and Color Doppler are used to assess the thickness and vascularity of nerve and help in making a definitive diagnosis.

Mitsuda skin test though of poor diagnostic value is positive in up to 100% of patients.

Although skin lesions are absent by definition, but skin biopsies performed from the skin along the distribution of the affected nerve, in a proportion of patients demonstrated leprosy pathology, revealing sub-clinical skin involvement. PNL precedes the development of skin lesions in up to 35% of the patients. A close follow up and development of skin lesions helps in revising the diagnosis and treatment.

**Treatment**

All patients with PNL are to be treated as MB disease because even when the symptoms pertain to one nerve, many nerves big or small and some not easily palpable may be affected. MDT does not halt the progression of nerve damage and some patients may even end up with more disability.

Nerve damage and lepra reactions can lead to lasting consequences of disability so the treatment should be instituted at the earliest. Steroids given for a longer period (6 months) are useful for the management of nerve function impairment of recent origin (< 6 months). All patients should be observed for a period of 2 years for reaction or deterioration of nerve damage.

Another aspect of management of PNL is disabling neuropathic pain requiring pregabalin, tricyclic, anti depressants, etc. Measures for pain relief, self care of the limbs and physiotherapy are important to prevent as well as manage disability.

In conclusion, PNL is a definite clinical entity with subtle findings which can be diagnosed by clinical, histo-pathological, bacteriological, electrophysiological and ultrasound criteria. Early diagnosis and treatment is required for better functional recovery and prevention of disabilities.

**References**

Pintu, 8 years old, noticed a swelling on the right arm which was painless. It was slow growing swelling and did not pay attention to it. However, his father noticed this and took him to a medical practitioner. He was examined thoroughly and prescribed some tests which included Fine Needle Aspiration Cytology from the lump. He was told that the blood tests were within normal range but the FNAC report had showed tuberculosis. The report had described caseation necrosis as one of the findings. The origin of the lump was not mentioned. A chest X-ray was ordered, which was normal. He was then started on anti TB medication on a daily regime. The child took the medication for 6 months. The swelling did not increase further.

After the completion of ATT, the father brought the child to the Leprosy Mission Hospital to consult a surgeon for excision of the lump. Pintu was examined, and the surgeon noticed the ulnar claw. When questioned, the patient and the son did not know anything about it. When pointed questions were asked about difficulty in using the right hand, the boy could not give any conclusive answers.

The child had sensory loss on the right palm, there were no anesthetic patches on the body and his BI was negative. There were no other thickened nerves and the right ulnar nerve was considerably thick with multiple knobbly swellings on the nerve. There was mild wasting of the small muscles on the ulnar border of the hand. He was diagnosed Pure Neuritic Leprosy with Rt Ulnar Abscess and Rt Ulnar Neuritis.

He was started on WHO MB MDT and planned for nerve decompression. Intra-operative findings showed multiple fusiform small swellings along the course of the ulnar nerve. Exercises were taught, and tendon transfer surgery was planned subsequently.

TLMTI’s participation in Immunocon – 2018
Dr. Itu Singh participated in “Immunocon – 2018 and 45th Annual meeting of Indian Immunology Society” She presented a paper entitled “Role of mimicking proteins (peptides) of host and M. leprae in the pathogenesis of type 1 reaction in leprosy”.

Operational research workshop
The Operational Research Workshop was conducted from 3-5 December at TLM Community Hospital, Naini. There were 31 participants represented from TLM India, Bangladesh, Myanmar and Nepal, including 6 facilitators. The participants were a healthy mix of clinical, social science, program, Lab and educational personnel.

The topics covered were basics of operational research, protocol, literature review, types of research, tools, validation and designing, budget, Gantt chart, developing a research question, sample size calculation, database management, informed consent and ethics.

There was group activity, brainstorming and interactive lectures. Facilitators could personally oversee and help each person. Most of them were able to develop a research question, do a literature review, write up the objectives and methodology and do a presentation at the end of the workshop.

Testimonial
I have a little experience in doing a study and depended on experts. After the workshop I’m able to do things on my own like writing an abstract, Literature review and I’m confident of completing this paper and publishing it. This workshop has built my capacity to a great extent.

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I got an opportunity to be trained at the lab at National Hansen Disease Programme (NHDP) at Baton Rouge, Louisiana, USA. It is the only facility in the US which is devoted to diagnosis, treatment, and research concerning Hansen’s Disease (HD).

The Laboratory Research Branch has pioneered many of the newer sophisticated molecular biology tools used today to study leprosy. On my first day of training, I met Dr Linda Adams, who is Chief of lab, scientists, post doc fellows and other staff of the lab.

I was trained on Whole Genome Sequencing (WGS) which is ostensibly the process of determining the complete DNA sequence of an organism’s genome at a single time. It has been used as a research tool and is the future of personalized medicine. Whole genome sequence data will be an important tool to guide therapeutic intervention. The tool of gene sequencing at single nucleotide polymorphism (SNP) level is also used to pinpoint functional variants from association studies and improve the knowledge available to researchers interested in evolutionary biology, and hence may lay the foundation for predicting disease susceptibility and drug response.

I visited their Clinic and I also got an opportunity to visit their Armadillo animal house facility. The Laboratory Research Branch has unique expertise in the propagation of leprosy bacilli, including the only colony of M.leprae-infected armadillos in the world!

I presented an overview of TLMTI and the work being done at the SB Lab. They were surprised to see the load of leprosy patients in our hospitals. Staffs were very curious about our environmental work. They asked many questions on this aspect and we had a very fruitful discussion on the same. They would be delighted to collaborate with us in our future studies.

My entire training was with Dr Alex, who is a senior post doc. She supported me and allowed me to do everything independently so that I would be able to set up this technique in our lab in India. My training for library preparation as well as running the libraries on Miseq (sequencing) was completed successfully. This was indeed a great opportunity for me to work in such a lab.

On my rest days, I could visit places like Audubon Butterfly Garden, Insectarium and French Quarter Audubon Aquarium of the Americas, in New Orleans, which is located adjacent to the Mississippi River. It was amazing experience.

I just went with the flow of time and it worked out fabulously!

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**Wandering for Knowledge....**

**Dr Mallika’s musings!**

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**Scientific Writeshop**

NLR India Foundation organized a workshop entitled “Scientific Writeshop”, from 3-7 in, IBIS Hotel, New Delhi, focusing on scientific writings. Medical practitioners, health workers, scientists and scholars from different countries as well as states got exposure and refined their skills.

Dr Mallika Lavania, participated as a facilitator and Ms Madhvi from SB Lab, Mr James George and Mr Harsha attended this workshop as a participant from TLMTI.

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**Poster presentation at the international conference**

Mr. Vikram Singh from Stanley Browne Research Laboratory presented a poster entitled “Insights into the Non-tuberculous mycobacterial World along with M. leprae in Environment of Leprosy Endemic Regions in India” in the international conference “World Congress on infectious diseases and antibiotics” Bangalore.
Announcement - The 20th International Congress, Manila, Philippines has called for submission of abstracts classified by topics.

Deadline: 30th January 2019.

Here is a quick guideline to abstract submission.
1. Online submission only
2. Last date to submit abstract is 30 January 2019
3. Notification regarding the abstract status (rejected, oral /poster presentation) is between 15 March - 15 April, 2019
4. All abstracts must be submitted and presented in clear English
5. Multiple submissions of the same abstract are not allowed.
6. The word limit is 400 (Objectives, Methods, Results and Conclusion)
7. Prescribed Format of Abstract is given below;
   TITLE: TYPE IN CAPITAL LETTERS; LIMIT TO 30 WORDS; ARIAL FONT, SIZE 11
   Authors: A.B. Alpha¹, D.E. Beta², H.R. Charlie³, R.R. Delta⁴

  ¹Institutional Affiliation of AB Alpha and HR Charlie,
   ²Institutional affiliation of DE Beta,
   ³Institutional affiliation of RR Delta

Objectives: Arial font, size11
Methods: Arial font, size11
Results: Arial font, size11
Conclusion: Arial font, size11

Limit to a total of 400 words

1. A New Instrument to Measure Leprosy Internalised Stigma:
The Leprosy Internalised Stigma Scale (LISS)
Govindharaj P, Srinivasan SK, Darlong J, Mahato B, Acharya P

2. Paucibacillary Leprosy: Reappraisal using Ziehl-Neelsen staining of slit skin smears and 16S rRNA Real Time Polymerase Chain Reaction of nasal swabs

3. The Incidence of Erythema Nodosum Leprosum In India: A Retrospective Follow-Up of the INFIR Cohort

Clin Microbiol Infect. 2018 Dec;24(12):1305-1310
https://doi.org/10.1016/j.cmi.2018.02.022

5. Association of non-tuberculous mycobacteria with Mycobacterium leprae in environment of leprosy endemic regions in India.
Turankar RP, Singh V, Gupta H, Pathak VK, Ahuja M, Singh I, Lavana M, Dinda AK, Sengupta U
https://doi.org/10.1016/j.meegid.2018.11.010

6. VDR polymorphism, gene expression and vitamin D levels in leprosy patients from North Indian population.
Singh I, Lavana M, Pathak VK, Ahuja M, Turankar RP, Singh V, Sengupta U
https://doi.org/10.1371/journal.pntd.0006823

Published papers