IADVL

IADVL SIG Leprosy (IADVL Academy) Newsletter

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WELCOME NOTE

Dr. Sujai K Suneetha

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Leprosy is a millennial disease that has affected humanity since ancient times. We have come a long way and today we are talking about 'Zero Leprosy' and 'Zero discrimination'. However the reality is that India still contributes to more than 60% of the world's total leprosy burden. The annual new case detection has remained the same or has marginally decreased; the number of multibacillary cases has increased; and childhood leprosy rate too has not decreased significantly. There is still a lot of work that needs to be done if we are to realize our dream of 'A leprosy-free World/ India'. The level of awareness about leprosy is still low in the general public and even among practitioners of specialties other than dermatology. We have tried to improve the awareness and change people's attitudes by organizing awareness walks and street plays and even CMEs for practitioners regularly.

The COVID pandemic this year did create some difficulties in the initial few months of lock-down and there were many concerns and questions of management of leprosy and its complications during this time. SIG leprosy members formulated and were instrumental in publishing the guidelines for management of leprosy during COVID. We also organized a round table meet of leprosy experts to discuss important management issues in leprosy like post exposure prophylaxis and management of leprosy patients with a high bacterial load and plan to publish the proceedings of the same.

In this issue we have tried to cover some of the important topics in leprosy like current updates in leprosy; epidemiology and management of type 2 reactions; the RPWD ACT of 2016 and its implications for leprosy cured persons with grade 2 disability; snippets from leprosy research; and interesting anecdotes from the times of the discovery of Mycobacterium leprae. We aim to bring out more such news letters in future on a periodic basis. We hope that this small attempt on part of SIG Leprosy proves to be informative to our readers. We are thankful to IADVL EC and IADVL Academy for their constant support and help in fulfilling the vision of the SIG in our endeavours. Please do share your valuable opinion, suggestions and comments so that we can improve it further.

FROM EDITORIAL TEAMS' DESK

Dr. Santosh Rathod
Assistant Editor

Dr. Abhishek Bharadwaj
Editor

Dr. Sunil Gupta
Assistant Editor

Dear Colleagues

The past year was unprecedented in our collective history. It may well have altered how Medicine, in general is perceived by everyone. The COVID pandemic continues to unravel and perplex. As Dermatologists, we are not as much in the limelight as our other infective disease colleagues. Nonetheless it's that much more pertinent that we continue to focus, especially in the 'neglected' realm of Neglected tropical diseases like Leprosy.

We at SIG Leprosy continued to work and published relevant literature including practice recommendations in Leprosy during the pandemic.

This newsletter is another offshoot from contributions of the members of our SIG.

It's a collective effort to collate thoughts on this enigmatic illness.

The attempt was to keep the sweep of this document as comprehensive as possible.

In the document on one hand, the reader will find himself enriched by lesser-known facts about the history of the disease while on the other there are must know facets about the illness. There is a digest for the quick reader who is seeking practical take-home tips, derived from the successful SIG Leprosy Webinar, held in August 2020. There is an interesting article on Rights of Persons with Disabilities (RPWD) Act, that now 'enables' persons with disabilities due to Leprosy. Reactions are times when a patient requires most hand-holding, an article covers updates on the particularly severe Type 2 Lepra reaction. The unique highlight of the newsletter is the snippets of recent research on Leprosy. It enables the reader to come at par with all research done on Leprosy in the recent times. And at the end, an interesting case scenario from an endemic zone and finally a 'fun' crossword to break the 'academic' monotony.

I sincerely hope that the newsletter will be thought provoking for all colleagues. We should not let our guards down on this ancient scourge which continues to challenge us even as it plays out a slightly unpredictable 'Endgame' in our country.

Lastly, on behalf of the SIG, I request all IADVL members to keep safe during the pandemic and wish them happy learning.

TWO INTERESTING ANECDOTES FROM THE TIMES WHEN MYCOBACTERIUM LEPRAE WAS DISCOVERED

Dr. Abhishek Bhardwaj
Additional Professor & Head, AIIMS, Jodhpur

We all revere Gerhard Henrik Armauer Hansen (1841-1912) for the discovery of the “Bacillus leprae”. It was for the first time in history, when it was being suggested that a chronic disease can be caused by a microbe. Interestingly discovery of the leprosy bacillus antedates the discovery of its more 'illustrious colleague', Mycobacterium tuberculosis by a full 9 years. And mind you, those were the times, when the concept of germs causing diseases was not popular. Only two human diseases till that time had been acknowledged to have a bacterial etiology namely, Anthrax in 1850 and relapsing fever in 1868.

The ultimate discovery of the bacillus is punctuated with the outcome of 2 interesting interpersonal relationships.

a. Hansen and Danielssen

Hansen was the eighth of fifteen children of Elizabeth Concordia Schram and Claus Hansen. Later, his merchant father faced bankruptcy. So, Hansen pursued his medicine and generated funds for study by simultaneously working in two jobs, one of them as a Prosector in Anatomy at the University of Christiania. After graduating with honors, and working first as a physician at Lofoten in Norway, he returned to Bergen in 1868. At the St. Jogren's Hospital, he came across the chief physician of the hospital and a celebrated dermatologist of the times Daniel Cornelius Danielssen. Like Hansen, Danielssen too had a modest beginning and had apprenticed to a pharmacist from the age of 13. His life was ravaged by Tuberculosis beginning by afflicting his hip joint at a young age and going on to claim his wife and daughters in due course of time. Danielssen, had a close collaboration with Carl Wilhelm Boeck and the two had published a much celebrated book, “Om Spedalskhed (On Leprosy)”.

Danielssen along with Boeck were of the opinion that leprosy was hereditary. Danielssen began to mentor and encourage Hansen, early in their association. Gradually Hansen, with his keen clinical and epidemiological bent of mind, realised that the disease is more specific and is likely to be due to an infectious agent. Again, this thought was not only radical at that time but also diametrically opposing to the theory of Danielssen. Despite this fundamental difference, Danielssen had the magnanimity to arrange a scholarship for Hansen to visit Bonn and Vienna to hone his histopathology skills. After the scholarship visit, Hansen spent many a midnight hour to finally discover the bacteria causing Leprosy on February 28, 1873, at the young age of 32. Later on, he fully backed his protégé when the claim of discovery of the bacillus came from one Albert Neisser (we will see later).

In the same year circa 1873 Hansen married Stephanie Danielssen, daughter of his mentor. Unfortunately, she succumbed to Tuberculosis within 1 year of walking down the aisle. Hansen got remarried to Johanne Margareth Gran. The couple had a son and as a befitting tribute to his mentor, Hansen named him Daniel Cornelius.

b. Hansen and Neisser

The other story has again two protagonists, Hansen and Albert Neisser. Now, this is the same Neisser after which Neisseria Gonorrhoeae would be named. In July 1879, Neisser a pupil of legendary Robert Koch visited Bergen to study leprosy. He was all of 24 when he met Hansen seeking his help, as Norway had a large number of cases and the city of Bergen with its 4 hospitals dedicated to leprosy, was the best ground to study the disease. Hansen, helped him and permitted him to collect some samples and take them back to Breslau (now Wroclaw, Poland). With the help of staining techniques learnt from Koch and Weigert, he could successfully stain the organism. In October, the same year, he presented his findings at a meeting of the Silesian Society for national culture and soon his work got published in the Breslau Medical Journal. Apparently he laid his claim for discovering the bacillus.

It will be pertinent to point out that Hansen had published his findings in 1874, in a communication to the Norwegian Medical Society. And chastened by Neisser's claims published an article in German that was intended mainly to defend his discovery, but at the same time did acknowledge the observation of Neisser with regards to better understanding of the staining property of Mycobacterium leprae. Neisser would later on claim that by staining he proved something that was uncertain in Hansen's expression. But, at that time the Norwegian Medical community rallied behind Hansen. Subsequently, in the first International congress held at Bergen in 1897, the fraternity acknowledged Hansen as the discoverer of Mycobacterium leprae. Thus, leprosy became one of the first grounds of plagiarism in medical literature. Sad but true.

Is it true that Hansen himself was guilty of reckless human experimentation without taking appropriate consent??.....well, that story some other day.

Acknowledgement

This article has utilized the following publications, besides curating the internet for adding the element of spice.

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iii. Ghosh S, Chaudhuri S. Chronicles of Gerhard-Henrik Armauer Hansen's life and work. Indian J Dermatol 2015; 60:219-21.
iv. Benedek TG. Albert L. Neisser (1855-1916), Microbiologist and Venereologist [Internet] available from: http://www.antimicrobe.org/h04c.files/history/Neisser.pdf

CURRENT UPDATES IN LEPROSY

Dr. Santoshdev P Rathod
Professor, Department of Dermatology, Smt. NHL Municipal Medical College, Ahmedabad

Introduction: This short write up summarizes the changes in the key indicators of leprosy in India; changes in the laws relating to leprosy-affected individuals in society; and highlights the role of IADVL in a recent evaluation of the national leprosy program in India.

1. Prevalence and prevalence rate

Prevalence in any disease or infection is the number of patients on treatment at a given point of time. On 31 March 2019, there were 85,914 patients on therapy for leprosy, this corresponds to a prevalence rate of 0.62 per 10000 population in our country. Over the last ten years, the prevalence rate has fallen from 0.72 in 2009 to 0.62 per 10000 population in March 2019, a reduction of 14%.[1]

2. Multi Bacillary Cases

In the last ten years (2008-2018), the proportion of MB disease among new cases has increased by 8% from 48.4% to 52.3%. There is a gradual shift towards MB, consistent with a decline in the epidemic. In most active field surveys, the MB proportion remains under 30% as against the high proportion of multibacillary cases, often above 50–80% in data from passive reporting, indicating that many early leprosy cases were missed out in passive reporting system. This finding also correlates well with high transmission in areas of high MB ratio proportion of cases. Thus, a policy for active case detection, in selective areas of high MB ratio (>40%), would aid in the estimation of the real burden of leprosy. This would also facilitate the policy for prevention of deformity in addition to the provision of timely and adequate treatment and rehabilitation support to the patients.[2] This, however, should be interpreted with caution because of operational changes including active case detection.[1]

MB leprosy is likely to increase with a decline in total cases because such cases are hard to treat and will cluster in the numerator while denominator decreases with relative faster decrease in PB cases. Therefore, an increase in MB cases suggests decreasing trend of leprosy in the community.[3]

Some interesting observations arise from a study from Argentina where elimination at the national level was declared in 2011 but where much like India, leprosy continues to simmer at the sub- national level. On applying statistical forecast tools to existing data of 23 years, a negative trend was clearly projected with regards to both number of new MB cases of leprosy over time, and the total number of cases too. In the relative short term though, they expect proportion of MB cases to increase proportionate to PB cases. It was proposed that this proportional increase is characteristic of the stage of leprosy elimination and could be due to the use of multi-drug therapy (MDT) for several years, because drugs acts efficiently on susceptible strains of *M. leprae* but drug resistant strains persist in MB cases. Further they warn that the proportion of Grade 2 disability can actually increase at such a juncture and should be observed with a keen eye by

administrators as it will be an indicator of quality of case detection activities.[4]

3. Number and proportion of children

The number of children diagnosed with leprosy has also decreased from 13,610 in 2008 to 9,227 in 2018 (a reduction of 32%).[1] Though this highlights that continued transmission in the community, the decreasing numbers indicate reduction in the transmission of the leprosy bacillus during the last decade. But, we must not let our guard down.

4. Grade-2 disability: number, proportion, and rate

The G2D rate (per million population) was 2.6 in 2018.[1] It has shown a decline in the last three years and if the same trend continues; it may be possible to reach the global target of "less than one new case with G2D per million population by 2020". The number of new G2D child cases (<15 years of age) is another indicator being maintained by WHO since 2014. Detection of a child with G2D indicates both delayed detection as well as ongoing transmission in the community and both of these are not good for the national leprosy programme.

INDEPENDENT EVALUATION OF THE INDIAN NATIONAL LEPROSY ERADICATION PROGRAMME

Report: 1-14 November 2019

This report mentioned the role of IADVL in leprosy care in India. IADVL was established in 1973. It currently has more than 12,500, members making it the second largest professional organization of dermatologists in the world. IADVL is an official partner of NLEP since 2018. National Leprosy Symposium were organized in New Delhi by SIG Leprosy with active support from IADVL in 2018 and 2019 with participation of NLEP office bearers.

IADVL conducted a *"Dermlep Survey"* to find out the number of leprosy patients managed by dermatologists in India. (IDOJ Aug 2020). Information was provided by 201 dermatologists: during a three-month period, wherein collectively 1,605 patients were diagnosed with majority being MB cases. Over the same period, care was imparted to 3688 persons affected with leprosy (like provision of MDT, management of reactions, disability care, etc.). This survey also revealed that approximately 43% of dermatologists are not reporting cases to the government authorities. The study provided evidence of a significant number of leprosy patients being managed by dermatologists and that data of most of these patients are not included in the national statistics.

The report **recommended** that IADVL should be involved in review meetings at central, state and district level as Dermatologists in India are involved in care of leprosy and are the key workforce as far as maintaining follow up is concerned. It is most likely that patients, once released from treatment will like to go back to the same Dermatologist in the event of onset of Lepra reaction, neuropathic ulcers or deformity.

Inclusion of Disability due to leprosy in 'Rights of persons with Disability Act, 2016':

There is a need to generate awareness of this act among dermatologists as it includes 'Leprosy Cured Persons' among the list of disabilities covered. The act replaces the Persons with Disabilities Act, 1995. Persons with 'benchmark disabilities' are defined as those certified to have at least 40 % of the disabilities specified. Benefits of this act include reservation in higher education (not less than 5%), government jobs (not less than 4%), reservation in allocation of land, poverty alleviation schemes (5% allotment) etc. have been provided for persons with benchmark disabilities and those with high support needs. Every child with benchmark disability between age group of 6 and 18 years will have right to free education. Who issues these disability cards, whom should the patient contact are important information that need to be imparted to the patients. The care providers and concerned departments need to develop neglected tropical disease clinics as these can separately address these ancillary issues and grant precious rehabilitative information thereby aiding in removing stigma associated with such diseases.

List of rehabilitation centers across India where reconstructive surgeries are performed.

	Name of the Centre	Address
1	Emmaus Swiss Referral Hospital & Leprosy Project	L.S. Farm, PO- Palamaner – 517408, Chhittor Distt. (ALES), Andhra Pradesh
2	Rural India Self Development Trust	Post Box 56, 20-63 Swaraj Nagar, A.C. Gardens, Kathipudi, Rajamundry- 533101 (ALES), Andhra Pradesh
3	Urban Leprosy Centre	Damien Foundation India Trust, Bkthavachala Nagar, A K Nagar Post, Nellore – 524004 (DFIT), Andhra Pradesh
4	Damien Leprosy Centre,	Vegavara, Gopannapalem, Eluru Tk 534450, W.G. Distt, (GLRA), Andhra Pradesh
5	Sivanand Rehabilitation Home	Kukatpally, Hyderabad – 500872 (GLRA), Andhra Pradesh
6	West Godavari District Leprosy Hospital	The Leprosy Mission, Narsapur, (TLM), Andhra Pradesh
7	Philadelphia Leprosy Hospital	The Leprosy Mission, Salur, Vizianagaram, District – 535591 (TLM), Andhra Pradesh
8	The Leprosy Mission Hospital	E. Godavari Distt, Ramachandrapuram- 533255, A.P. (TLM), Andhra Pradesh
9	The Leprosy Mission Hospital	P.O. Ramma, Muzaffarpur- 842002 Bihar (TLM)
10	Bethesda Leprosy Home and Hospital	The Leprosy Mission, P.O. Champa Janjgir District – 495671, Chattisgarh (TLM)
11	Chandkhuri Leprosy Hospital and Home	The Leprosy Mission, PO_ Baitalpur, Via- Hirri Mines, Bilaspur District – 495222, Chattisgarh (TLM)
12	Hubli Hospital for Handicapped	Post Box No- 54, Anand Nagar Road, Hubli – 580020, Darwad District, Karnataka – 580020 (ALES)
13	Sri Ramakrishna Sewa Ashram	Swami Vivekananda, Integrated Rural Health Centre, K R Extension, Tumkur, Pavagada, Karnataka – 561020 (DFIT)
14	Belgaum Leprosy Hospital	The Leprosy Mission, Vengurla Road, Hindalga, Belgaum District – 591108, Karnataka (TLM)
15	St. Joseph Leprosy Centre	Post Bag – 1, Sanawad- 451111, Distt. Khargaon (LEPRA) M. P.
16	Sishu Prem Samaj,	101/C- Mountana Building, Road No- 2, Lokandwala Complex, Andheri West, Mumbai – 400053, Maharashtra (GLRA)
17	Kothara Leprosy Hospital,	The Leprosy Mission, P.O. Paratwada, Amravati District – 444805, Maharashtra (TLM)
18	Richardson Leprosy Hospital,	The Leprosy Mission, Miraj, Sangli District – 416410, Maharashtra (TLM)
19	The Leprosy Mission Hospital	Poladpur Raigad District – 402303, Maharashtra (TLM)
20	HOINA Leprosy Research Trust	Post Bag 1, Muniguda, Rayagada Distt. – 765020, Orissa (LEPRA)
21	Schieffelin Leprosy Research & Training Centre	Karigiri – 632106, Vellore Distt., Tamil Nadu
22	Sacred Heart Leprosy Centre	Karaikal Road, Sakkottai, Kumbakonam RS 612401, Tanjore Distt., Tamil Nadu (ALES)

	Name of the Centre	Address
23	Holy Family Hansenorium	Fathimanagar PO, Tiruchirapalli Distt., Tamil Nadu (DFIT)
24	Leprosy Relief Rural Centre	Chettipatty 636455, Via – Omalur, Salem Distt.Tamil Nadu (GLRA)
25	GREMALTES	5, Gajapathy Street, Shenoynagar, Chennai – 600030, Tamil Nadu (GLRA)
26	The Leprosy Mission Hospital	Vadathorasalur, P.O. Tiyagadurg, V.R.P. Distt – 606206, Tamil Nadu
27	Dayapuram Leprosy Centre	The Leprosy Mission, Manamadurai, Sivagangai DIstt- 630606 Tamil Nadu (TLM)
28	Faizabad Leprosy Hospital	The Leprosy Mission, P.O. Motinagar, Faizabad Distt-224201, Uttar Pradesh (TLM)
29	The Leprosy Mission Hospital	P.O. Naini, District Allahabad – 211008, Uttar Pradesh (TLM)
30	Purulia Leprosy Home and Hospital	The Leprosy Mission, P.O. Box-9, Purulia – 723101, West Bengal (TLM)
31	Premanada Memorial Leprosy Hospital	The Leprosy Mission, 259 – A, A P Chandra Road, Kolkata – 700005 , West Bengal (TLM)
32	The Leprosy Mission Hospital	The Leprosy Mission Hospital, Nandnagri, Shadhara, Delhi – 110 093

Post-exposure prophylaxis (PEP): Current recommendations

India implemented giving post-exposure prophylaxis as a part of national leprosy eradication program(NLEP) since 2nd August, 2019. The operational guidelines for the same have been published by government of India and WHO. In last two years, total of 1334556 contacts of active leprosy cases have been identified and 872182 (65%) of them have been administered single dose rifampicin (SDR) as PEP. (Source Dr. Megha Khobragade, ADDG Leprosy, GOI). England and Singapore are two other countries who have already implemented SDR PEP. Recently, there has been some evidence to suggest limitations of use of SDR as tool for PEP and a more effective regime as PEP++ consisting of three standard doses of rifampicin 600 mg (weight adjusted when given to children) plus moxifloxacin 400 mg given at two– or four-weekly intervals, although this was later set at four weeks to coincide with MDT practices. For children and for adults with contraindications for moxifloxacin, moxifloxacin should be replaced by clarithromycin 300 mg (weight adjusted).

References and Acknowledgements

1.Evaluation of India's Leprosy Eradication Programme. https://ilepfederation.org/evaluation-of-indias-leprosy-eradication-programme/

2. Anil Kumar, Sajid Husain, "The Burden of New Leprosy Cases in India: A Population-Based Survey in Two States", *International Scholarly Research Notices*, vol. 2013, Article ID 329283, 8 pages, 2013. https://doi.org/10.1155/2013/329283

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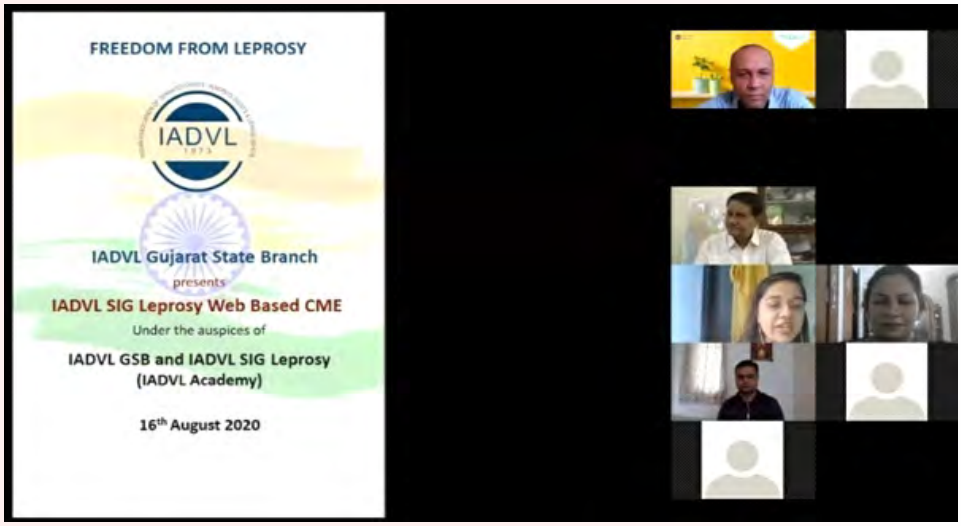
4. Odriozola EP, Quintana AM, González V, Pasetto RA, Utgés ME, Bruzzone OA, Arnaiz MR. Towards leprosy elimination by 2020: forecasts of epidemiological indicators of leprosy in Corrientes, a province of northeastern Argentina that is a pioneer in leprosy elimination. Mem Inst Oswaldo Cruz. 2017 ;112 :419-427.

5. World Health Organization. Regional Office for South-East Asia. (2020). Leprosy/Hansen disease: Contact tracing and post-exposure prophylaxis. World Health Organization. Regional Office for South-East Asia. https://apps.who.int/iris/handle/10665/336679. License: CC BY-NC-SA 3.0 IGO

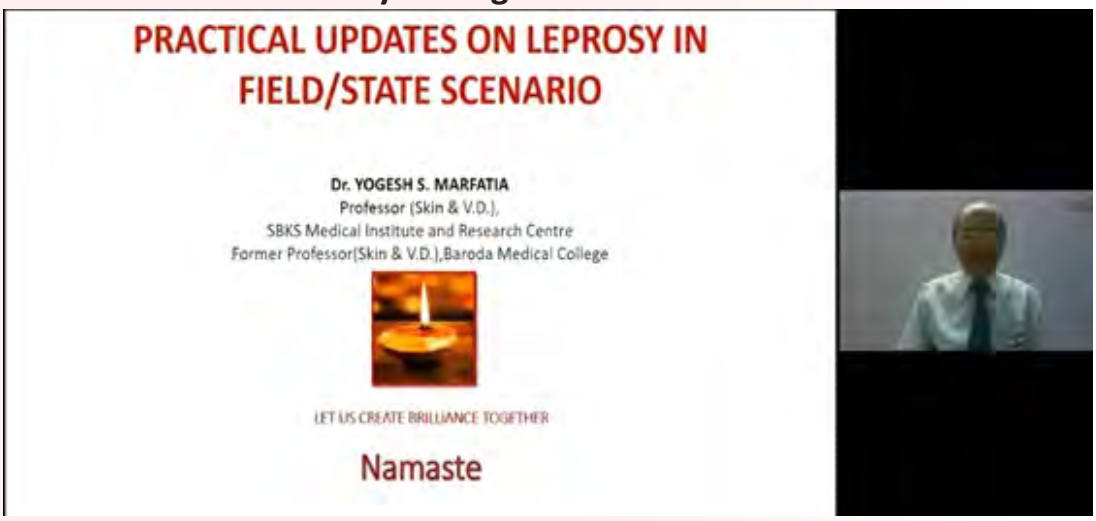
DETAILED REPORT OF SIG-LEPROSY WEBINAR

IADVL SIG LEPROSY Webinar- Gujarat State Branch
(Compiled by resident doctors of Dr. Shardaben General Hospital, Smt. NHL Municipal Medical College, Ahmedabad)



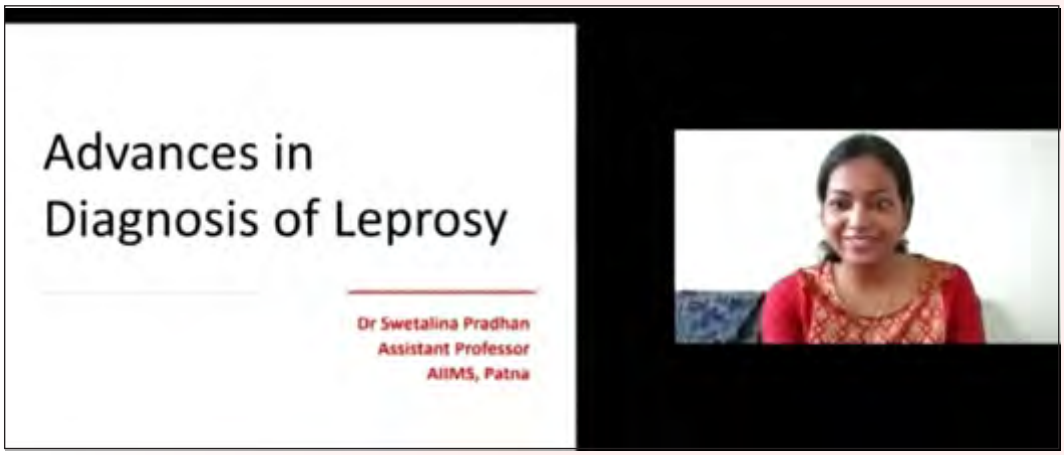
An SIG Leprosy Web based CME was organized by IADVL Gujarat State Branch in association with IADVL SIG Leprosy and IADVL academy on 16th August, 2020 with the theme of *'Freedom from Leprosy'*. The program included plenary talks and a case based panel discussion. The program was well attended by more than 350 delegates including consultant dermatologists and post graduate students. In this brief activity report- we bring you the salient points discussed in the webinar.

Talk on PRACTICAL UPDATES IN LEPROSY IN STATE AND FIELD SCENARIO by Dr. Yogesh S Marfatia.



The elimination of leprosy as a public health problem (PR<1/10,000) was achieved globally in 2000. India achieved the WHO target of elimination (PR<1/10,000) in 2005, but still continues to account for 60% of new cases reported globally each year and is among the 22 “global priority countries” that contribute 95% of world numbers of leprosy. In Gujarat, prevalence rate in March 2020 was 0.36/10,000. Fixed duration MDT has had a little impact on reducing new case detection rate. In a pilot study, by ICMR; MIP vaccine has been introduced in leprosy control wherein the index leprosy case will receive both MIP vaccine and MDT and the contacts will get two doses of MIP vaccine at an interval of 6 months. Another development is the Leprosy post exposure prophylaxis which includes contact tracing, screening and single dose Rifampicin to all the eligible contacts.

ADVANCES IN DIAGNOSIS OF LEPROSY
by Dr. Swetalina Pradhan



- In cases of early or suspected leprosy or in situations where all 3 cardinal features of leprosy are not present, we may require advanced diagnostic tests besides the skin biopsy and histopathology. The antigen detection tests like *M leprae* specific PCR using *M. leprae* DNA (sensitivity 2-8 bacilli) is a sensitive assay to diagnose leprosy even in cases of paucibacillary or indeterminate leprosy. RT PCR and q PCR are also being utilised in clinical trial settings for quantification of viable or total bacillary load in patients who are on treatment and may be helpful in studies on newer drug regimes in leprosy.

- There are a lot of serological assays like PGL antibody assay, ML flow test using immunochromatographic method, ND-O-BSA dipstick assay,35 kda based serology but the problem with these tests is that they may not detect paucibacillary patients. However they may prove useful to detect subclinical cases, pure neural Hansen or in cases of early lepromatous leprosy which may not be detected easily in the field. Some experts also feel that these tests can be useful in contact tracing and PEP programmes.

- Drug resistance is being reported from India and other parts of the world, new molecular methods which can detect resistance to rifampicin, ofloxacin and dapsone by PCR, line probe assays, etc are also available which are being used in drug resistance surveillance in India. Ultrasonography is also a new tool which may prove to be useful in the diagnosis and management of neural leprosy; HRUSG (10-14MHZ probe to detect nerve thickness, echotexture, consistency useful in differentiating neuropathies) and Colour Doppler may also prove to be useful to detect lepra reactions in which increased vascularity can be detected early.

MANAGEMENT OF LEPRA REACTION AMIDST COVID-19 PANDEMIC:
Dr. Deepika Pandhi

· Management of reactions during the covid pandemic is a big dilemma, there is fear of inducing immune-suppression leading to increased susceptibility to the infection and, if these reactions are not managed promptly, they may lead to significant deformities and disabilities. Leprosy patients on corticosteroids >60mg/day or total cumulative dose >700mg are immunocompromised and are at a higher risk of developing COVID-19 infection.Patient with chronic ENL require corticosteroid for longer period thus increasing the chances to be infected by COVID-19 virus, but based on risk-benefit ratio, we should continue steroid at the minimum acceptable dose in such patients.

· According to European Academy of Dermatology and Venerology taskforce: Drugs increasing risk of COVID-19 are: Azathioprine, Methotrexate, Cyclosporine, Prednisolone. We should try to avoid these immune-suppressants as far as possible. Thalidomide is an effective option for treating severe and recurrent ENL. Other immune modulators like chloroquine, hydroxychloroquine, colchicine, high dose clofazimine and minocycline can be used in cases with mild to moderate ENL or for maintenance therapy of recrurrent or Chronic ENL.

· Stress reduction is a very important aspect and stressors should be looked for and eliminated in cases with chronic or recurrent ENL to prevent disease flare.

Immunotherapy and Immunoprophylaxis in Leprosy :

Dr. Ashwini PK
MBBS, MD, FRGUHS (Dermatosurgery)
Associate Prof., JSS Medical College, JSSAHER, Mysore

BCG: The protective efficacy of BCG vaccine is around 50%, it is better in MB spectrum and younger individuals. BCG with Single dose rifampicin- together provide upto 80% protection against transmission. BCG with MDT - induces more effective therapeutic response and reduces the frequency and intensity of lepra reactions. although there were concerns that it might lead to increased frequency or severity of neuritis and may lead to nerve function impairment but studies from India have shown no significant increase in neuritis and it may even be protective as far as nerve function impairment is concerned. It is contraindicated with chemoprophylaxis (if BCG given first, give chemoprophylaxis after 1 month and if chemoprophylaxis given first then give BCG after 24 hours).

Other vaccines that have been used in leprosy prophylaxis are -BCG + killed M. leprae in italics however in the trials from Venezuela and Malawi, there was no significant difference in efficacy between BCG plus killed M. leprae or BCG at 5–9 years. *M. Vaccae; which is a* non-pathogenic species of mycobacterium living in soil Again its efficacy was not proven in studies on leprosy patients or contacts.*M. Habana* was also a live vaccine. One Indian study reported Lepromin conversion post vaccination, however there are not many studies on its efficacy in prophylaxis or as immunotherapeutic vaccine.

MIP: *Mycobacterium Indicus Pranii* (*Mycobacterium Welchii*) is an indeginious vaccine from non-pathogenic, rapidly growing atypical mycobacterium developed by Talwar et al. it has been used as an immunotherapeutic adjunct to MDT in a number of trials and has led to significant improvement in clinical and bacteriological clearance as well as histological upgradation in patients with MB leprosy. It has been approved by DCGI and FDA. A large clinical trial in Kanpur reported that the prophylactic effect of vaccine was 68.6%, 59%, and 39.3% at the end of the first, second, and third follow-up survey, respectively, which was at 3, 6, and 9 years after the initial vaccination and these effects were sustained upto 7-8 years.

ICRC vaccine- It is a gamma-radiation inactivated ICRC bacilli, (Cultivable mycobacterium belonging to *M avium intercellulare* complex) which are a group of leprosy-derived cultivable slow-growing mycobacteria; it provided around 65% protection in the south India immunoprophylaxis study

Recombinant vaccines: BCG vaccine confers a 50-60% protection against leprosy , hence recombinant BCG vaccines are being tried which will increase its efficacy and immunogenicity. Some examples are, rBCG overproducing Ag85A and it reduced the multiplication of *M. leprae* in the foot pads of mice. Another is BCG-SM, a recombinant BCG strain that secretes MMP-II (matrix metalloproteinase-II), which is an immune-dominant antigen, activated both naïve CD4+ T cells and naïve CD8+ T in mice

Lepvax: single tetravalent fusion protein. Consists: ML2028, ML2055, ML2380, ML2531 antigens. They are used in conjunction with approved “GLA-SE” adjuvant (glucopyrinosyl lipid in stable emulsion). The antigenicity of each component of vaccine is retained and antibodies develop against each component, which is an important feature. 85% reduction in *M. leprae* load in post-exposure experimental animals 12 months' post-vaccination. Good safety profile, nerve protective, delays motor nerve impairment.

Video demonstration of rehabilitation in leprosy
Dr Sunil K Gupta

Leprosy is one of the Neglected Tropical Disease and associated with stigma, discrimination, and deformity. Unfortunately, India represents a major bulk of global leprosy caseload with miserable cases of childhood leprosy. Grade 1 disability (loss of sensation) & Grade 2 disability (visible deformity) of hands/feet/eye occur due to late diagnosis and management, multibacillary leprosy, Lepra reaction involving nerves and lack of awareness about self-care in leprosy. So the best way to prevent disabilities is early diagnosis and prompt treatment with WHO MDT, along with education and awareness regarding leprosy and rehabilitation.

The primary goal of rehabilitation should be reversing the physical impairments caused by leprosy, while the secondary goal should be customising lifestyle modifications for the individual patients, their families, and their communities. Rehabilitation of a leprosy-affected individual should start at diagnosis and continue until the patient can return to an active normal life.

The physical rehabilitation of the leprosy-affected includes- (1) Identifying nerve function impairment (NFI) (2) Monitoring impairments (3) Preventing further deterioration of impairments. Leprosy may affect an individual's performance of the activities of daily living (ADL) as well as of work- and leisure-related activities.

The goal of occupational rehabilitation is to enhance or enable meaningful participation in the work- and leisure-related activities that are important to the clients served with the help of (1) Assistive technology/devices (2) Special training (3) Tendon transfer surgery (4)Vocational and diversional activities. The occupational therapist uses vocational activities to divert as well as to enhance the skill level of clients.

Self-Care & Foot-wears- Every patient with a leprosy-related impairment needs to be educated about self-care. The education needs to be participatory and problem-based. Effective self-care interventions or lifestyle modifications adopted by the patients will help reduce their impairments. A self-care group is a group of leprosy-affected patients, and even their family members, who meet to discuss various aspects of self-care including daily care of eyes, hands and feet.

Feet that have sensory loss are at a high risk of thermal and repetitive pressure injuries, as well as injuries from sharp objects. Footwear made of Micro Cellular Rubber (MCR) is considered to be the most appropriate because the microcells in the rubber cushion the feet. MCR also helps redistribute pressure and provides adequate protection from external pressure.

Community-Based Rehabilitation is an important part of leprosy rehabilitation which is multidimensional and involves different aspects like health, education, livelihood, social and empowerment of leprosy-affected people so that they can live a healthy, happy and social life in the community.

MANAGEMENT OF PATIENTS WITH HIGH BACTERIAL LOAD

Dr.Tarun Narang

Patients with high bacillary index (BI) are probably the single most important reservoir of leprosy transmission and should never be missed, or under-treated. Adequate management of these patients is crucial for success of our dream of a Leprosy free world. WHO fixed duration multidrug therapy(MDT) for 12 months may not be adequate for patients with high bacillary load as these patients continue to harbour live bacilli even after one year of MDT and continue to suffer from reactions and recurrences. These patients especially the polar lepromatous leprosy are anergic and may relapse or get reinfected if they are released from treatment after one or two year of treatment. An ideal approach in these patients would be prolonged MDT till smear negativity but that is not practical as it may compromise the compliance, hence we need approaches like intensive therapy initially or immunotherapy with vaccines like BCG and MIP along with MDT. We can also give alternate leprosy treatment with potent bactericidal drugs like clarithromycin, minocycline and ofloxacin or moxifloxacin to patients who show clinical or microbiological non responsiveness to WHO MDT. Contact tracing and treatment of contacts with chemotherapy or immunotherapy is an important part of management of these patients. Prolonged therapy with monthly doses of rifampicin, ofloxacin and minocycline may also be an effective way to prevent relapses and recurrences in this subset of patients. All these interventions have to go hand in hand with socio-economic upliftment and improvement in standard of living for achieving a target of ZERO transmission of Leprosy and eventually a leprosy free world.

Panel discussion on CHILDHOOD LEPROSY
Dr. Timir Mehta, Dr. P Narasimha Rao and Dr. Sujai Suneetha

One of the most important sources of infection in childhood cases is familial contact with leprosy. Detection of a case of childhood leprosy may provide an opportunity to detect the index case, usually within the family and sometimes even community. The course of childhood leprosy is unpredictable. Progression or regression of lesions is common. There may be three possible outcomes when a child is infected with *M. leprae*;

(a) the child does not develop leprosy;

(b) early lesions like indeterminate leprosy may appear, which may remain stationary or disappear due to self-healing; and

(c) the indeterminate lesion/s may progress to a determinate type. Leprosy in children presents predominantly as PB disease. The spectrum of leprosy in children is reported mostly to be tuberculoid (TT), borderline tuberculoid (BT), mid-borderline (BB), and indeterminate forms. Single skin lesion and indeterminate leprosy were seen to be a common early presentation in most of the studies.

Molecular diagnostic tests like multiplex PCR can help in the diagnosis of IL with limited clinical manifestations. However, one has to be very careful while giving a diagnostic label of leprosy in a child for obvious psychological trauma and social stigma.

The frequency of reactions in children is reported to vary from 3.1% to 33.9% as compared to adults where more than 50% of the patients develop reactions.

Since the demonstration of classical histological features of leprosy or AFB in cutaneous lesions of IL is difficult; hence, a reasonable period of observation is recommended if the diagnosis cannot be confirmed at the time of presentation.

Treatment dropout rates in children range from 10% to 20% in some programmes, main cause being the child's refusal to cooperate in swallowing tablets. Child-friendly treatment options such as flavoured syrups are the need of the hour for improvement in dosing and compliance.

Parental education is essential before starting MDT for the child. Parents and young patients need to understand the following:

1. There is no need to isolate child with disease
2. How to recognize common sand serious side effects of MDT
3. How to recognize symptoms of Lepra reaction
4. Clearance of lesions will take time
5. MDT is freely available at all government centres

Panel Discussion on Tuberculosis and Leprosy co-infection
Dr. Rashmi Mahajan, Dr. Bela Shah, Capt. Sridhar J. and Dr. Abhishek Bhardwaj

Although an increased frequency of pulmonary TB in patients with lepromatous leprosy may occur as a result of malnutrition, TB occurs across the spectrum of leprosy. The incubation period of both the infection differs as in leprosy it varies from 6 months to many years, whereas in TB, it ranges from few weeks to months. The duration of the gap between the development of leprosy and TB varied between 2 months and 10–15 years

The main problem in screening a patient with concomitant leprosy and tuberculosis is that interferon-gamma release assays (IGRAs) to test for latent TB is confounded by the cross-reactivity of T-cell response with the protein homologs in M. leprae and the mantoux or the Purified Protein Derivative (PPD) skin test may have some utility in the diagnosis of latent TB in the setting of paucibacillary leprosy (PBL); however, “giant reactions” to PPD testing have been documented in mono-infection with multibacillary leprosy (MBL) which may lead to more confusion or dilemma. However, a positive IGRA or PPD test in a patient with Leprosy should not be considered false positive without ruling out active TB. All investigations based on the symptoms should be performed like chest X ray, Ultrasound abdomen, FNAC from lymph node etc.

Treatment:

CAT-I anti-tuberculous drug and to continue MDT without rifampicin 600 mg monthly dose.

- Sometimes cutaneous lesions may also pose a diagnostic challenge and it is difficult to differentiate between borderline tuberculoid Hansen and cutaneous lupus vulgaris even on histopathology.When in doubt, PCR from skin tissue should be done. A therapeutic clue may sometimes help as lesions of cutaneous tuberculosis shows rapid improvement within 4-6 weeks whereas lesions of leprosy take longer time to regress.

RPWD ACT 2016 AND ITS IMPLICATIONS FOR LEPROSY CURED PERSONS WITH GRADE II DISABILITY

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Introduction

The Act replaces the Persons with Disabilities (Equal Opportunities, Protection of Rights and Full Participation) Act, 1995. It fulfills the obligations to the United National Convention on the Rights of Persons with Disabilities (UNCRPD), to which India is a signatory. The Act came into force in December 2016. [1]

Disabilities covered

The types of disabilities have been increased from existing 7 to 21 and the Central Government will have the power to add more types of disabilities. Leprosy cured persons have been added in recent list. "Benchmark disability" is defined under the Act as one that is certified to have at least 40 per cent disability.

WHO grading of disability in leprosy

EHF (Eyes, Hands, Feet) grade score is calculated. Highest grade for each eye or hand or foot is 2. Higher the score, greater the disability. Maximum EHF score possible is 12.

Grade	Eyes	Hands	Feet
0	No eye problem due to leprosy; no evidence of visual loss	No anesthesia, no visible deformity or damage	No anesthesia, no visible deformity or damage
1	Eye problem due to leprosy present, but vision not severely affected as a result of these (vision: 6/60 or better; can count fingers at 6 metres).	Anaesthesia is present but no visible deformity	Anesthesia present, but no visible deformity or damage
2	Severe visual impairment (vision worse than 6/60, inability to count fingers at 6 metres). Also includes lagophthalmos, iridocyclitis and corneal opacities	Visible deformities or damage like ulcers, fissures, contractures,claw hands, ape thumb, etc	Visible deformity or damage present (suchs cracks/wounds, claw toes, foot drop, contractures, amputation etc.)

Muscle power is tested clinically by voluntary muscle testing of commonly examined peripheral nerves and graded as per the Medical Research Council, London Scale.

Computation of disability percentage

1. EHF Score is 0-1, then % of disability is up to 20%.
2. EHF Score is 2-3, then % of disability is 20% to 40%.
3. EHF Score is 4-5 then % of disability is 41% to 60%.
4. EHF Score is 6-7 then % of disability is 61% to 70%.
5. EHF Score is 8-9 then % of disability is 71% to 80%.
6. EHF Score is 10-11 then % of disability is 81% to 90%.
7. EHF Score is 12 then % of disability is 91 to 100%.

Rights and entitlements

1. It has been cast upon the appropriate governments to take effective measures to ensure that the persons with disabilities enjoy their rights equally with others.
2. Additional benefits such as reservation in higher education (not less than 5%), government jobs (not less than 4 %), reservation in allocation of land, poverty alleviation schemes (5% allotment) etc. have been provided for persons with benchmark disabilities and those with high support needs.
3. Every child with benchmark disability between the age group of 6 and 18 years shall have the right to free education.
4. Government funded educational institutions as well as the government recognized institutions will have to provide inclusive education to the children with disabilities.
5. For strengthening the Prime Minister's Accessible India Campaign, stress has been given to ensure accessibility in public buildings (both Government and private) in a prescribed time-frame.

Penalties for offences

1. Act provides for penalties for offences committed against persons with disabilities (PwDs) and also violation of the provisions of the new law.
2. Any person who violates provisions of the Act, or any rule or regulation made under it, shall be punishable with imprisonment up to six months and/ or a fine of Rs 10,000, or both. For any subsequent violation, imprisonment of up to two years and/or a fine of Rs 50,000 to Rs five lakh can be awarded.
3. Whoever intentionally insults or intimidates a person with disability, or sexually exploits a woman or child with disability, shall be punishable with imprisonment between six months to five years and fine. Special Courts have been designated in each district to handle cases concerning violation of rights of PwDs.

Experience of patients

In Feb 2020, one of our leprosy cured patients at INHS Asvini, Mumbai was issued a Disability Certificate as per proforma

given in RPWD Act [2] with 60% disability assessment for ulnar claw and drop foot deformities. With the certificate, the individual applied for Unique Disability Identity (UDID) card, also known as 'Swavlamban Card' in his native state of Madhya Pradesh. The application for UDID card was processed online and delivered to his home (Fig 1).

At present Disability Certificates issued in one state are not easily recognized in others. The UDID card helps the differently-abled to tide over problems that they face at railway counters and even educational institutions across the country. This card comes with number of benefits as follows [3]:

1. The card is of standard credit card size and easily fits in one's wallet (Figure 2).
2. UDID Card is valid anywhere in India to prove one's disability condition.
3. The card has a unique number which if fed on the website would help an authority to access all details.
4. The card has also a microchip through which information can be easily read with a card reader device.
5. It is easy to identify the extent of person's disability by the coloured strip on the left hand margin as follows:
   (a) Less than 40% disability - white stripe.
   (b) 40 to 80 % disability - yellow stripe.
   © Above 80% disability - blue stripe.
6. Real time data about disabled persons is available to the government to monitor implementation of the Act.
7. Disability related data across the country will not get duplicated as computer system ensures uniqueness of all data related to disabled individuals.
8. System can be easily up scaled if more disability conditions get recognized by the government.
9. UDID card will help government to track a number of aspects of implementation, for example:
   (a) Whether benefits of welfare schemes are reaching to the disabled persons.
   (b) How the beneficiaries are getting benefited.
   (c) If schemes are contributing to the progress of UDID card holder.
10. Other than the above benefits of UDID card, our patient is also getting following benefits:
   (a) Concession while travelling by Indian Railways.
   (b) Concession in competitive exam fees and preference in job in government sector.
   (c) Income tax benefits as disability deduction under section 80DD and 80U.
   (d) Preference in queue at all government institutions and banks.

Conclusion

RPD Act, 2016 is making a significant impact on the social rehabilitation and dignity of leprosy cured persons. The UDID card that is given by states on the basis of Disability Certificate issued by the Dermatologist is valid proof of disability across the country. It has opened hitherto closed doors of opportunities for leprosy cured persons.

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UPDATES ON ERYTHEMA NODOSUM LEPROSUM

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While cases of leprosy are declining due to the joint efforts of World Health Organization (WHO) and National Leprosy Eradication Program, the annual new case detection rate has remained constant over the last 10 years. Reactions in leprosy are a major clinical concern and up to 50% of the leprosy patients experience a reaction at least once during their lifetime. Two main types of reactions seen in leprosy are: Reversal Reactions (RR) or type 1 reaction and Erythema Nodosum Leprosum (ENL) or type 2 reaction. ENL is a Gell & Coombs type 3 hypersensitivity reaction affecting approximately 50% of patients with lepromatous leprosy and 10% of borderline lepromatous leprosy. Available data indicates that ENL incidence ranges between 0.7-4.6% of all multibacillary leprosy cases.

CLINICAL PRESENTATION

Type 2 reaction classically presents with tender, erythematous, evanescent nodules together with constitutional features and visceral involvement. Atypical clinical manifestations have also been reported like pustular, bullous, necrotic, annular ENL, lichenoid papules, erythema multiforme-like reaction; reactive perforating; and Sweet's syndrome-like presentation. Uncommon variants of ENL are often misdiagnosed in patients. Hence, a high index of suspicion is required in such cases to avoid delay in diagnosis which may result in complications like deformities and disabilities.

IMMUNOPATHOLOGY

ENL is an immune-mediated complication of leprosy. The bactericidal effect of MDT or other antibiotics on M. leprae results in the release of an enormous amount of bacterial breakdown products that are recognized by the innate immune reaction as antigens resulting in activation of pro-inflammatory cytokines and attraction of CD4 + T cells to the location of the infection. ENL is associated with circulation- and tissue- deposition of immune complexes and occur in patients with dominant Th2 response.

During ENL, DNA sensing via TLR9 has a key role as demonstrated by higher levels of TLR9 within the lesions and in the circulation of ENL patients compared to BL/LL controls without reactions.

A subpopulation of circulating neutrophils of ENL patients that exclusively expressed IL-10R1, providing evidence that IL-10R1+ neutrophils are present in ENL lesions. Circulating and lesional neutrophils in ENL exclusively express CD64 which isn't the case in leprosy patients without reaction. Macrophage migration inhibitory factor levels are also elevated.

IMMUNOGENETIC RISK FACTORS

Immunogenetic factors are used for research purpose to contribute to the early detection, prognosis, understanding of pathophysiology and improvement in the treatment of the disease. These markers also explain why some of the ENL

reaction is mild and response early while some become chronic and recalcitrant. Some of the important factors for ENL are-

-Decreased C4, C4B and IL6

-Elevated anti-M. leprae antibodies

-TLR9 genes,

-HLA genes (HLA-DRB1 and HLA-DQA), HLA-linked genes (TAP, MICA, and MICB)

-Nucleotide-binding oligomerisation domain containing 2 (NOD-2),

-Vitamin D receptor (VDR),

-Natural resistance-associated macrophage protein 1 (NRAMP-1).

BIOMARKERS

Over the past few years, a significant amount of research on biomarkers for lepra reactions have been done to predicting the severity and prognosis of Type 2 reactions. These are: -

-High serum TNF-α levels

-CD64 is an early biomarker also as a predictor of severity in ENL.

-Elevated levels of α 1- acid glycoprotein, which induce TNF- α secretion,

-Anti-PGL-I Ab and anti-LID (Leprosy IDRI antigen)-1 levels showed prognostic value for ENL in patients with a positive Bacillary Index (BI) at diagnosis.

-The pentraxin PTX3 (TNF-inducible gene protein). This protein binds with high affinity to the complement component C1q which is a diagnostic marker for active ENL reactions also used for monitoring ENL treatment. It is inversely correlated with ENL.

-CCL-11, (produced by monocytes, a chemoattractant for eosinophils and Th2 lymphocytes).

TRIGGERS

Though there are several triggering factors for the ENL including initiation of MDT, superinfection, stress and pregnancy but recent literature also observed the role of chronic infections with soil-transmitted helminths (STH). STH is known to induce systemic immune dysregulation towards Th2 predominant immune response. Furthermore, in India, the areas like Bihar/Eastern UP are endemic for lymphatic filariasis & leprosy as well which may be a precipitant for ENL.

DIAGNOSIS

FNAC has also been found to be an important diagnostic modality for early diagnosis of ENL.

The cytological features of ENL are similar to the histomorphological counterpart and include the presence of acute inflammatory infiltrate, focal necrosis, foamy macrophages, and high acid-fast bacilli positivity.

NECROTIC ENL vs LUCIO PHENOMENON

Although it may be difficult to differentiate between the two, necrotic ENL is more common than Lucio phenomenon in India. The management of these two is also different so careful differentiation between the two entities is important; systemic manifestations in the form of fever, joint pain, malaise and myalgia, tender lymphadenopathy, ocular complaints, and orchitis are more common in Necrotic ENL. In Lucio phenomenon, clinical lesions may be similar to Necrotic ENL but systemic manifestations are usually absent. AFB in the endothelial cells has been described as a hallmark of Lucio phenomenon but some studies have described it in Necrotic ENL as well in association with vasculitis.

ENL SEVERITY SCALE

ENL has been classified as mild, moderate, or severe. To standardize the classification, the Erythema Nodosum Leprosum International Study (ENLIST) Group has developed an objective scale, the ENLIST ENL Severity Scale which is the first validated severity scale of ENL in the world [see the table]. We should encourage the proper incorporation of such tool by the clinicians and paramedics in leprosy clinics across the leprosy endemic countries like India, to reduce the chance of misdiagnosing and help in the proper selection of drug regimen for the effective management of ENL.

TREATMENT

Erythema nodosum leprosum may appear before, during or after the treatment of leprosy. When ENL occurs or continues to occur after release from treatment, it may indicate disease activity or high bacillary load or sometimes drug resistance, hence these patients should also be evaluated on these lines and depending on the results, we may have to start the patient on alternate leprosy treatment (if drug resistance is detected) or restart MDT (if no drug-resistant bacilli are detected). Oral steroids are the mainstay for management of ENL. The mRNA expression in blood and skin lesion for TNF, IFN-γ, IL-1β, IL-6, and IL-17A significantly reduced in patients with ENL after treatment, while mRNA expression for IL-10 and TGF-β was significantly increased both in blood and skin lesion after treatment. This is the first study examining the effect of prednisolone on the kinetics of inflammatory and regulatory cytokines in patients with ENL reactions before and after prednisolone treatment. The recent findings of significantly increased prednisolone-induced LDL and TG levels, in patients with chronic ENL reactions, highlight the importance of monitoring lipid profiles during treatment of patients to minimize the long-term risk of prednisolone-induced complications. Current study on genetic polymorphism of the TNF gene and the CYP2C19*2 explains about the poor response to oral steroid and thalidomide. During treatment of ENL with the combination of oral steroid and thalidomide, there is an increased incidence of deep vein thrombosis which require the use of acetylsalicylic acid (Aspirin) 100mg/day as prophylaxis. Though there are reports of the use of minocycline, azathioprine, methotrexate, TNF-α inhibitors like etanercept and infliximab in chronic recalcitrant ENL with variable results but a recent study showing the efficacy of Apremilast in patients of recalcitrant ENL is promising. Medications like metformin, pomalidomide, TNF-α inhibitors such as adalimumab, certolizumab pegol, golimumab, IL-17 inhibitors like secukinumab, xanthine derivatives like bupropion could be tried in ENL as targeted therapies in future.

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Table- ENLIST Severity Scale

		Points			
	Item	**0**	**1**	**2**	**3**
1	Visual scale of pain (in mm)	0	1-39	40-69	70-100
2	Fever	Absent (37.5 or less)	No fever at the moment, but having occurred in the last 7 days	37.6–38.5	Above 38.6
3	Number of lesions of erythema nodosum	Absent	1-10	11-20	>20
4	Inflammation of the lesions	Absent	Erythematous	Painful	Complex
5	Extent of skin involvement	0	1-2 regions	3-4 regions	5-7 regions
6	Peripheral edema	Absent	1 place amongst hands, feet, or face	2 places	Edema in 3 places

		Points			
	Item	**0**	**1**	**2**	**3**
7	Bone Pain	Absent	Present, but not disrupting daily activities	Disrupting sleep or daily activities	Incapacitating
8	Arthritis and/or dactylitis	Absent	Present, but not disrupting daily activities	Disrupting sleep or daily activities	Incapacitating
9	Lymphadenopathy	Absent	Increased	Pain or tenderness	Pain or tenderness in two or more group
10	Neuritis	Absent	Absent, if attention is distracted	Present, even when distracted	Withdraws limb on examination
	Total				

SNIPPETS FROM RECENT RESEARCH ON LEPROSY

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In recent years there has been a considerable amount of research in the field of leprosy which has added to our knowledge regarding the condition. Various aspects of pathogenesis and factors responsible for the development of leprosy have been published as scientific papers. This compilation is an attempt in summarizing the information available in the research articles on Leprosy, in the last five years.

A. Genetic clues:

1.Sartori PV, Penna GO, Bührer-Sékula S, Pontes MA, Gonçalves HS, Cruz R, Virmond MC, Dias-Baptista IM, Rosa PS, Penna ML, Fava VM. Human genetic susceptibility of leprosy recurrence. Scientific reports. 2020 Jan 28;10(1):1-5.

Host genetic susceptibility to leprosy has been intensely investigated over the last decades, however, studies on role of genetic variants in disease recurrence are lacking. Sartori et al in their scientific report on human genetic susceptibility of leprosy recurrence, suggested that leprosy patients with 'high- susceptibility genetic profile' can have more chances of disease recurrence. A clinical trial for uniform six doses of MDT for leprosy patients was conducted in Brazil. Among the cases who presented with recurrence, whole genomic sequencing and analysis was done. No mutations associated with drug resistance were detected in the genomes studied. Thus it was reasonable to conclude that leprosy recurrence was not due to any characteristics of the etiological agent. And it could be due to increased host -susceptibility genetic background. 19 single nucleotide polymorphism(SNP) distributed across 11 loci were genotyped. Their findings, that the enrichment of certain risk alleles being observed in patients presenting with recurrences, highlights the importance of genetic susceptibility.

It is hypothesised that early onset leprosy is more heavily dependent on genetic mechanisms, whereas late onset disease is a balanced combination of genetic and environmental factors.

A higher frequency of risk allele is observed for markers of several well - known leprosy susceptibility genes – IL 10, PACRG(parkin coregulated gene), NOD2(nucleotide binding oligomerisation domain), HLA-DRB1/DQA1, LTA(lymphotoxin alpha), GATA3 and TLR1- in relapse cases compared to controls. The data thus indicates that genes associated with susceptibility to leprosy may also play an important role in recurrence. Combination of alleles in different genes may confer hyper-susceptibility to leprosy. Since this particular study was conducted on a limited sample size of six patients, further studies involving larger number of subjects with recurrence of leprosy would throw better light on this area of research.

2. Benjak A, Avanzi C, Singh P, Loiseau C, Girma S, Busso P, Fontes AN, Miyamoto Y, Namisato M, Bobosha K, Salgado CG. Phylogenomics and antimicrobial resistance of the leprosy bacillus Mycobacterium leprae. Nature communications. 2018 Jan 24;9(1):1-1.

Benjak et al s study revealed few MDT-resistance mutations additional to the known ones. The study involved extracting the DNA from 109 human skin biopsy samples from clinically well characterised patients. The Bacteriological index ranged from 0-6 in these samples. Surprisingly, successful genomic coverage could even be achieved with some specimens whose

BI was as low as 1+. A total of 154 M leprae genomes were analysed, of which 120 were newly sequenced. The cohort comprised of 147 human samples, 6 from red squirrels and 1 from armadillo. 30 of these strains were from patients who had relapsed or not responded to MDT and the remaining ones from drug susceptible strains. They opined that some of the previously undescribed mutations do occur in genes. Interestingly, three genes (fadD9, ribD, pks4) were mutated almost exclusively in MDR strains. High frequency of mutations in ribD and fadD9 were associated with drug resistance. The discovery of these mutations would encourage further research in order to establish their role in anti-microbial resistance, especially to clofazamine.

B. Epidemiological aspects:

1. Ploemacher T, Faber WR, Menke H, Rutten V, Pieters T. Reservoirs and transmission routes of leprosy; A systematic review. PLoS neglected tropical diseases. 2020 Apr 27;14(4): e0008276.

A systematic review on reservoir and transmission of leprosy was done. This systematic review assessed publications of possible non-human environmental reservoirs and transmission pathways of M. leprae and M. lepromatosis. The results show a wildlife reservoir of M. leprae in armadillo species in the southern United States and a wildlife reservoir of M. leprae and M. lepromatosis in British and Irish red squirrels.

It was also stated that RNA indicating the presence of viable M. leprae was found in environmental soil and water samples in Brazil and India.

In addition, it was found that amoebae are capable of taking up M. leprae by phagocytosis. Inside amoebae, M. leprae remained viable for days to weeks. This mechanism might contribute to environmental survival in the absence of a mammalian host. Moreover, M. leprae can also accumulate in amoebae. This gives amoebae a possible role as a vector in transmission.

Animals can be affected by leprosy-like diseases, caused by pathogens phylogenetically closely related to M. leprae. These mycobacteria have been proposed to be grouped as a M. leprae-complex.

C. Diagnostic aids:

1. Van Hooij A, Fat EM, Richardus R, Van Den Eeden SJ, Wilson L, Claudia J, Faber R, Alam K, Richardus JH, Corstjens PL, Geluk A. Quantitative lateral flow strip assays as user-friendly tools to detect biomarker profiles for leprosy. Scientific reports. 2016 Sep 29; 6:34260.

In this report the authors have discussed about applying quantitative user friendly lateral flow assays for four immune markers. The subjects included MB patients, PB patients, Healthy household contacts, House hold contacts vaccinated with BCG, new cases and endemic controls. The protocol prepared by the authors merge detection of innate, adaptivecellular as well as humoral immunity, thereby leading to a convenient tool for assessing M. leprae infection using a field-friendly technology.

2. Van Hooij A, Fat EM, da Silva MB, Bouth RC, Messias AC, Gobbo AR, Lema T, Bobosha K, Li J, Weng X, Salgado CG. Evaluation of immunodiagnostic tests for leprosy in Brazil, China and Ethiopia. Scientific reports. 2018 Dec 18;8(1):1-9.

Leprosy still remains persistently endemic in several areas. New case detection reflects the ongoing transmission. Low

complexity tools, to detect the infection, suitable for large scale screening are required .Hooij et al studied the diagnostic performance of few such assays in Asia, Africa and South America.

The IFN gamma inducible protein (IP 10) correlates with M leprae exposure and thereby the risk of infection. IP 10 response to M leprae specific proteins indicates exposure to M leprae. Chemokine C-C motif ligand 4 (CCL4), a component of innate immunity, can be used to identify immunity against M leprae. It is found to be increased in patients, partly in household contacts but not in endemic controls. Levels of anti- PGL-I IgM antibody, IP-10 , CCL4 and CRP were measured in blood from leprosy patients, household contacts and healthy controls from each area. Combined detection of these parameters, which reflect both humoral and cellular immunity, significantly improved the diagnostic potential, particularly for paucibacillary case detection. IP-10 was the most significant cellular marker to identify both LL/BL and BT/TT leprosy cases. CCL4 was found to be helpful indetecting BT/TT cases. It was seen that anti- PGL IgM and CRP were relevant in diagnosis of LL/BL cases.

3.Barbieri RR, Manta FS, Moreira SJ, Sales AM, Nery JA, Nascimento LP, Hacker MA, Pacheco AG, Machado AM, Sarno EM, Moraes MO. Quantitative polymerase chain reaction in paucibacillary leprosy diagnosis: A follow-up study. PLoS neglected tropical diseases. 2019 Mar 5;13(3): e0007147

The diagnosis of paucibacillary (PB) leprosy cases remains a challenge because of the absence of a confirmatory laboratory method. The quantitative polymerase chain reaction (qPCR) has been shown to provide reliable sensitivity and specificity in PB diagnoses. Around 2437 household contacts were included in the study. Among them 2.8% were either diagnosed as having leprosy during the initial visit or developed leprosy throughout the study. In a group of 2383 remaining contacts 797 refused to donate samples. Of the 1586 household contacts, 25 presented with difficult-to-diagnose leprosy like skin lesions and a total of 1561 contacts had skin scrapings collected for qPCR. The group of 25 were evaluated by PCR and skin biopsies where 8 of them confirmed leprosy. Noteworthy 50% of these were qPCR positive. It was seen that qPCR presented a sensitivity of 50% and specificity of 94% when skin biopsies were used for molecular diagnosis of suspect contacts with leprosy-like lesions. But unfortunately the use of qPCR in earlobes of healthy contacts does not appear to be a good predictive marker of disease progression. But it can be used for routine screening among difficult-to-diagnose suspected cases. It improves the precision in diagnosing PB leprosy.

4.Van Hooij A, van den Eeden S, Richardus R, Fat ET, Wilson L, Franken KL, Faber R, Khatun M, Alam K, Chowdhury AS, Richardus JH. Application of new host biomarker profiles in quantitative point-of-care tests facilitates leprosy diagnosis in the field. EbioMedicine. 2019 Sep 1; 47:301-8.

A study including patients from Bangladesh, identified three new biomarkers for leprosy (ApoA1, IL-1Ra, S100A12), and confirmed five previously described biomarkers (CCL4, CRP, IL-10, IP-10, αPGL-I IgM).

Since antibodies against M.leprae phenolic glycolipid I (PGLI) indicate infection and are associated with bacillary load , rapid diagnostic tests detecting anti-PGL-I antibodies have been developed. However, these are still not yet widely implemented in the field due to limited availability. It is said that both cellular and humoral markers should be included in diagnostic tests.The biomarker profiles including cellular and/or inflammatory biomarkers such as CCL4, IL-10, IP-10, CRP

combined with M.leprae specific anti-PGL-I antibodies, increased sensitivity for leprosy. Apart from IL-10, IL-1Ra and CCL4 the other biomarkers were directly detectable in plasma, hence suitable for rapid POC tests.

Most of these tests use fingerstick blood (though in the present study plasma was used) which is easy and simple to perform and does not require overnight stimulation they can be used as rapid tests. Indeed, lateral flow assays (LFAs) utilizing this five-marker profile detected both multi- and paucibacillary leprosy patients with variable immune responses.

A plasma biomarker signature including αPGL-I IgM, IP-10, S100A12, ApoA1, CRP accurately detected leprosy patients irrespective of type with high sensitivity (86%) and specificity (90%) indicating the diagnostic value of this signature in leprosy as it identifies both patients with high and low bacillary loads.

5. Vinay K, Kamat D, Chatterjee D, Narang T, Dogra S. Dermatoscopy in leprosy and its correlation with clinical spectrum and histopathology: a prospective observational study. Journal of the European Academy of Dermatology and Venereology. 2019 Oct;33(10):1947-51.

Dermoscopy has emerged as a non-invasive tool aiding diagnosis of various skin conditions. The dermatoscopicfeatures consistently seen in Leprosy, according to a study by Vinay et al, were yellowish orange areas and vascular structures like linear branching vessels and crown vessels correlating with the presence of dermal granulomas and dilated vessels. Broken pigment network, paucity of appendageal structures were seen in addition. The study was done in a set of 30 leprosy patients. Findings like vascular structures and broken pigment network may not be specific for the condition. Further studies in larger group of patients in each spectrum, with varied clinical findings would help in providing better clarity regarding the role of dermoscope as an adjuvant in managing leprosy.

6. Queiroz EA, Medeiros NI, Mattos RT, Carvalho AP, Rodrigues-Alves ML, Dutra WO, Félix-Lana FC, Gomes JA, Correa-Oliveira R. Immunological biomarkers of subclinical infection in household contacts of leprosy patients. Immunobiology. 2019 Jul 1;224(4):518-25.

A study on immunological markers in Hansens patients and their household contacts was done. Monocyte and CD4 + T lymphocytes frequency was significantly higher in patients. Both CD4+ and CD8 + T lymphocytes had a reduced CD25 expression in their household contacts. The immunoglobulin (Ig)M profile anti- NDO-HSA, LID-1, and NDOLID antigens was significantly higher in cases. This study points to the monocyte and CD4+ lymphocyte frequency, as well as specific IgM profile, as predictors of subclinical infection in the household contacts.

7**. Saini C, Srivastava RK, Kumar P, Ramesh V, Sharma A. A distinct double positive IL-17A+/F+ T helper 17 cells induced inflammation leads to IL17 producing neutrophils in Type 1 reaction of leprosy patients. Cytokine. 2020 Feb 1; 126:154873.**

Saini et al s study states that the inflammation noted in lesions of T1R is because of a different phenotype of Th17 which produces double positive IL-17A+IL17F+ and also contributes IL-17 producing neutrophils. Studying the levels of IL-17 would be useful for monitoring, diagnosis and treatment response before reactions episodes.

D. Management snippets:

1.Narang T, Bishnoi A, Dogra S, Saikia UN. Alternate Anti-Leprosy Regimen for Multidrug Therapy Refractory Leprosy: A Retrospective Study from a Tertiary Care Center in North India.The American journal of tropical medicine and hygiene. 2019 Jan 9;100(1):24-30.

Inspite of being on MDT there can be a set of patients who are "non responders". The criteria for the diagnosis of "nonresponsiveness" to MDT were as follows: 1) persistent/new lesions after completing ≥ 12 months of WHO-MDT-MBR (reactions excluded) and 2) persistent positive/increasing values of the morphological index (MI) and a 2 log increase in the bacteriological index (BI) after ≥ 12 months of WHO-MDT-MBR.

Narang et al s study highlights the use of alternate anti-leprosy treatment comprising minocycline, ofloxacin, and clofazimine in treating WHO-MDT-MBR refractory leprosy patients, in the absence of facilities for resistance studies. Anti-leprosy therapy comprised minocycline 100 mg/day, clofazimine 50 mg/day, and ofloxacin 400 mg/day for 6 months (intensive phase), and ofloxacin 400 mg/day and clofazimine 50 mg/day for the next 18 months (maintenance phase) was used which showed beneficial results in these patients.

2. Polavarapu K, Preethish-Kumar V, Vengalil S, Nashi S, Lavania M, Bhattacharya K, Mahadevan A, Yasha TC, Saini J, Sengupta U, Jabeen S. Brain and Spinal Cord Lesions in Leprosy: A Magnetic Resonance Imaging–Based Study. The American journal of tropical medicine and hygiene. 2019 Apr 3;100(4):921-31.

Skin and peripheral nerve affliction in leprosy has been extensively studied and published, but reports on involvement of the central nervous system (CNS) and proximal nerves are extremely rare. Polavarapu et al described MRI brainstem and spinal cord lesions and brachial and lumbosacral plexus abnormalities in eight patients with leprosy. They demonstrated lower brainstem MRI lesions involving the seventh cranial nucleus and its nerve and the nucleus ambiguous corresponding with clinical findings highlighting the importance of considering CNS manifestations in leprosy.

3. Richardus R, Alam K, Kundu K, Roy JC, Zafar T, Chowdhury AS, Nieboer D, Faber R, Butlin CR, Geluk A, Richardus JH. Effectiveness of single-dose rifampicin after BCG vaccination to prevent leprosy in close contacts of patients with newly diagnosed leprosy: A cluster randomized controlled trial. International Journal of Infectious Diseases. 2019 Nov 1; 88:65-72.

Study by Richardus et al concluded that Single dose Rifampicin(SDR) after BCG vaccination reduced the incidence of PB leprosy among contacts by 42%. This was a statistically non-significant reduction due to the limited number of cases after SDR was administered. To what extent SDR suppresses excess leprosy cases after BCG vaccination is difficult to establish because many cases appeared before the SDR intervention. Further research would throw light on the area.

4. Liu H, Wang Z, Bao F, Wang C, Sun L, Zhang H, Yu G, Mi Z, Li J, Li L, Zhao Q. Evaluation of prospective HLA-B* 13: 01 screening to prevent dapsone hypersensitivity syndrome in patients with leprosy. JAMA dermatology. 2019 Jun 1;155(6):666-72.

Prospective HLA-B*13:01 screening and subsequent elimination of dapsone from MDT for patients with HLA-B*13:01–positive leprosy may significantly reduce the incidence of DHS.

5. Fairley JK, Ferreira JA, de Oliveira AL, de Filippis T, de FariaGrossi MA, Chaves LP, Caldeira LN, Dos Santos PS, Costa RR, Diniz MC, Duarte CS. The burden of helminth coinfections and micronutrient deficiencies in patients with and without leprosy reactions: A pilot study in Minas Gerais, Brazil. The American Journal of Tropical Medicine and Hygiene. 2019 Nov 6;101(5):1058-65.

Vitamin A, D and Iron deficiencies and helminth infections were prevalent in leprosy patients, though not statistically co relating with clinical severity, suggesting a potential role for additional treatment interventions

Emanuel de Jesus et al.Botulinum toxin type A in chronic neuropathic pain in refractory leprosy March 2019. **https:doi.org//10.1590/0004-282x20190053**

The study comprised of 15 patients with chronic neuropathic pain of leprosy defined by painful condition of at least two years after treatment with MDT or after three months with continuous or uninterrupted pain, associated or not with leprosy reaction, with no evidence to suggest other causes such as infected ulcer. Botulinum toxin A- 100 U was used with dilution in 2ml of 0.9% saline solution, where each 0.1cc match 5U of Botulinum toxin –A. The injection was administered subcutaneously along dermatomes or affected nerve endings. Pain intensity evaluation showed significant reduction (p=0.0057) from days 10 to 60. Probably a longer follow up of the patients would tell us regarding the sustainability of the improvement following a single injection. Since the study did not mention about the improvement in relation to spectrum of disease the patients belonged to, further research would be needed to determine its role in neuropathic pain of leprosy.

6. Samaan M, Musa HA, Hassan Y, Saeed MI. Fungal carriage and infection among leprosy patients in Sudan. LEPROSY REVIEW. 2020 Jun 1;91(2):139-44.

Hay R. Trophic leprosy ulcers-what is a secondary infection. Editorial. Lepr rev(2020)91.126-129)

Foot ulcers caused by diabetes are known to be more prone for surface invasion with bacteria such as staphylococcus aureus. Most studies focus on secondary bacterial growth and fungal cultures are performed rarely. But research in this aspect shows that there was growth of fungal species like Fusarium species, candida species and mucormycetes. This highlights the role of fungal biofilms, contributing to the non- healing nature of these ulcers. Adding anti- fungals, to the standard wound care, significantly improved the healing rate of wounds. The yeast biofilms are said to increase bacterial colonisation. The paper from Sudan said that species like Candida and Aspergillus were isolated from leprosy ulcers and also from ear, nose and eyes of leprosy patients compared to controls. This says that there is a higher chance of carriage of organisms in case of leprosy. There is lot to understand about the role of multiple micro- organisms and their biofilms, in the pathogenesis of leprosy ulcers and whether addition of an anti -bacterial or an anti -fungal agent would help in better healing of leprosy ulcers.

7. Lockwood DN. Chronic aspects of leprosy—neglected but important. Transactions of The Royal Society of Tropical Medicine and Hygiene. 2019 Dec 1;113(12):813-7.

Nerve damage is caused by inflammation of affected nerves in leprosy. About 66% of multibacillary patients will develop

nerve damage. The peripheral nerve damage leaves people unable to feel and with weakness in their hands and feet. They are at risk of damaging their hands and feet, causing the disabilities and deformities. The WHO disability grading does provide a useful measure of disability. But a more sophisticated measure would be the EHF scoring- eye, hands and feet score. This scores the damage caused to the eye, hands and feet. Use of graded nylon monofilament to assess sensation is known. More work needs to be done to develop this as a screening tool in leprosy clinics. Assessing nerve damage and treating patients with steroids in leprosy programmes needs to be strengthened. The World Health Organization has a successful programme for supplying antibiotics for treating leprosy infection. They should take responsibility for providing steroids to national programmes since this is a core part of the treatment of neuritis says the paper by Lockwood DN.none of the problems with giving steroids would be the morbidity associated with the medication. Adding azathioprine to steroid treatment can improve the outcome. Patients with recent nerve damage improved better than the patients with chronic nerve damage. Effectiveness of methotrexate in erythema nodosum leprosum is on the track. Patients with neuropathic pain can be treated with amitriptyline, gabapentin if not alleviated by analgesics alone. The paper proposes that thalidomide should be made available more widely and steroids should be provided to national leprosy programs for optimal management of neuritis. But this would require keen monitoring of patients to observe for any adversities related to the medications per se.

8. Duthie MS, Pena MT, Ebenezer GJ, Gillis TP, Sharma R, Cunningham K, Polydefkis M, Maeda Y, Makino M, Truman RW, Reed SG. LepVax, a defined subunit vaccine that provides effective pre-exposure and post-exposure prophylaxis of M. leprae infection. npj Vaccines. 2018 Mar 28;3(1):1-9.

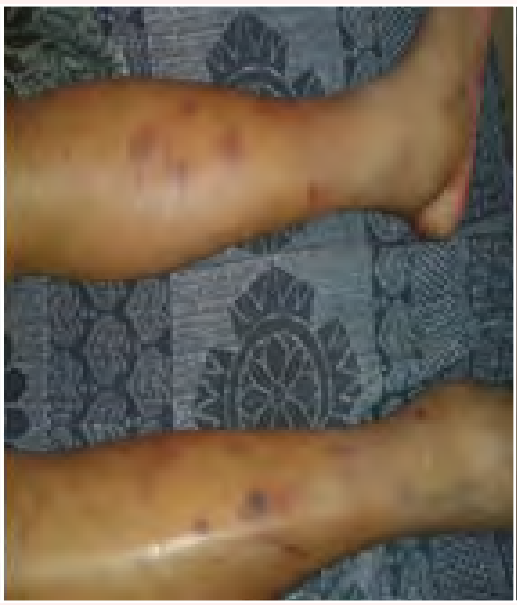
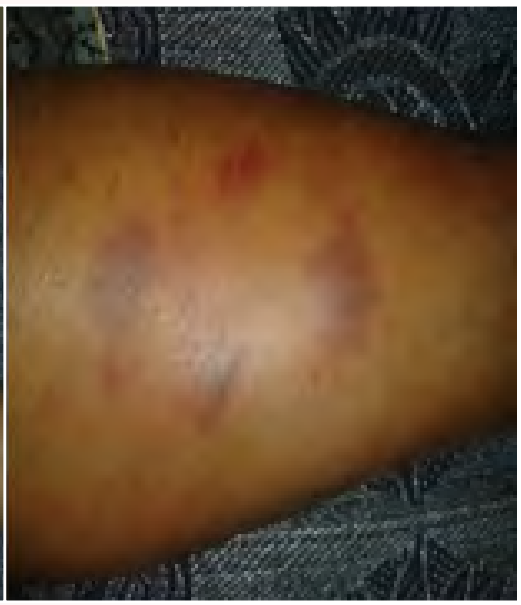
Unlike drug treatment , vaccines provide active and sustained protection by promoting immune memory response. Lepvax is a single chimeric fusion protein used in conjunction with approved Glucopyranosyl lipid adjuvant in stable emulsion. The trial on mice and armadillo gave conclusive evidence that when given prophylactically the vaccine reduced the M leprae outgrowth and in post exposure set up it is efficient against motor nerve damage. The role of the vaccine in providing beneficial protection to cutaneous nerves was evident. Advancement of lepvax vaccine to clinical testing appears prudent, with the potential to provide sustained, active protection to M leprae. Further research would reveal more regarding the role of vaccine in clinical set up.

A RARE CASE SCENARIO

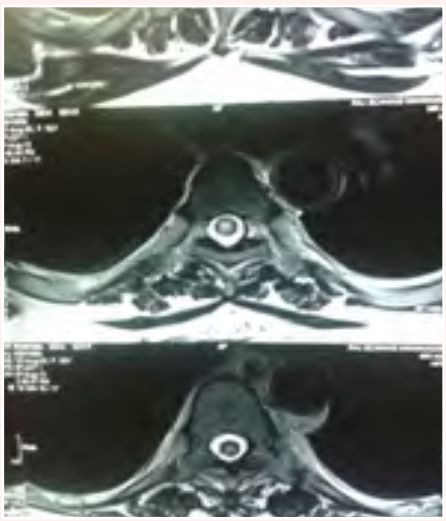
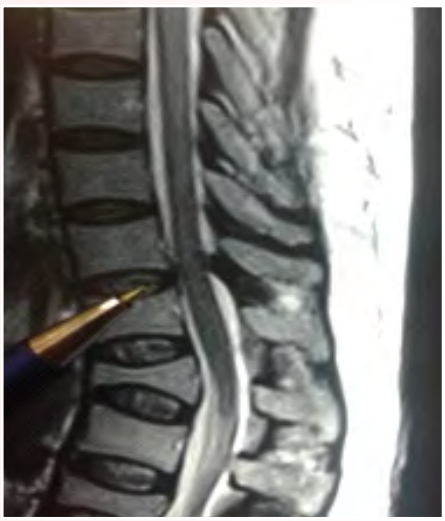
Acute transverse myelitis due to type 2 lepra reaction

Dr. Sunil Kumar Gupta
Associate Professor, AIIMS, Gorakhpur

A 50 years old lady was admitted in the hospital with multiple erythematous, tender nodule on both lower legs associated with intermittent high grade fever. On examination, bilaterally symmetrical diffuse infiltration of skin with gloves and stocking type anaesthesia was present. Peripheral cutaneous nerve trunks were not thickened. CBC, LFT, KFT were normal except mild neutrophilia. Blood sugar was normal and HBsAg, HIV & HCV negative. X-ray chest was normal. ANA and VDRL were negative. Slit skin smear from right ear lobule showed a BI of 5+. Biopsy from nodule revealed ENL.

After 2 days of admission, she developed sudden weakness of both lower limb. MRI was done which revealed altered signal intensity intramedullary area in dorsal cord at D3-D4 level. Cord edema was seen extending from C3 to D10. CSF examination was not done.

On the basis of above findings a diagnosis of Lepromatous Hansen with ENL and Acute Transverse Myelitis (due to reaction) was made. The patient was treated under multidisciplinary approach involving Dermatology, Medicine and Physical & medical rehabilitation departments. Oral prednisolone 40 mg was prescribed by the physician under strict vigilance with MBMDT. The steroid was tapered after 2 weeks when muscle power in lower limb started to recover. After one-month therapy patient had only mild muscle weakness and was discharged with advice of regular follow ups. Patient responded well to the treatment with MDT and steroids.

There is paucity of literature on leprosy and central nervous system involvement. However two interesting reports in which the first case had histopathological and molecular evidence for CNS involvement by leprosy in a living patient who had clinical features which mimicked a low grade glioma.[1] The second case report was about a 27-year-old Brazilian woman presented with a 7-month history of progressive pain, tingling, numbness, and weakness of the left upper limb, and paroxysmal dysesthesia affecting the left foot. On examination, there were erythematous, anesthetic patches of skin overlying the metacarpophalangeal joints and on the palmar surfaces of the hands. Skin biopsy showed hyperkeratotic and mildly hyperplastic epidermis with several well-defined non-necrotizing granulomas in the dermis. These were composed of epithelioid histiocytes, lymphocytes, and occasional Langhans giant cells. These were seen mainly in a perineural/periadnexal distribution but also involved the papillary dermis in an interstitial pattern. The MRI of the patient revealed expansion of the cervical cord with an intramedullary, enhancing area of high signal at C5-C7 and ganglionitis. The signal changes were most apparent on short T1-inversion recovery pulse sequences.[2]

On the basis of these reports and other evidence in literature, it is time that we should revisit the relationship between the Leprosy and the Central Nervous System.

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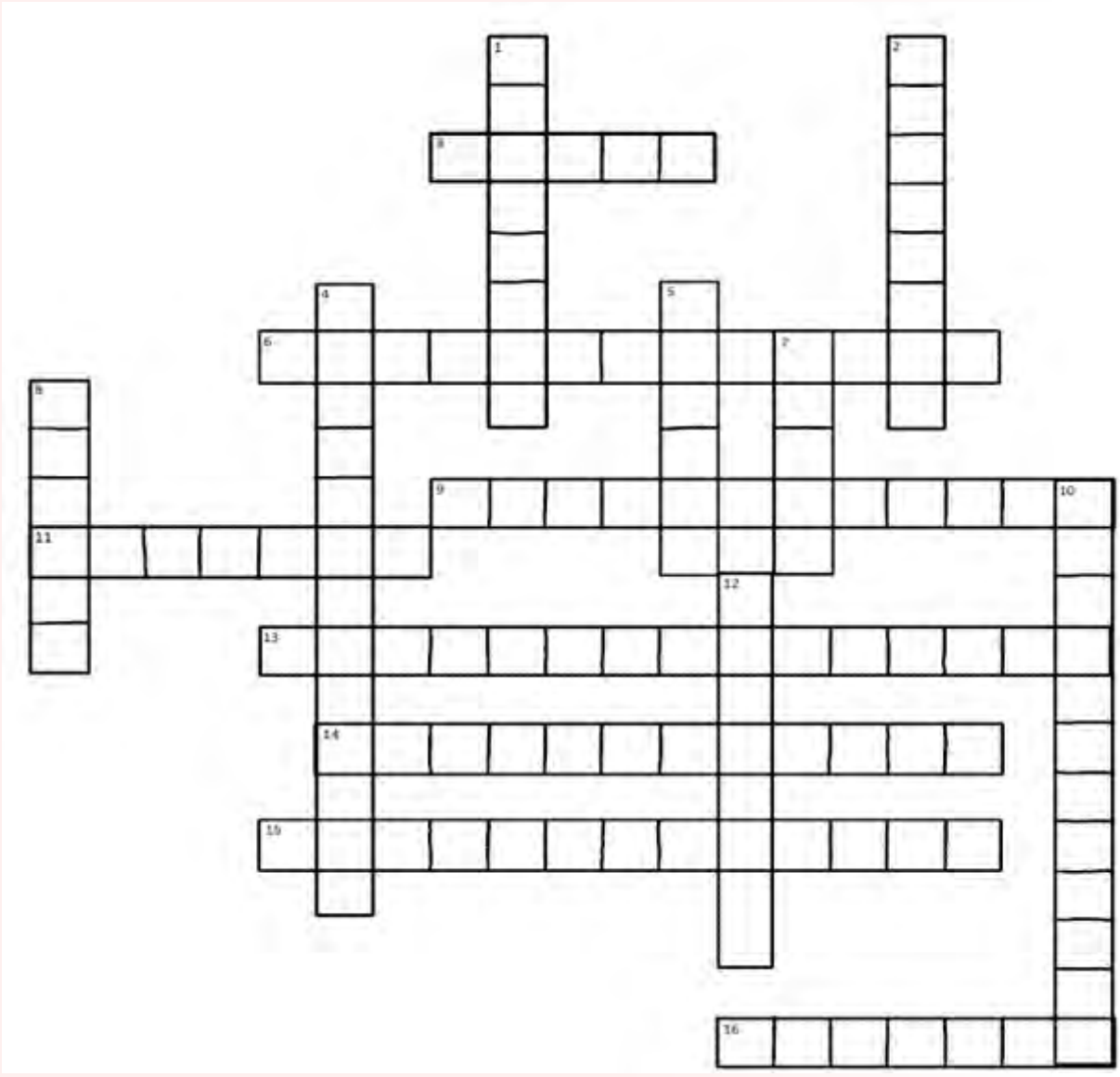
1. Lee KH, Moon KS, Yun SJ, Won YH, Lee JH, Lee MC, Jung S. Brain involvement by leprosy presenting as a frontal cystic lesion. J Neurosurg. 2014 Jul;121(1):184-8. doi: 10.3171/2014.1.JNS131429. Epub 2014 Feb 14. PMID: 24527821.

2. Rice CM, Oware A, Klepsch S, Wright B, Bhatt N, Renowden SA, et al. Leprous ganglionitis and myelitis. Neurology - Neuroimmunology Neuroinflammation. 2016;3(3):e236.

CROSSWORD ON LEPROSY: TICKLE YOUR NERVES

Dr. Varun Rajagopal S & Dr. Abhishek Bhardwaj
All India Institute of Medical Sciences, Jodhpur



DOWN

1
Sulphone pioneer, in leprosy

2
Ulcerating variant, courtesy an exaggerated type 1 reaction.

4
Swiss-cheese, seen in??

5
Oh Leprosy! Even you can be so attractive.

7
Pure and primitive form of leprosy with jagged, multiangulated purpura and ulcers

8
Without you, we would still be blaming Leprosy on the Gods.

10
Southern Indian plant that served as the source of an oil used to treat leprosy.

12
Grape like succulent, though on normal skin.

HORIZONTAL

3
Squeeze the wrist in a Leprosy patient, sign of wincing.

6
Arguably 'the' most famous duo in Leprosy.

9
It has a 36 in its name and the most Leprosy patients.

11
method in which 104 bacilli are inoculated in mouse foot pad to yield 106 after 5-6 months.

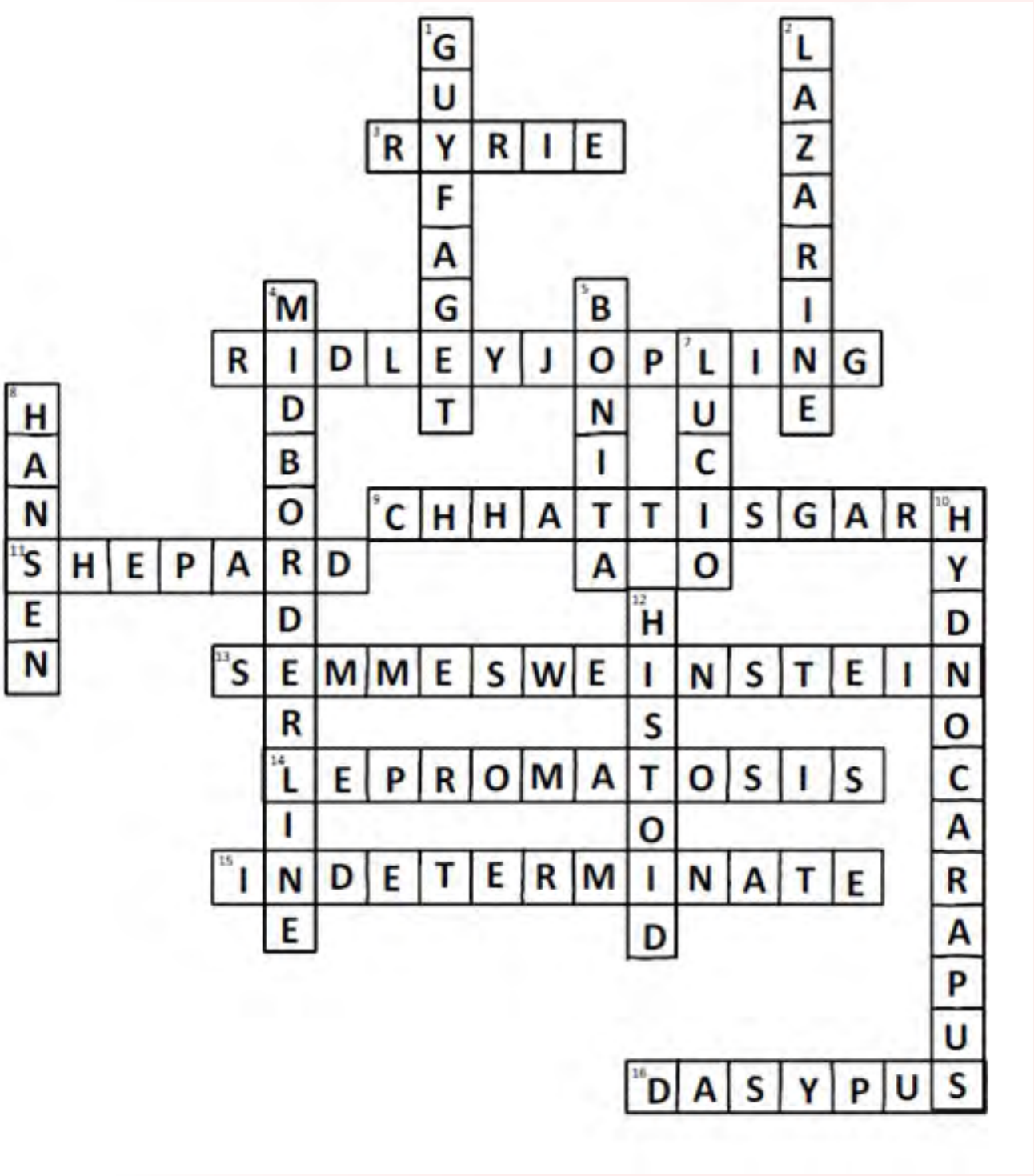
13
Ideal means of checking sensations.

14
The new kid on the block; as far as Mycobacterium is concerned.

15
So, what's that ill-defined, dry looking area on the cheek of the child of our Leprosy patient?

16
Want to study Leprosy, but not in humans? Look out for this guy.

SOLVED CROSSWORD



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