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NEURITIC LEPROSY

Leprosy is a chronic disease which mainly affects skin and nerves. The outcome of infection depends upon the cell mediated immunity (CMI) of the host. Individuals with adequate cellular immunity develop tuberculoid disease while those who lack this get lepromatous disease with varied system organ affection. In most instances, it has been considered that the skin is the primary site of invasion with secondary centripetal spread into the nerves, the pathology stopping short at the dorsal nerve root ganglion. However, in many individuals, the infection primarily affects the nerves with resultant initial lesion inside one or more of the nerves bundles. Thus, at least for some time, these patients have nerve involvement without obvious primary skin lesions. The type of disease where patients have clinical evidence of nerve deficit and involvement in the form of nerve thickening with or without tenderness but without signs of skin inflammation or historical evidence of having had a skin lesion is termed 'neuritic' or 'polyneuritic' leprosy.

The very existence of this form of leprosy has been debated by many workers in the field who were of the the view that these patients must have had initial skin lesion which over the years may have regressed. In recent years, there has been a rsurgence of interest in this type of disease since the number of these patients is not insignificant. Among the south Indian population, their proportion has been reported to be as high as one sixth of all leprosy patients with the number increasing with age[1]. Among the self reporting patients, workers from Bombay have reported that of the 11581 patients registered at Acworth Leprosy Hospital in 2 years, 4.3 per cent had neuritic leprosy[2]. In a retrospective study among army personnel 10.7 per cent of all patients with paucibacillary leprosy seen in an institution, were of neuritic type[3]. Though, there is a complete lack of epidemiological information from other centres or parts of the world, it is mentioned that pure neural leprosy occurs in under one per cent of black patients in Africa[4]. Clinic based observations at the Central JALMA Institute for Leprosy (CJIL), Agra, suggest that among the self-reporting cases, about 6 per cent patients have this type of disease (unpublished observations). A recent report also indicates occurrence of neuritic type of disease among experimentally infected monkeys[5].

It is, thus, clear that neuritic type of disease occurs frequently yet till recently these patients had not been studied in detail. Apart from a few case reports[6-8], published information is limited. Of the available reports, two are from south India[9,10], one from Bombay[11] and one from north India[12]. Whereas the studies from south India[9,10] and Bombay[11] have focussed on the classification and the diagnostic value of nerve histology in neuritic leprosy respectively, studies from CJIL, in addition have brought out the clinical and immunological profile of disease, determination of parameters, if any, that can indicate the severity of disease[12] and also the course of this type of leprosy under specific chemotherapy.

Division of Publication & Information, ICMR, New Delhi - 110 029

The first series studied in south India consisted of 17 patients with clinical evidence of neuritic leprosy[9]. Jacob and Mathai[10] in their work on diagnostic value of nerve biopsy in neuritic leprosy, studied 77 patients of peripheral neuropathy who did not have skin lesions, positive skin smears for acid fast bacilli (AFB) or skin histology consistent with leprosy. Researchers from Bombay[11] on the other hand had 12 selected patients with thickened nerves for their histopathological investigation. The CJIL study was on 108 consecutive untreated patients with neuritic leprosy, who in addition to having some evidence of nerve deficit, had definite nerve thickening of one or more nerves but no evidence of any skin lesion or history of any skin patch in the past[12].

The age range and sex distribution of patients with neuropathy in the above reports is shown in Table I. The findings clearly indicate that the disease affects males more than females and it is in the 20 to 40 years age group that the disease manifests more frequently.

Table I. Age range and sex distribution of patients with peripheral neuropathy

	Age (years)		Male	Female	Total
	Mean	Range			
Pannikar *et al*[9]	All adults		15	2	17
Uplekar and Antia[11]		15-55	11	1	12
*Jacob and Mathai[10]		16-60	57	20	77
Kaur *et al*[12]	37.19 ±11.3	8-65	102	6	108

*Several patients with peripheral neuropathy due to other causes also included.

Superscript numbers refer to the serial number in the list of references.

As with other types of leprosy, most of the patients remain asymptomatic and hence there is a tendency to ignore the sensory deficit. Thus, by the time the patient is detected in the field or reports to the clinic, a significant delay in time occurs. In the CJIL study, on untreated patients, the mean duration of illness, at the time of presentation was 29±31 months. Some patients, however, present much earlier, specially, if they have problems like nerve pain and/or suddenly appearing deformities which could be paralytic or secondary to sensory loss. It was observed by CJIL workers that 85 per cent patients presented with only sensory impairment. This loss of senory perception ranged from localized impairment to glove and stocking type of sensory deficit, similar to what is observed in other types of peripheral neuropathy. Symptoms in the form of abnormal sensations (paraesthesia), were the presenting features in a quarter of patients. Two patients of neuritic leprosy have been reported to present with initial symptoms of acute neurologic pain in the distribution of trigeminal nerve[13]. Eighteen per cent patients came with deformities, whereas only 5 per cent presented with pain in the nerve trunks. Several of the patients had more than one presenting symptom.

The extent and number of clinically involved nerves vary among neuritic patients. It is seen from Table II that in all the studies more than 40 per cent patients had thickening of only one nerve and almost 50 to 55 per cent of patients of neuritic leprosy had thickening of multiple nerves. In a significant proportion, this thickening of multiple nerves was symmetrical and was associated with peripheral sensory deficit.

Table II. Nerve involvement in patients with peripheral neuropathy

	Pannikar *et al*[9]	Uplekar and Antia[11]	Kaur *et al*[12]	Jacob and Mathai[10]
	No. of patients			
Only one nerve thickened	6	10	49	Mononeuritic multiplex 25
Multiple nerve thickening	7	2*	59**	Distal polyneuropathy 48
No nerve thickening	4	–	–	Motor neuropathy 5

*One patient had 2 and another multiple nerve thickening.

**Localized and asymmetrical in 42 and symmetrical in 17.

In all the reports, the ulnar and common peroneal were two most frequently affected nerves, similar to what is observed in patients across the leprosy spectrum. Though these are the nerves usually examined in patients, the problem is in the confirmation of diagnosis as biopsying these nerves is not without the hazard of causing motor deformities and/or increased sensory deficit.

One of the important features of neuritic leprosy is skin smear negativity. Response to lepromin has been studied with the aim of delineating the CMI status of these patients. In our series[12] using Dharmendra antigen, approximately 50 per cent of the patients showed positive response after 24 to 48 hours. A similar veriation was found in leucocyte migration inhibition test (LMIT) using Dharmendra antigen

sonicates. Both lepromin and LMIT response showed no correlation with the extent of disease as measured in terms of the number and distribution of affected nerves. Similar observations had earlier been reported with regard to lepromin response and *M. leprae* induced lymphocyte blastogenesis[14]. Three weeks response to Mitsuda antigen has also been studied. A higher positivity using this reagent has been found by some workers possibly becuase of a higher proportion of patients with single nerve affection[9,11].

Nerve conduction studies undertaken in neuritic patients, have shown that the affected nerves have abnormally slow conduction velocities and low compound motor action potentials, suggesting axonal degeneration, as has been observed in other sensory/motor neuropathies[4].

The most important investigation in patients with neuritic leprosy is the histology of the affected nerves. In all the studies where thickened nerves were taken for histological assessment, almost all patients showed definite evidence of leprosy; the entire leprosy spectrum having been observed in the nerves (Table III). It is seen from the table that a significant proportion of patients show

Table III. Nerve involvement in patients with neuritic leprosy

	No. of nerves biopsied	Leprosy confirmed	TT/BT	BB	BL/LL	I	Non-specific	AFB positive
Pannikar *et al*[9]	17*	11	–		6	–	5	10
Uplekar and Antia[11]	12†	12	9	3††				
Jacob and Mathai[10]	77**	38	10		10	7	11	18
Kaur *et al*[12]	39***	34	10		14	10	0	36

*Only radial cutaneous nerve biopsied.
†Affected nerves.
**Regional cutaneous nerves (whether thick or not) taken.
***Affected thickened cutaneous nerves biopsied.
††2 showed upgrading reaction.

lepromatous histology. Detailed analysis of results of the above studies revealed that even when patients have just one thickened nerve, finding of lepromatous morphology (BL/LL) in the nerve is not uncommon. In addition to these reports, lepromatous histology in nerve biopsies from pure neuritic patients has earlier also been reported[15]. Results of Uplekar and Antia[11] showed that in the majority, the histology was towards the tuberculoid pole. In this series 10 of the 12 patients had only one affected nerve.

More significant is the observation of finding of AFB in the nerves in practically all patients of neuritic disease. The bacilli were found in large numbers in almost half the patients. In contrast, none of the skin biopsies taken from areas with sensory deficit showed any histological abnormalities and presence of AFB.

All the available reports thus, indicate that in a very large proportion of patients with thickened nerves, the diagnosis of leprosy can be confirmed if nerve biopsy is done. Conversely, it is also evident that there is a fair amount of certainty in diagnosis of leprosy on the basis of the neural deficit together with clinical thickening of nerve. CJIL figures show that of 39 nerve biopsies taken, 34 had unequivocal evidence and classifiable leprosy within the nerve[12]. Of the remaining 5, two showed AFB despite the absence of specific infiltrate again suggestive of leprous infection. In only 3 was the histology normal in spite of the nerves being thick. Even here, it is possible that either the site chosen was not proper or the affected fasicles were missed. Similar concurrence has been reported between clinical findings and histology by others also[9-11].

To find whether clinically observed differences in the number and distribution of nerve involvement, symptomatology and/or immune status of patients give any indication of underlying severity or spectral classification the data were analysed accordingly. The CJIL findings (Table IV) reveal that no parameter other than histology helps in grading the severity of these patients because even

Table IV. Clinical vs histological classification of patients with neuritic leprosy

		CLASSIFICATION			
Group	No. of patients biopsied	I	TT/BT	BL/LL	Normal/ Regressed
I	14	5	3	6	3(2*)
II	13	2	5	3	0
III	5	1	1	2	1
IV	7	2	1	3	1

Groups indicate number of nerves affected and their distribution. I–only one nerve thickened, II–two or more nerves thickened but localized to one part. III–two or more nerves thickened, distant but asymmetrical. IV–multiple and symmetrical nerve thickening.

*Occasional AFB present but without any tissue reaction.

AFB content–few in 12, several in 10 and numerous in 14.

when only one nerve was thickened, 40 per cent patients had BL/LL histology with several having fair amount of bacteria. The converse was also seen. In patients with thickening of multiple symmetrically placed nerves, indeterminate or TT/BT histology was not uncommon and so was lepromin and/or LMIT positivity. Thus, in the absence of any clear clinical criteria to split this group into pauci- and multibacillary categories, it seems appropriate to maintain the neuritic type as a separate entity for purposes of management.

In the National Leprosy Eradication Programme, patients belonging to this class of leprosy have been included in the paucibacillary group based on the observations that all these patients are skin smear negative, many are lepromin (Mitsuda) positive and in several earlier case reports, nerve histology showed tuberculoid picture[6,7]. However, it may be more appropriate to include these patients in the multibacillary group rather than group them with paucibacillary patients as more than 90 per cent of patients with neuritic leprosy have demonstrable bacilli. Further, more than half the patients have significant bacterial load as revealed in the biopsy sections. An argument against this could be that even though bacilli are seen in the nerve biopsies, the total number of organisms within the whole body may still be small. But with the revised definition of paucibacillary leprosy[16] it is to be seen whether neuritic patients have a total load less than that in 1+ or 2+ positive patients. An earlier work in this regard may also be significant, wherin it has been shown that distant uninvolved nerves, too, show evidence of disease[17].

Follow up studies have also been done to assess the course of these patients under treatment. In the study by Pannikar *et al*[9], 4 of 17 patients under a two year follow up showed skin lesions. These lesions were clinically classified as tuberculoid and borderline tuberculoid type, although 2 of them had been classified as BL and 2 as indeterminate on nerve histology. Two of the 12 patients in the series reported by Uplekar and Antia[11] likewise developed skin lesions after 3 and 3 1/2 months of MDT. Observations of workers at the CJIL, Agra, on a series of another 40 patients observed for over 3 and a half years indicate that about 35 per cent of neuritic patients develop skin lesions of mostly BT leprosy (unpublished observations). Further, in the CJIL study on evolution of disease, it has been found that almost two-thirds of patients with suspicious disease pass through a short lived phase of neuritic disease before developing skin manifestations[18]. Talwar *et al*[3] also came across 8 patients (among 62) who after 2.6 to 3 months of the start of treatment developed cutaneous lesions. In 7 patients the lesions were I, TT or BT while one had BL leprosy. In addition, few other case reports[1,19] of similar transition are also available in literature. A possible explanation for this could be that under specific treatment, some patients undergo reversal reactions and shift towards the tuberculoid pole, in the process any skin site which has the, antigen develops the lesions.

In conclusion, neuritic leprosy which is a defined type of leprosy occurs in a significant proportion of patients and in some patients evolves into typical spectral disease. There is a need to critically review the subjects from treatment point of view as these patients have a rather large but hidden load of bacilli, irrespective of the fact whether there is one or multiple nerve affection.

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85TH ANNIVERSARY CELEBRATIONS OF ICMR

AIDS was the theme selected for the dissemination of scientific information in the month of December, 1995.

All the Bombay-based ICMR Institutes/Centres *viz*, the Institute for Research in Reproduction, the Institute of Immunohaematology, Enterovirus Research Centre and the ICMR Genetic Research Centre jointly organised an awareness programme on AIDS at the Haffkine Institute, Bombay on December 22, 1995. The programme included a talk on "Shared Rights and Shared Responsibilities by Dr. J.J. Rodrigues, screening of video films and a poster exhibition on the subject. College students and staff of Haffkine Institute as well as the staff of all the four ICMR Institutes participated in the programme.

The National Institute of Cholera & Enteric Diseases, Calcutta, in collaboration with the ICMR Unit for Research on AIDS in North-Eastern States of India, organized an open house on December 29, 1995 highlighting the activities of ICMR in the field of AIDS. Doctors and students from various medical colleges and nursing staff from the Infectious Diseases Hospital, Calcutta, participated in the programme. Lectures/discussions were followed by an exhibition on different aspects of AIDS and screening of video films.

The Central Jalma Institute for Leprosy, Agra, organised an AIDS awareness camp in the Sadar Bazar of Agra on December 20 and 21, 1995. An open day was also organised in RBS Degree College, Agra, on December 22, 1995 for creating awareness regarding AIDS.

The Vector Control Research Centre, Pondicherry, organized a lecture on AIDS by Dr. Venkateswaralu, Project Director, AIDS Cell, Pondicherry on December 8, 1995 for the benefit of the VCRC staff. Another lecture by Dr. Raghavan, Chief of the District AIDS Cell, Allepey was arranged on December 27, 1995 for the members of the Bhagat Singh Arts and Sports Club Omkareswaram, Shertalli. Screening of a video film on AIDS was organized at the Tagore Arts College, Pondicherry on December 12, 1995.

At Pune, the National AIDS Research Institute (NARI) organised several awareness programmes on AIDS. Dr. J.J. Rodrigues, Director-in-Charge, NARI, delivered a talk on "Shared Rights and Shared Responsibilities" on December 1, 1995 which was followed by screening of a video film entitled "Karate Khiladi". The Institute put up an exhibition at Shree Ganesh Kala Krida Rangmanch on December 1, 1995. The Institute also organised an exhibition and a talk on "HIV-1 Subtype Identification by Heteroplex Analysis" by Dr. D.A. Gadkari, Dy. Director, at the Poona University on December 27, 1995, and a talk on "Paediatric AIDS" by Dr. Mridula Phadke, Dean, B.J. Medical College, Pune, at the Lokamanya Hospital, Chinchwad, Pune on December 28, 1995. A poster competition was also organized by the Institute on the topic "Impact of HIV on the Society".

The National Institute of Nutrition, Hyderabad, organized a lecture on "Social Aspects of AIDS" in December, 1995.

Institute of Cytology and Preventive Oncology, New Delhi, organized a lecture on "Pathological and Microbiological Aspects of AIDS and its Laboratory Diagnosis" by Dr. Shobha Broor, Addl. Professor, Dept. of Microbiology, All India Institute of Medical Sciences, New Delhi on December 18, 1995.

The Institute of Pathology, New Delhi, organized a lecture on "AIDS : National and International Scenario" by Dr. Sudershan Kumari from the South-East Asia office of the WHO, New Delhi on February 9, 1996.

The Rajendra Memorial Research Institute of Medical Sciences, Patna, organized a symposium on AIDS on December 19, 1995. This was followed by a debate and quiz competition for school children.

CJIL Field Unit at Avadi, Madras, organised an AIDS awareness programme for general public in Somangalam town of Sriperumbudhur taluk of Chengai–MGR district on January 4, 1996. Audio and video programmes were also screened for the benefit of the public.

The Regional Medical Research Centre for Tribals, Jabalpur, organized AIDS awareness programmes at Govt. Medical College, Mahakaushal Arts College, Mankuwarbai Women's College and Home Science College of Womens, Jabalpur on December 1, 7, 8 & 11, 1995 respectively. The programmes included talks, question-answer sessions and screening of video films.

The Desert Medicine Research Centre, Jodhpur organized an open house on AIDS awareness and prevention at the premises of the Jodhpur Truck Union in Basani Phase-I area of Jodhpur on December 15, 1995.

ICMR NEWS

The 51st meeting of the Scientific Advisory Board of the ICMR was held on January 30-31, 1996, at the ICMR Headquarters, New Delhi.

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Meetings of the Expert Group/Scientific Advisory Committee held at New Delhi.

Expert Group on Otolaryngology	January 29, 1996
Scientific Advisory Committee of the ICMR-NIC Centre for Biomedical Information, New Delhi.	February 6, 1996

Participation of ICMR Scientists in Scientific Events:

Dr. S.K. Subbarao, Dy. Director, Malaria Research Centre, Delhi, participated in a Task Force meeting on Malaria Vector Control Research in Africa at Nairobi (February 4-8, 1996)

Dr. S.P. Pani, Dy. Director, Vector Control Research Centre (VCRC), Pondicherry, participated in the III meeting of the WHO Steering Committee of the Applied Field Research on Tropical Diseases at Geneva (February 5-9, 1996).

Dr. S.P. Pani and Dr. P.K. Das, Dy. Director (Senior Grade), VCRC, Pondicherry, participated in the consultative meeting on the Application of Modelling to Control Strategies in Lymphatic Filariasis at Geneva (February 14-16, 1996).

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The Indian Council of Medical Research participated in the 12th World Book Fair held at New Delhi (February 3-11, 1996).

ICMR AIDED SYMPOSIA/SEMINARS/WORKSHOPS/COURSES/CONFERENCES

Symposium/Seminar/Workshop/ Course/Conference	Date & Place	Contact Address
Symposium on Casava in Nutrition and Health.	February 10-11, 1996; (at Thiruvananta-puram)	Dr. K. T. Shenoy, Organising Secretary of the Symposium, Department of Gastroenterology, Medical College, Thiruvanantapuram.
XI National Pain Conference and III International Palliative Care Conference.	February 11-14, 1996; (at Cuttack)	Dr. S. Nayak, Organising Secretary of the Conference, Acharya Harihar Regional Cancer Centre, Cuttack.
National Symposium on Molecular and Cellular Biophysics.	February 18-21, 1996; (at New Delhi)	Dr. V. Kothekar, Convenor of the Symposium, Department of Biophysics, All India Institute of Medical Sciences, New Delhi.
V National Conference of Biomechanics.	February 22-24, 1996; (at Madras)	Dr. S. Radhakrishna, Organising Secretary of 5NCB, Department of Applied Mechanics, Indian Institute of Technology, Madras.
Internationl Conference on Current Status and Challenges in Medical and Veterinary Microbiological Research particularly in Third World Countries.	February 26-28; 1996; (at Jabalpur)	Prof. S.M. Singh, Organising Secretary of the Conference, Department of Biological Sciences, R.D. University, Jabalpur.
Symposium on Schizophrenia: The Indian Scene	March 22-23; 1996; (at Chandigarh)	Dr. P. Kulhara, Additional Professor, Department of Psychiatry, Postgraduate Institute of Medical Education and Research, Chandigarh.

COUNCIL'S TRAINING PROGRAMMES FOR 1996-97

Leprosy

At the Central Jalma Institute for Leprosy, Agra:

- Multidrug Therapy Orientation Course in Leprosy for Medical Officers (March 11–22, September 9–20, 1996).

Virology

At the National Institute of Virology, Pune:

- Diploma in Medical Virology (June 1996–May 1997).

Reproductive Biology

At the Institute for Research in Reproduction, Bombay:

- Training Course on Immunoassay Techniques (June 3–15, 1996).
- Training Course on Current Trends in Management of Infertility and Reproductive Disorders (September 2–13, 1996).

Endocrinology

At the National Institute of Nutrition, Hyderabad:

- Annual Training Course on Endocrinological Techniques and their Applications (August 1, 1996–September 15, 1996).

Nutrition

At the National Institute of Nutrition, Hyderabad:

- M.Sc. in Applied Nutrition (June 1, 1996–February 28, 1997).
- Annual Training Course in Nutrition (December 1, 1996–February 28, 1997).

Medical Entomology

At the Vector Control Research Centre, Pondicherry:

- M.Sc. in Medical Entomology (from August 1996; for 2 years).

Laboratory Animal Technology

At the National Centre for Laboratory Animal Science, National Institute of Nutrition, Hyderabad:

- Training Course for Laboratory Animal Technicians (June 15–July 31, 1996).
- Training Course for Laboratory Animal Supervisors (September 1–November 30, 1996.

Haematology

At the Institute of Immunohaematology, Bombay:

- Training Course in Transfusion Medicine for Blood Bank Medical Officers (August 5–October 4, 1996).
- Training Course in Blood Group Serology and Blood Bank Methodology for Technicians (August 5–September 4, 1996).
- Training Course in Advanced Haematology and Immunohaematology (September 17–October 4, 1996).

Biostatistical Techniques

At the Institute for Research in Medical Statistics, Madras:

- Training Course for Doctors in Biostatistical Techniques in Controlled Clinical Trials (March 4–15, 1996).

INDIAN COUNCIL OF MEDICAL RESEARCH

Grant-in-aid for organising Seminars/Symposia/Workshops

The Council provides partial financial assistance for organising Seminars/Symposia/Workshops. Applications for grant of financial assistance (complete in all respects in the prescribed proforma), will be considered only if furnished **at least four months before the date of commencement of the Seminar/Symposium/Workshop,** *etc.*

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