AMBADY ORATION 1982

Challenges in Leprosy - A Clinician's Overview—Delivered by Dr. Rachel Mathai at the X Annual Conference of IADVL at Hyderabad on 5—1—82

Thank you Mr.Chairman for the very kind words. I am indeed most grateful to you.

What I wish to say is the old saying again. But, repeat it as often as one needs to, listen to it as often as one has to; it neither gets stale nor does it sound improper. My predecessors on similar occasions have said it and I say it again because, I believe 'words have meaning'.

I deemit indeed a very great privilege to have been asked to deliver the oration which bears the name of Dr. Bhaskara Menon Ambady. Perhaps to a large section of the audience in this hall, B. M. Ambady is just another name. Let me therefore introduce him to you briefly.

A graduate of the Madras Medical College, Dr. Ambady took specialist's training abroad. He headed the department of Dermatology and Venereology of the Trivandrum Medical College for several years. A founder member of the Indian Association of Dermatologists and Venereologists, he was later elected as President of the Association. He had a number of publications to his credit in both dermatology and venereology. He not only excelled himself in his professional field, but had many other areas of interest. To name a few; at Trivandrum he was Vice-President of the Foot Ball Association, President of the Weight Lifters' and Wrestler's Association and President of the Lion's Club.

And this is what they say about him.

For myself, I have two distinct memories of Dr. Ambady. I was less than a beginner when I first met him, and he a pillar of the association. We journeyed from Patna to Madras via Calcutta. I met him at Calcutta where both he and I were left unsure of our onward reservation. We eventually boarded the train, Dr. Ambady's compartment far behind mine, which I had to share with 2 other gentlemen. At every station where the train halted, Dr. Ambady got off to check on my comfort and what more? my safety. Something only my father would have done under similar circumstances.

I next met Dr. Ambady in 1975. He was the hero of the success story of that year's annual conference held at Trivandrum, his home town. Many others might have worked very hard behind the spot light to make that conference what it was. But without Dr. Ambady's welcome smiles and pervading spirit that conference would have lacked its charms.

I am left with the revered memory of a man, gentle, kindly, fatherly and unassuming but above all, a great soul.

For this year's Ambady oration I have chosen Leprosy as the subject. "Leprosy — A Clinician's overview". Primarily a dermatologist with the background training of an internist, I am not a leprologist in the true sense of the word. What then are my claims to speak on this subject?

In the department of Dermatology and Venereology of the Christian Medical College Hospital at Vellore, where I have the privilege of working for almost 2 decades, 10% of the clinical material relates to leprosy.

I am faced with questions related to widely varying aspects of leprosy – epidemiological, immunological, diagnostic and therapeutic — for which I still have found no answers.

Leprosy counselling has become part of my professional commitment. I find myself a counsellor on schooling, marriage, child bearing, divorce, remarriage, career and so on. To play this role effectively I need to find specific answers in the various epidemiological aspects related to all these situations and much more. Answers are not available in books because the books do not necessarily deal with our population with its own specific environment. We have to find our own answers and so we begin to search.

I boast myself of nothing but being a clinical investigator; dealing with living people and handling unsettled questions.

The challenges of medical science, and its charms will remain as long as these quesitons remain and answers are to be found.

I want to speak this morning on certain aspects of leprosy wherein we faced these challenges and answers were found.

Our leprosy work is carried out in a general hospital set-up where no special isolation is practised for leprosy patients. In such a situation, infection can spread from leprosy patients to nonleprosy patients and from leprosy patients to hospital personnel.

What are the risks of treating leprosy in a general hospital?

The question was tackled by analysing the cases of leprosy discovered among the staff and students of The Christian Medical College Hospital who are drawn from various States in the country. 85% of staff and 34% of students belong to Tamil Nadu where the institution is situated. All students and large majority of the doctors and nurses live within the instiiution campus. Every employee and student is screened prior to entry into the institution and thereafter subjected to routine annual examination. Of those who at initial screening had no evidence of leprosy, 24 acquired the disease. This attack rate of 0.5% is significantly lower than the incidence or prevalence of leprosy in the area. Our answer to the question is that staff and students serving in a general hospital where leprosy is also practised on par with all other infectious diseases, the risks of contracting leprosy is no more than the risk in the general population for our area.

I go on to another aspect of leprosy that we have been able to study.

Immunology was in its infancy in the 1940s, when dapsone was first introduced as a therapeutic agent for leprosy. Consequently the pathogenesis of erythema nodosum leprosum (ENL) was ill-understood at that time and the management of ENL–to say the least–was messed up for a very long time. For almost 2 decades after the advent of dapsone it was widely believed that this drug was the major incriminating factor in the precipitation as well as persistence of chronic ENL reactions. The natural result of such a widely held view was, that patients with chronic ENLs did not receive dapsone for long periods. The situation was both unfortunate and alarming at a time

when dapsone was the only satisfactory drug available for treatment of the disease.

Bugged with the problem, we set out on a careful retrospective study of patients with chronic ENLs with specific reference to the role or otherwise of dapsone in the causation of ENLs. We reviewed our first series of 47 cases in 1966. The result of that study convinced us that ENLs are neither precipitated nor worsened by dapsone. In about 40% of our patients with chronic ENLs the first episodes were either before starting treatment with dapsone or more than 6 months after a patient had discontinued therapy. Over 10 years ago when these findings were presented to a group of specialists, these were promptly rejected by most, and declared to be a suicidal proclamation by some. Clinical findings, however, have to be reckoned with. Many later workers have been since then able to agree with our findings on the basis of their own observations. Today immunology has advanced to the stage where the pathogenesis of ENLs is clearly understood. A sound clinical observation made years earlier had been supported by sound immunological facts.

Leprosy has posed no less a challenge on the diagnostic front.

To the experienced and observant clinician, leprosy can be the most obvious of diagnosis in the vast majority of patients who suffer from it. The combination of skin and peripheral nervous system involvement is the hall mark of the disease. Leprosy can unfortunately be, though rarely, the most subtle diagnosis when it presents symptoms common with other diseases. One of these symptoms is peripheral neuropathy. We have been intrigued and interested in the problem of leprosy presenting as a pure peripheral neuropathy.

Peripheral neuropathy (PN) is the term used to describe a variety of conditions with different etiology and pathology but having a clinical similarity. The similarity of the clinical picture is the impairement of function of multiple nerves, the signs of which are most marked peripherally.

The causes of peripheral neuropathy are multifarious.

Table 1 gives a broad etiological classification of peripheral neuropathies that have been seen in our clinic either as a diagnostic problem or because of a complication related to secondary skin changes. The most common condition in this group is undoubtedly leprosy.

TABLE 1

Causes of Peripheral Neuropathy

1. Infections : Acute
   Chronic – Leprosy
   Syphilis
2. Metabolic Disorders :
   Diabetes Mellitus
   Uremia
   Porphyrias
   Refsum's Disease
3. Hereditary and Familial Disorders :
   Hereditary Sensory Neuropathies and Variants
   Peroneal Muscular Atrophy and Variants
   Hypertrophic Interstitial Neuritis
4. Toxic and Allergic :
   Drugs – Alcohol
   INAH
   Metals Lead
5. Diseases of Spine and Spinal Cord :
   Canal Occlusion
6. Collagen Vascular Disorders :
   Polyarteritis Nodosa
   Root Compression
7. Nutritional Deficiencies :
   Anemias, Avitaminosis
8. Malignancies
9. Miscellaneous – Sarcoidosis
10. Idiopathic

I wish to share and discuss in detail some of our findings related to 68 patients who presented with PN of undetermined etiology. They were investigated primarily with the aim of confirming or ruling out the possibility of leprosy.

Table 2 shows the age and sex distribution of the 68 patients. The youngest patient was 12 years old and the oldest 65 years. The 0-15 group was least represented. Maximum number of patients constituting 36.7% belonged to the 41 – 60 year group. There were 54 males and 14 females giving a male: female ratio of 3.8 : 1.

TABLE 2
Age and sex distribution in 68 patients

Age in years	Number Male	Female	Total	Percentage
0-15	2	0	2	2.6
16-30	18	3	21	30.8
31-40	12	4	16	23.5
41-60	19	6	25	36.7
61 and above	3	1	4	5.8
Total	54	14	68	99.4

After a detailed history and clinical examination, all patients were subjected to conventional screening tests for leprosy. These constituted skin smears for AFB from 4 upto 13 sites and skin biopsies in those who showed skin changes even remotely suspicious of leprosy. All patients yielded negative results. Routine laboratory tests like hemoglobin, leukocyte counts, urine and stools also gave normal values in all patients. Additional tests were then performed.

Table 3 shows the type of tests done, the number of patients in whom these were carried out and the results of the test. As is evident, all patients were not subjected to the same battery of tests. The choice of tests for each patient depended on the history and findings at clinical examination. For example, blood sugars were estimated in the older age group more prone to have diabetes mellitus.

TABLE 3
Additional laboratory tests

Tests	No.	Normal	Abnormal
GTT Blood Sugar	32	27	5
Blood VDRL	15	14	1
EMG/Nerve conduction velocity	8	4	4
X-Ray spine	5	3	2
Collagen work-up	5	5	—
Porphyrins	2	2	—
CXR	3	3	—
CSF	3	3	—
B. Marrow	1	1	—

Among 32 patients checked for diabetes mellitus 27 gave normal values and 5 abnormal. Blood VDRL was done in 15 patients and was normal in 14. EMG and nerve conduction velocities were done where clinical pattern of PN suggested nerve trunk involvement. Among 8 patients, 4 had normal and 4 abnormal results. X-ray spine was done where a nerve root involvement had to be ruled out. Among 5 patients, 2 gave abnormal results. Collagen work-up, porphyrin estimations, Chest X-ray, CSF examination and bone marrow gave normal results.

Various clinical forms of PN are recognised. These are broadly classified into 3 groups namely pure motor neuropathy, mononeuritis multiplex and distal polyneuropathy. Cases with motor involvement without affection of sensory modalities are classified under pure motor neuropathy. Where neurological deficit pattern indicates involvement of one or more peripheral nerves at the level of the nerve trunks, the neuropathy is classified under mononeuritis multiplex. In these, all modalities of function are impaired, namely, autonomic, sensory and motor. Cases classified as distal PN belong to a heterogenous group. These may have

bilateral and symmetrical loss of sensation in upper and/or lower extremities or patchy distal areas of sensory loss with and without distal muscle palsies. Table 4 shows the number of cases with the various types of PN and the correlation between the clinical types and diagnosis in relation to leprosy.

TABLE 4
Correlation between types of P. N. and Diagnosis in relation to leprosy

Types	Patients No.	%	H. D. No.	%	Non H. D. No.	%
Pure motor Neuropathy	1	(1.4)	0	(0)	1	(100)
Mononeuritis Multiplex	24	(35.2)	9	(37.5)	15	(62.5)
Distal Polyneuropathy	43	(63.1)	31	(72.2)	12	(27.8)
Glove and stocking anesthesia	28					
Patchy sensory deficit	9	43				
Sensory-motor deficit	6					
Total	68		40		28	

Among the 68 patients, one had pure motor neuropathy who on investigation gave no evidence of leprosy. 24 patients had mononeuritis multiplex. Of these 9 (37.5%) were proved to have leprosy and 15 (62.5%) gave no evidence of the disease. 43 (63.1%) patients had distal polyneuropathy. 28 had glove and stocking type of anesthesia, 9 had pure patchy sensory loss and 6 had both sensory and motor involvement in a distal distribution. Among these 43, 31 (72.2%) were proved to have leprosy and 12 (27.8%) showed no evidence of the disease.

Keeping in mind the possibility that 2 common conditions both capable of causing PN can coexist; even when positive evidence of one disease was obtained on the basis of tests performed, it was felt that a cutaneous nerve biopsy may give additional useful information.

Indications for nerve biopsy is presented in Table 5. The 68 patients investigated with nerve biopsy could be divided into 3 categories.

TABLE 5
Indications for Nerve Biopsy

Indications	No. of cases
Peripheral Neuropathy (PN) without Hypopigmented patches	55
P.N. with Hypopigmented patches showing non-specific H/P	8
Treated Leprosy with progressive Neuro deficit	5
Total	68

Patients with PN which was not associated with any hypopigmented patch. There were 55 such patients.

Patients in whom PN and hypopigmented patches were both present but skin biopsy from the patch gave non-specific picture. There were 8 such patients.

Patients with known leprosy had taken antileprosy treatment elsewhere in the past. They presented to the clinic because of progressive neurological deficit of recent origin. There were 5 such patients.

Table 6 indicates sites of biopsy. Biopsy sites depended on the sites of neurological deficit. Where both glove and stocking anesthesia was present, radial cutaneous nerve was biopsied. Where legs and feet were the sites of neurological deficit cutaneous branch of the CPN or sural cutaneous nerve was biopsied. Sliver biopsy of ulnar nerves at the elbow was performed on 2 patients. Multiple nerve biopsies had to be done in 3 patients where result on one nerve was inconclusive.

A total of 72 biopsies were done on 68 patients.

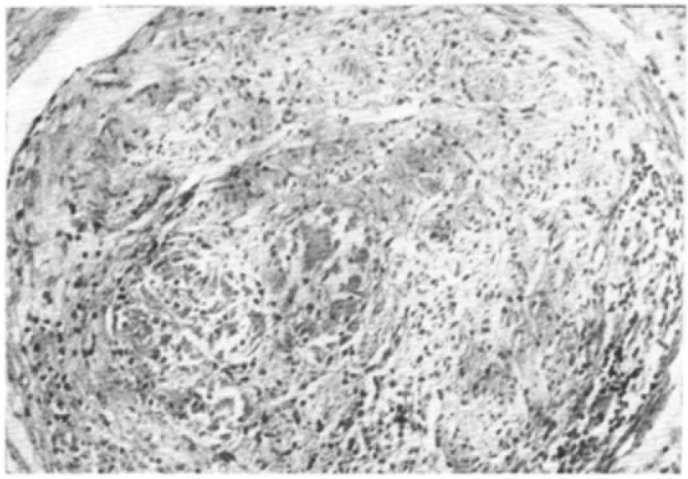

Fig. 1
Nerve showing tuberculoid pathology with collections of epithelioid cells and giant cells

TABLE 6
Biopsy Sites

Nerve	Number
Cutaneous branch-Radial nerve	26
Cutaneous branch-CPN	34
Cutaneous branch-Sural nerve	10
Ulnar nerve-At elbow	2
Total	72

Multiple nerve biopsies were done in some patients.

Histological changes in nerves in 68 patients are shown in Table 7.

4 nerves showed changes consistent with that of tuberculoid leprosy. Fig (1). These had collections of eipthelioid cells and giant cells, 11 nerves which showed features of borderline leprosy represented the full spectrum of the disease from borderline tuberculoid to borderline leproma. (Fig. 2 & 3). 8 patients had nerves showing lymphocytic infiltration. (Fig. 4) and many AFB (Fig. 5). In 16 patients nerves showed minimal to moderate lymphocytic infiltration. One patient was reported to have nonspecific neuritis where scattered lymphocytes were present intraneurally. 14 patients showed degenerative changes in the nerves reported as demyelination, hyalinisation and axonal degeneration in varying combination of severity (Fig.6). No significant lesion was reported in 11 patients. In 3 patients biopsies were inadequate.

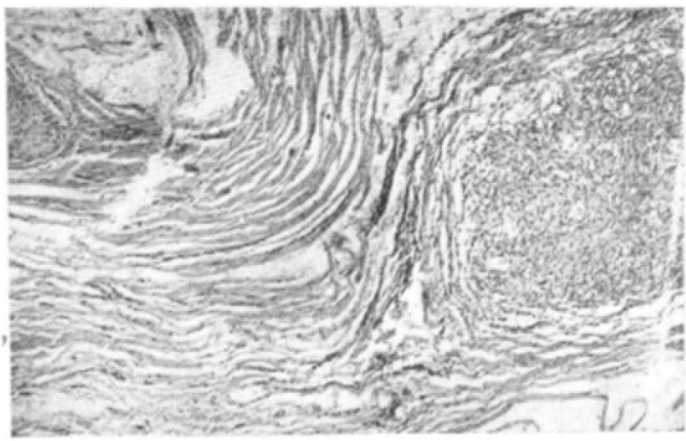

Fig. 2
Nerve showing features of borderline leprosy low magnification

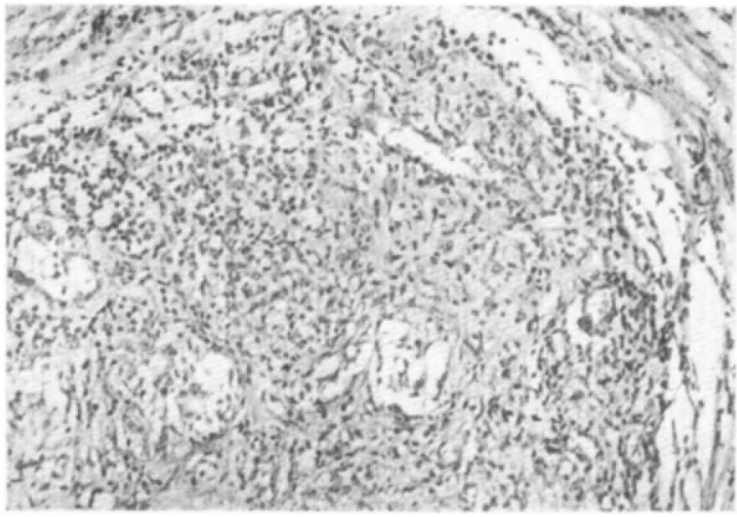

Fig. 3 Nerve showing features of borderline leprosy. Foam cells and epithelioid cells are seen (High magnification)

TABLE 7
H/P Changes in nerves in 68 patients

H/P	Number
Tuberculoid Leprosy	4
Borderline Leprosy	11
Lepromatous Leprosy	8
Leprous Neuritis	16
Non-Specific Neuritis	1
Demyelination, Hyalinisation and Axonal Degeneration	14
No significant lesion	11
Inadequate Biopsy	3
Total	68

Table 8 shows the demonstration of AFB from various sites tested. Skin smears done from 4 sites upto 13 sites in all 68 patients yielded negative results. It was particularly interesting to note that in 2 of these smears from finger tips were also negative. In 11 patients, skin biopsies were done. Histological section stained for AFB gave negative results in all except one patient. In contrast, AFB in small or large numbers were detected in nerves in 19 patients.

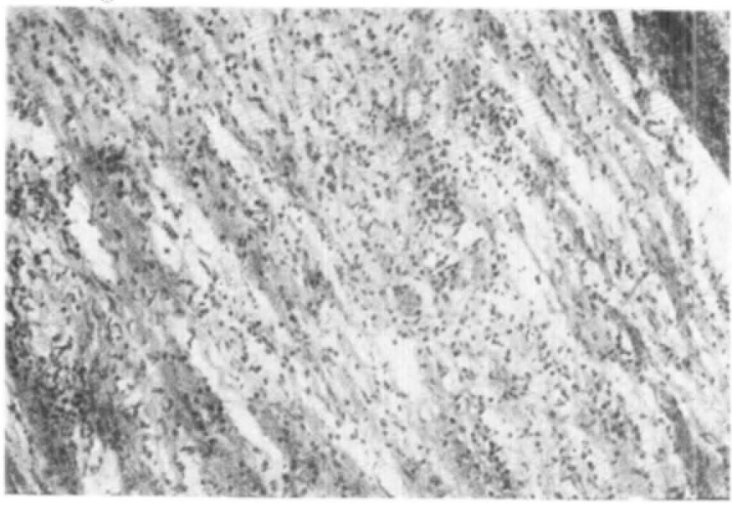

Fig. 4
Nerve showing lymphocytic infiltration

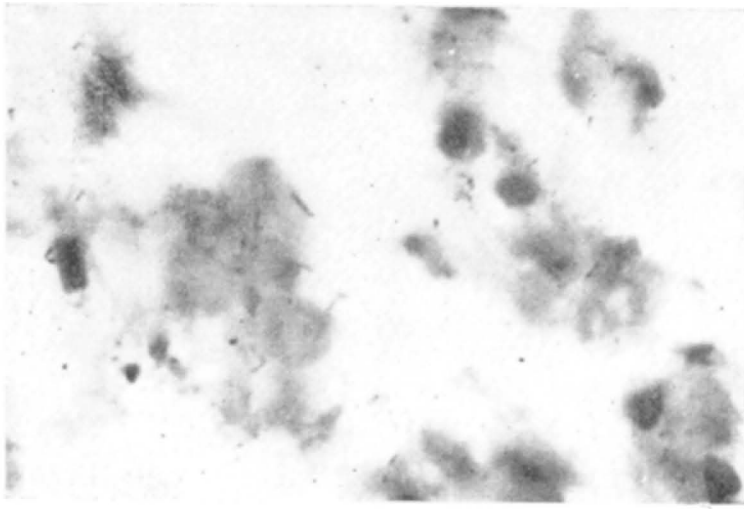

Fig. 5 Lepromatous leprosy nerve with many AFB

TABLE 8
Demonstration of A. F. B.

Site	No.	A. F. B.
Skin smears (4-13) (Including finger tips)	68	—
Skin Biopsy		
Patches/Anesth. Areas	11	1
Nerve Biopsy	68	19

Table 9 shows comparison between clinical thickening of nerves and the histological findings. Of the 43 clinically enlarged nerves only 33 showed changes consistent with leprosy. 29 nerves were considered to be normal on the basis of clinical examination. 16 of these showed changes suggestive of leprosy.

TABLE 9
Clinical enlargement Vs H/P

Clinical	H/P		
	Number	Leprosy	Non-Leprosy
Enlarged	43	33	10
Not Enlarged	29	16	13
Total	72	49	23

These observations indicate the value of cutaneous nerve biopsies in the

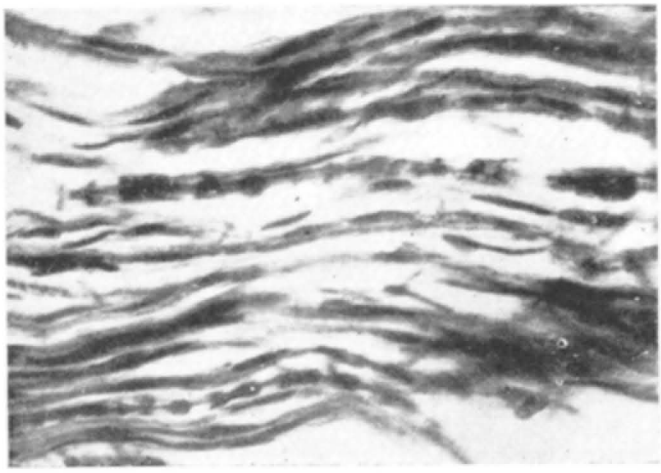

Fig. 6
Nerve showing degenerative changes

diagnosis of PN. 68 patients in whom the cause of PN could not be determined otherwise, histological examination of the nerves established the diagnosis of leprosy in 40. The classification of leprosy was also possible in 23 out of these 40 cases because of the distinctive histological features.

14 patients showed nerves with degenerative changes as shown in Table 10. Among these 2 had diabetes mellitus, 1 demyelinating disease and 1 traumatic neuropathy. Degenerative changes in one patient was suspected to be the result of leprosy, because of evidence of resolving neuritis. One patient had evidence of hypertrophic interstitial neuritis. In 8 patients no definite etiological diagnosis was made.

TABLE 10

Diagnosis on 14 patients showing degenerative nerve changes

Diagnosis	Number
Diabetes mellitus	2
Demyelinating disease	2
Traumatic neuropathy	1
Resolving leprosy	1
Total	6

In 8 remaining patients no specific diagnosis could be made.

11 patients showed normal nerve histology thus ruling out at least a diagnosis of leprosy. The final diagnosis in these patients is presented in the Table 11. Spinal canal occlusion and root compression were diagnosed in 2 patients each. One patient had diabetes mellitus and another sarcoidosis. PN in each of these patients was attributed to the diabetes mellitus and sarcoidosis respectively. In one patient a lipomatous tumour had caused a compression neuritis. In 4 patients no definite diagnosis could be made.

PN is not uncommon in our country. Once established, the ravages secondary to damage to the peripheral nerves will remain potential problems of a life time. We may therefore pause to ask the question, Is a study into the etiology of PN purely on academic exercise? The answer would be No. A scientist who has to handle a problem effectively must have an insight into the root cause.

TABLE 11

Diagnosis on 11 patients with normal nerve histology

Diagnosis	Number
Canal occlusion	2
Root compression	2
Diabetes mellitus	1
Sarcoidosis	1
Pressure neuritis	1
Total	7

In 4 remaining patients no diagnosis could be made.

There are 3 diseases in which cutaneous nerve histology is diagnostic. These are leprosy, progressive hypertrophic interstitial neuritis and primary amyloidosis. Rarely sarcoidal PN may give diagnostic nerve histology. Our patient with sarcoidosis and PN gave normal nerve histology. The possibility of an associated leprosy could be ruled out in this patient.

Cutaneous nerve biopsies are simple office procedures of much diagnostic value in our experience. Perhaps it should be recommended as one of the routine diagnostic tests to be used in PN particularly in areas endemic to leprosy. Without this diagnostic aid it is our impression that dermatologists and leprologists in this country over diagnose leprosy whereas physicians and neurologists under-diagnose the same.

I chose to speak on leprosy as the prototype of an every day problem. There is danger of viewing some of our daily problems as matters of routine.

To the young scientific minds in this audience I have an advise and a plea. Do not miss the challenges of clinical medicine. There are unopen vistas. To each of us is given the opportunity to be a physician-scientist. An exalted title perhaps ?

You can stop to learn always from your books. The books teach you what someone else has learned. You can learn yourselves and teach others too. Learn from your patients. No laboratory facilities can surpass the human body in its ability to provide material for learning.

I conclude with a note of 'Thank you' to all those who have been responsible for giving me the opportunity and the honour to speak this morning.

And Thank you for a patient hearing.

Announcement

Dr. F. Handa Prizes : for the best paper presented or published by persons below 35 years. It is proposed to initiate this prize at the ensuing XI All India Conference of IADVL to be held in January 1983 at Mangalore. Members desirous of being considered for the prize should intimate the scientific chairman when submitting their abstract and-or submit their published paper for consideration not later than October 31, 1982.

M. G. M. Medical College Medal instituted by the organisers of IX Annual Conference of IADVL (Indore)-for the best paper by a young scientist. It is proposed to initiate this prize at the ensuing XI All India Conference of IADVL to be held in January 1983 at Mangalore. Members desirous of being considered for the award should intimate the scientific chairman when submitting their abstract not later than October 31, 1982.

Only members and associate members of the Association are eligible for the above prize and award.