

however differs significantly from the CS of both the control group and the paucibacillary patients. The results support our hypothesis that a loss of corneal sensation

in leprosy patients is mainly due to secondary atrophy of corneal nerves or to multiple ocular pathology.

## PATHOLOGY

### PA1

HISTOLOGICAL AND IMMUNOHISTOCHEMICAL CHANGES OF ECCRINE SWEAT GLANDS IN LEPROSY

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Histopathological and immunohistochemical changes of eccrine sweat glands were investigated in skin biopsies taken from four hundred leprosy cases covering the whole spectrum of the disease and including indeterminate group. The histological findings which may indicate the impairment of sweat function are 1) intraluminal retention of secretory material, 2) cystic dilation of ductal and secretory segment, 3) atrophy, vacuolation, absence and the formation of giant vacuoles in the secretory segment, 4) periglandular fibrosis of the surrounding connective tissue and 5) a decrease in the density of capillary plexus, apart from the destruction directly by inflammatory infiltration. With the immunohistochemical staining using antibody against neuron-specific enolase, a rich network of autonomic nerve fibers around the eccrine sweat glands could be demonstrated on paraffin embedded tissue sections. The involvement of autonomic nerve fibers was a predominant finding in all types of the disease. That the involvement was also sensitively detected in the indeterminate cases indicates that it is a hopeful approach to the diagnosis of leprosy at an early stage.

### PA2

DEMONSTRATION OF PGL-I & LAM-B ANTIGENS IN PARAFFIN SECTIONS OF LEPROSY SKIN LESIONS

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An investigation on the demonstration of PGL-I and LAM-B antigens in thirty-four paraffin embedded skin biopsies taken from leprosy patients who covered the whole spectrum of the disease and in four control specimens was carried out. Neither the PGL-I antigen nor the LAM-B antigen was demonstrated in the normal skin specimens that were used as negative control; and only the LAM-B antigen appeared in the tuberculosis specimens in which the PGL-I antigen was negative. The antigens were identified as intracytoplasmic bacillary staining, in solitary, granular as well as debris patterns; and as soluble antigenic staining, in vacuolar or amorphous pattern. The PGL-I antigen was demonstrated on thirty-three samples except one IT sample and the LAM-B antigen on all samples by the immunohistochemical staining technique. In addition, it is interesting to note that the immunohistochemical staining was able to differentiate foamy change from hydropic degeneration. We also found that the PGL-I

antigen reduced after MDT treatment and increased when relapse happened while the LAM-B antigen was relatively unchanging. The results indicate that the specificity and sensitivity of the immunohistochemical staining technique used in this study are suitable for both the application of the diagnostic pathology and the research on the pathogenesis of leprosy. Particularly the immunohistochemical staining is an aid to the differentiation between reversal reaction and relapse.

### PA3

IMMUNOHISTOCHEMICAL DEMONSTRATION OF PGL-I ANTIGEN IN THE SKIN AND NERVOUS SYSTEM OF LEPROSY PATIENTS

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Immunohistochemical demonstration of *M. leprae* specific phenolic glycolipid-I (PGL) antigen is important for the definite pathological diagnosis of leprosy. We could demonstrate the localization of PGL antigen as well as cross-reactive BCG antigen in formalin fixed paraffin-embedded skin, peripheral nerve and brain stem of leprosy patients.

**Materials and methods:** Skin biopsy of lepromatous leprosy (n=26), nervous system of clinically cured (BI- more than 10 yrs) leprosy autopsy (L: n=6, T: n=6) were immunohistochemically stained by anti-PGL monoclonal antibody and anti-BCG polyclonal antibody using ABC method.

**Results and discussion:** (1) PGL and BCG were clearly stained in leprosy skin biopsies. By both antibodies, solid bacilli were stained as granular pattern, and degenerated bacilli as vacuolated pattern. Even in the resorption stage and Fite's staining is negative, immunostaining remained to be positive, which indicate the efficacy of PGL immunohistochemistry for the definite diagnosis of doubtful leprosy cases using routine paraffin sections. (2) In all the autopsy cases of cured lepromatous leprosy, PGL and BCG staining was observed in sciatic nerve, dorsal root ganglia, posterior spinal roots, spinal cord (posterior horn and anterior horn neurons), medulla oblongata (mainly in ambiguus, facial, hypoglossal, cuneate and gracile nuclei), while most of the cured tuberculous leprosy were negative. These findings indicate that *M. leprae* specific antigen remains in the peripheral nerves and central motor nerves long after the clinical cure of lepromatous leprosy

### PA4

*TGFβ* in leprosy

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Growth factors release from inflammatory cells with multiple activities such as transforming growth factor- $\beta$  (TGF $\beta$ ) have been implicated in the progression of several inflammatory injury. This peptide is an important regulator of matrix formation, enhancing the synthesis of collagen, fibronectin in proteoglycans and has also been shown to be a chemoattractant for monocytes and fibroblast and has some effect as a negative immunoregulator.

The role of TGF in the genesis of the lesion of leprosy patients was investigated by immunohistochemical studies of skin biopsies from patients with different clinical forms of these disease using a polyclonal TGF $\beta_1$  antibody. Our results show the presence of moderate reaction located in basal epidermal cells of normal as well as in leprosy skin. However in patients with erythema nodosum leprosy type ENL and lepromatous leprosy LL we also observed the presence of intense staining in dermal and hipodermal inflammatory infiltrate while lighter staining occurred in these infiltrate present on the skin biopsies from patients with tuberculoid leprosy TT. No reaction was observed in these biopsies when the TGF $\beta_1$  antibody was preincubate with TGF coupled to sepharose resin. These results suggest that TGF $\beta_1$  may be an important factor on the development of the skin injury and fibrosis observed in these patients.

### PA5

#### APPLICATION OF S-100 PROTEIN STAIN IN THE DIAGNOSIS OF LEPROSY

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Twenty-three cases with clinical diagnosis of TT-BT(PB) requiring confirmation by histopathology were detected by the immunoperoxidase technique with S-100 protein. The result showed that 18 cases were confirmed to have leprosy on the basis of the nerve damage in the epithelial granulomas, but only 11 of 23 cases were confirmed to have leprosy on because of the presence of AFB in the skin sections. The significant difference was noted between the two methods( $X^2=4.572$ ,  $P<0.05$ ). The result of 37 cases with multibacillary leprosy(MB) detected by S-100 protein showed that the swollen cutaneous nerve branches were infiltrated with inflammatory cells, and the perineurium were proliferated. There are many bacterial blue particles stained by this method. These data show that the use of S-100 protein stain provides an efficient aid for the diagnosis of leprosy, especially for histopathologically bacilli-negative leprosy.

### PA6

#### THE EFFECT OF *M. LEPRAE* IN PERIPHERAL NERVE ON THE SKIN OF PATIENTS WITH LEPROSY

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*M. leprae* infecting peripheral nerve trunks are a potential reservoir for spread of infection, relapse and hypersensitivity reactions, but the way in which these effects might be induced is unclear.

Forty-one concurrent nerve and skin biopsies from untreated patients presenting with clinical neuropathy, without reaction, and follow through biopsies from 15 reacting patients, provided evidence that *M. leprae* residing in peripheral nerve influenced the involvement of the associated area of skin. The density of bacilli did not appear to be of direct causal importance either for spread of bacilli to uninvolved skin, or in the development of hypersensitivity reactions. It appeared that neural destruction, associated with large intraneural epithelioid cell granulomas due to the presence of bacilli, exerted a primary influence on both spread of infection and reaction in the associated skin area.

### PA7

#### HISTOPATHOLOGICAL ANALYSES OF LEPROMIN TESTS PERFORMED AT BCG-IZED AND NON-BCG-IZED REGIONS OF MULTIBACILLARY LEPROSY PATIENTS UNDER MULTIDRUG THERAPY.

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Ten lepromatous and two borderline-lepromatous patients were injected intradermally with 0,1ml dose of BCG vaccine (Moreau-Rio strain, Ataulpho de Paiva Foundation) on a three-month basis, six doses total, at the deltoid region of the right arm. All of them were previously untreated, lepromin-negative and submitted to multidrug therapy as recommended by W.H.O.

Between two and six months after the last BCG shot, two doses of 0,1ml Lepromin were applied simultaneously. The first was done at an hypocromic rings surrounding the sixth BCG injection place; the other was done at the deltoid region of the left arm, where no Leprosy Lesion could be seen. Both Lepromin tests were read after twenty-one days, and also biopsied for histopathological examination.

The results will be presented, analysed and discussed by the authors.

### PA8

#### HISTOPATHOLOGICAL ANALYSIS OF SPECIMENS OF BCG-IZED REGIONS OF MULTIBACILLARY LEPROSY PATIENTS UNDER MULTIDRUG THERAPY.

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Fifteen lepromatous and two borderline-lepromatous patients were injected intradermally with 0,1ml dose of BCG vaccine (Moreau-Rio strain) on a three-month basis, six doses total, at the deltoid region of the right arm. All of them were previously untreated, lepromin-negative and submitted to multidrug therapy as recommended by W.H.O.

Three months after the sixth dose biopsy specimens were collected from three sites: A) Near the first B.C.G. injection; B) An hypocromic ring surrounding the sixth BCG injection place, and C) the deltoid regional of the left arm, where no leprosy lesions could be seen.

The results will be presented, analysed and discussed by the authors.

### PA9

#### MORPHOLOGICAL AND IMMUNOHISTOCHEMICAL FINDINGS IN ERYTHEMA MULTIFORME IN LEPROSY

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Erythema Multiforme (EM) is an uncommon manifestation of a reactional episode in lepromatous patients. It is probably due to a recrudescence of the same mechanisms involved in the pathogenesis of



Erythema Nodosum Leprosum (ENL), with which it shares clinical signs and concomitant lesions. To further characterize the morphological changes and the types of inflammatory cells in evolving lesions, 8 cases of EM and 8 cases of ENL were studied by histological and immunohistochemical techniques.

Our results showed that vascular changes were prominent in both groups, with dissociation of the walls by edema and infiltration of mononuclear cells, mainly CD4+ T cells. Fibrinoid necrosis was never seen but proliferated small blood vessels whose endothelial cells express Ulex europaeus, ICAM-1 and HLA-DR antigens were found throughout the biopsy area, surrounded by TNF- $\alpha$  cells.

Those vascular findings in association with a usually thickened epidermis also expressing HLA-DR antigen by keratinocytes, suggests that a cell-mediated immunity response cytokine-dependent is involved.

This study was financed by WHO grants.

### PA10

#### LEPROSY - STUDY OF 20 PLACENTAS AND THE REPERCUSSION ON THE NEWBORN

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Maternal Leprosy has effects on the fetus leading to low body weight, prematurity and death. Even though leprosy has a high prevalence rate in Brazil, there are no reports concerning the placental lesions. We studied the pathology of 20 placentas from patients with different forms of leprosy, evaluating the occurrence of alterations related to the presence of *M. leprae* and investigating the transmission of specific antibodies (anti PGL-1 IgM) from mother to newborns.

The placentas were grossly examined according to Fox's criteria and fixed with 10% formalin. After routine processing for light microscopy the slides were stained with HE and auramine-rhodamine fluorescent technique.

Acid-fast bacilli were found in eleven placentas and nine of them also showed villitis. Twenty percent of the newborns were premature and 25% had less than 2500 g.

Newborns from mothers with lepromatous leprosy showed in average a sevenfold higher serum anti PGL-1 antibodies.

Placental examination as well as the study of the newborn immune status may allow us an early diagnosis of leprosy and to clarify some aspects of congenital transmission of leprosy.

Supported by CNPq grants.

### PA11

#### HISTOPATHOLOGICAL ANALYSIS OF SKIN BIOPSIES PERFORMED IN LEPROSY PATIENTS: REACTION OR RELAPSE ?

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The study aimed at identifying the histopathological changes in paucibacillary leprosy patients who presented with cutaneous lesions suggestive of either reaction or relapse following completion of the WHO-recommended therapeutic regimen.

### PA12

#### HISTOPATHOLOGICAL ALTERATIONS IN AREAS OF CUTANEOUS SENSORY LOSS IN THE DIAGNOSIS OF LEPROSY

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A retrospective study of altered histopathological findings in skin biopsies of patients presenting only with altered cutaneous sensory loss took place. Of the 158 patients included, 15.2% showed histopathological alterations sufficient to diagnose leprosy.

### PA13

#### ROLE OF SKIN AND CUTANEOUS NERVE BIOPSIES IN PAUCIBACILLARY (PB) BORDERLINE TUBERCULOID HANSEN'S DISEASE (BTHD)

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Aim: To determine whether skin smear negative patients with BTHD are in the multibacillary (MB) spectrum by studying their skin and cutaneous nerve biopsies.

Method: Twentyfive patients with clinical features of BTHD who had received less than 3 months of prior treatment and were skin smear negative from 6 sites were included. All had skin biopsies and lepromin test done. Twenty of them also had cutaneous nerve biopsy. AFB stain was done on skin and nerve biopsies.

Results: Multiple patches were seen in 64% of patients. Maximum number of patches was 14. 88% of patients had enlarged nerves. An unusual clinical feature was detection of areas of anaesthesia in addition to patches in 64%. 80% of such patients showed AFB in the skin and/or nerve. Clinico-histological concordance by skin biopsy was seen in 76% and by nerve biopsy in 55% of patients. Histological correlation in the skin and nerve was seen in 50%. Among histologically diagnosed BTHD patients, 58% showed AFB in the skin biopsy while 90.9% had AFB in the biopsied nerves. Lepromin was positive in 83.4% patients.

This study emphasizes that present classification of MB and PB HD by skin smears alone is inadequate, since 80% of patients who were skin smear negative showed AFB in the skin and/or nerve.

### PA14

#### CLINICAL AND HISTOPATHOLOGICAL CORRELATION IN THE CLASSIFICATION OF LEPROSY

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The study reports our observations on the correlation between clinical and histopathological diagnosis of classification of leprosy. The histopathological classification of leprosy in 1351 cases, was done as per Ridley-Jopling criteria and was compared with the clinical diagnosis of the same. These 1351 cases included 79 cases which were diagnosed as having reaction clinically. However, the histopathologist could not detect any evidence of reaction in 16 of these 79 cases (20%). Of remaining 1272 cases, 68 (5%) were reported as 'no evidence of leprosy' by the histopathologists. 37 out of these 68 were found to be of the clinically Indeterminate type. Histopathological and clinical diagnosis of classification of leprosy concided in 69% of the cases. Concordance between the clinical and histopathological diagnosis for different types of leprosy was: Indeterminate (I)=35%, Tuberculoid (TT)=50%, Borderline tuberculoid (BT)=77%, Borderline (BB)=25%, Borderline lepromatous (BL)=43%, and lepromatous (LL)=91%. When some of the types were combined together (BT with TT, BL with LL), the overall figure of concordance was 76%, concordance for the TT/BT group was 80% and for the BL/LL group it was 93%. As both TT and BT are considered paucibacillary and LL or BL are considered multibacillary for treatment purpose, differentiating TT from BT or BL from LL is perhaps therapeutically irrelevant. However for classification purposes, it appears that weightage given to different signs and/or histopathological parameters for classifying the leprosy cases specially TT, BB and Indeterminate need to be re-assessed.

**PA15**

A SEMI-QUANTITATIVE ASSESSMENT OF THE CELLULAR IMMUNE RESPONSE TO *MYCOBACTERIUM TUBERCULOSIS* IN HIV-INFECTED PATIENTS

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In the histologic classification of leprosy, features of significance include the cellular composition of granulomas and the bacillary index. There is a spectrum of granulomatous response to *Mycobacterium tuberculosis* in HIV positive patients which may be related to immunosuppression, and as with leprosy, histologic classification may prove useful prognostically and in clinical trials. We assessed the level of cellular response and graded the histologic patterns from 1 (classic granuloma) to 4 (anergic tuberculosis) in lymph nodes from ten HIV positive Zairians with tuberculous adenitis. Acid-fast bacilli (AFB), Grocott Methenamine Silver (GMS), and Jones stained sections were examined. Successive sections were studied for the quantitation of L26 positive cells (B lymphocytes), CD4 positive cells (T helper cells), UCHL-1 positive cells (T cells), and KP-1 positive cells (histiocytes). Histologic grade, relative proportions of cell types, AFB counts in tissue, peripheral CD4+ lymphocyte counts, WHO clinical stage of HIV disease, and PPD reaction were compared. Nine non-tuberculous HIV positive Zairian patients matched for age, sex and peripheral CD4+ count were also studied to compare the lymphadenopathy of HIV infection alone to tuberculous lymphadenopathy in HIV infection.

In the tuberculous cases, relative proportions of cell types vary according to the histological grade. In patients with severe immunosuppression, the caseous granulomatous response was replaced by a pyohistiocytic infiltrate and coagulative necrosis. PPD anergy correlated with absence of Langhans giant cells. AFB counts in tissue were inversely related to peripheral CD4+ counts and histological grade, and in patients with advanced AIDS (CD4+ <10%) were not affected by anti-mycobacterial treatment. The cellular response to *Mycobacterium leprae* in patients co-infected with HIV has not been well described. The above techniques will be applied to cases of HIV-leprosy available in our registries.

**PA16**

MAST CELLS IN HISTOID LEPRONA

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Five male patients with histoid leproma occurred in the lepromatous leprosy were observed histopathologically. Age ranged from 23-37 years. The duration of the lesions varied from 2 months to 1.5 years. Skin biopsy was taken from the nodule with surrounding healthy skin of histoid leproma. The specimens were fixed in 10% buffered formalin solution and processed for paraffin embedding. 7 $\mu$  thick sections were cut and stained with hematoxylin and eosin, toluidine blue, Giemsa and Harada's acid-fast method.

In histoid leproma, in addition to the dense infiltrates of macrophages, fibroblasts etc., the proliferation in various degree and the degranulation of mast cells were found, while in the surrounding normal healthy skin the mast cells were only occasionally seen and mainly intact.

Finally the possible role of mast cells in the histopathogenesis of the lesions was discussed.

**PA17**

MYCOBACTERIUM LEPRAE IN MAST CELLS IN HISTOID LEPRONA

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In this paper, a leprosy patient in relapse with wide-spread lesions of histoid leproma was presented. Histopa-

thological examination confirmed the diagnosis of histoid leproma with high BI (6+). With Giemsa stain, the slide showed that the number of mast cells in the lesion was much more than that in the surrounding healthy skin. Under TEM, the close contact or apposition of mast cells to *M. leprae* was found. Meanwhile, in the cytoplasm of some mast cells, the intact *M. leprae* were seen. These findings had not been reported previously. The possible role of mast cells in the histopathogenesis of the lesion was discussed.

**PA18**

CONJUNCTIVAL BIOPSY IN PATIENTS BEARING HANSEN'S DISEASE.

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The authors have examined 120 patients's eyes with Hansen's disease, who were equally divided among the forms: Tuberculoid (30), Indeterminate (30) Borderline (30) and Lepromatous (30).

The investigation was made with biopsy of the bulbar conjunctiva on the upper temporal quadrant of the right eye.

The patients were from 3 groups: 1) untreated patients, 2) during treatment and 3) those who were in observation after the end of medicamentous treatment.

This study tried to identify the presence of *M. leprae* in conjunctive and it was found in four cases: one borderline and three lepromatous patients who were being treated with multidrug therapy.

**PA19**

LIVER & LEPROSY: HISTOPATHOLOGICAL/BIOCHEMICAL CHANGES

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A prospective study of liver involvement in leprosy was conducted in 30 patient (10 non lepromatous, 7 borderline & lepromatous, 4 erythema nodosum and 1 indeterminate. Illness ranged from 6 months to 6 years with 61% having illness less than 1 year) duration 36.7% (1-5 year) duration. M:F ratio was 77.6% 23:4%. Histopathological evaluation showed granuloma in 12, more commonly in patients having disease of less than 1 year duration (4 each in borderline, lepromatous and erythema nodosum leprosum). Acid fast bacilli was demonstrated in 13.3% Lymphocytic infiltration (92%), focal cell necrosis (64%), Kupffer cell hyperplasia 28%, Mild fibrosis (4%) and hepatolysis (12%) were seen. Patients having granulomas more frequently showed liver function test abnormalities. Biochemical abnormalities in the form of serum proteins decrease was seen in 16.7% and increase in serum globulins in 53.3% of subjects. SGOT, SGPT and alkaline phosphatase were raised in 23.3, 26.7 and 23.3% but was statistically significant only in patients of lepromatous leprosy as compared to controls. Serum bilirubin, serum cholesterol and thymol turbidity were not found to be significantly altered. Hence biochemical and histopathological hepatic involvement is commonly seen in leprosy.

**PA20**

QUANTITATIVE MORPHOLOGICAL METHODS FOR ASSESSMENT OF THE EFFECTIVENESS OF ANTILEPROSY THERAPY

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Morphological methods (quantitative and enzymochemical assays) are well suited for the assessment of the efficiency of antileprosy therapy. Based on the principles of volume stereometry and using a set of various ocular metric systems, skin granulomas in biopsied skin lesions from 50 leprosy patients were studied by the following parameters: volumes percent of "leprosy" macrophages (LM), histiocytes-monocytes (H-M), bacterial index of granuloma (BIG), lymphocytes (L) and epithelioid cells (E). Active LL patients show the following cytohistogram: LM-80%, H-M-8%, BIG-70% (4, 5+), L-0%, E-0%. As the disease regresses, the cyto-



histogram changes: volume percent of LM decreases to 15%, H-M increases to 40%, BIG - 50% (3+), L - 5%, E remains unchanged. These parameters are convenient to be represented on radius histogram and to be stored in a computer memory. The ratio between functionally inactive cells of the epidermis and hyperfunctioning "leprosy" macrophages is expressed by esterase coefficient (EC). In active leprosy patients the index of histochemical reaction to nonspecific esterase of epidermis is significantly low (EC<1,0), in regressed skin lesions EC increases to 1,0 and more. In oligobacterial forms of leprosy and the illnesses suspected for leprosy the assay should be supplemented by cytophotometry of immunoperoxidase deposits of *M. leprae* antigens.

## PA21

### PRE AND POST HISTOPATHOLOGICAL EVALUATION OF FIFTY LEPROSY PATIENTS, UNDER MULTIDRUG THERAPY:-

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#### AIM:

- 1. To observe the histopathological changes in Leprosy patients under multidrug treatment and to see whether W.H.O recommendations hold good in treatment.

#### METHODS:

Every Leprosy patient underwent a biopsy before starting the treatment and again a biopsy next to the original site after 1 year and at the end of 3 years.

#### RESULTS:

Not much histopathological changes were seen in 90% of the patients at the end of 1 year. 80% of the paucibacillary patients showed resolution of granuloma and no inflammatory infiltrate around the nerves at the end of three years. But multibacillary patients showed definite histopathological evidence of Hansen's, even at end of three years of treatment.

#### DISCUSSION:

In this study we have observed that paucibacillary patients do not show any changes histopathologically even at the end of 1 year treatment. If the treatment is stopped at the end of six months and patient develops relapse due to any debilitating diseases, patient may not respond to the same drugs. Due to debilitating conditions the body immunity may go down and the dormant bacteria can become active.

So when we have drugs like Rifampicin, Dapsone and Clofazamine which are virtually devoid of side effects, the treatment can be continued till histopathological resolution has occurred, otherwise we may land up with an era where Leprosy may be resistant to Dapsone and call for a higher and costlier drug may arise.

#### CONCLUSION:

1. W.H.O recommendation of time period is not sufficient.
2. If W.H.O recommendation is followed strictly, after a gap of few years, a generation of patients who are resistant to Dapsone can be encountered.

## PA22

### REACTION TYPE II OF HD (ENL) WITH VISCERAL INVOLVEMENT: INDEX FOR THE SEVERITY OF THE DISEASE. CLINICAL, LABORATORIAL AND AUTOPSY STUDY OF 34 PATIENTS.

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The clinical, laboratorial and autopsy data of 34 patients with type II reaction (TIIR) of Hansen's Disease were collected. The clinical and laboratorial aspects were evaluated and correlated with the anatomo-pathological findings. The TIIR of the disease in severely ill patients are more significant in males, white, old, long time and progressive course of the disease, Virchowian form of the disease, presence of cutaneous, mucosal and neurological sequelae, irregularity of the treatment, high serum levels of bilirubin, leucocytosis and high erythrocyte sedimentation rate.

The anatomo-pathological findings related with severe forms were acute inflammatory and necrotic suppurative lesions, multiplicity of affected regions by the Virchowian form of the disease and/or generalised and extensive necrotic-ulcerative cutaneous lesions. The TIIR may be directly related with the death of the patients but often is the result of infectious complications or renal amyloidosis.

## PA22

### GRANULOMA PERSISTENCE AFTER CLINICAL INACTIVITY

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Histological findings on 220 biopsies from 56 LL, 26 BL, 106 BT and 32 TT cases were presented. Biopsies were taken from MB cases after 24-36 doses and from PB cases 6-12 doses of MDT. Histopathological examination showed granulated bacilli in 40% and persistent macrophage granuloma in 58% of cases. The macrophages were markedly vacuolated with few giant vacuoles containing acid fast dust. Evidence of cellular or bacterial activity was absent. In PB cases epithelioid cell granuloma persisted in 40% of cases. There was follicular pattern with dense collar of lymphocytes around the epithelioid cell nests.

The highest granuloma fraction was 40 and 25 in macrophage and epithelioid cell granuloma respectively.

Of the cases without a granuloma 30% of lepromatous and 28% of tuberculoid cases had focal collection of lymphocytes and the remaining ones had only atrophic changes.

The individual cells of a granuloma appear to take long time to die and disappear in the absence of disease activity and it seems unreasonable to continue treatment until disappearance of the granuloma.

## PA23

### ANALYSIS OF 98 AUTOPSY CASES IN A JAPANESE LEPROSARIUM

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In a Japanese Leprosarium Hoshizuka-Keiaien, 151 patients died of disease from 1982 to 1992, and 98 cases of them were autopsied (average age 78.1; M:60, F:38; L:57, B:1, T:39). All the cases were cured or quiescent stage of leprosy. Main causes of death were malignant tumors (33.34%), respiratory disease (29.30%), cardiovascular disease (15.15%), cerebro-vascular disease (10.10%), alimentary disease (5.5%) and others (6.6%). Malignant tumors were 32 carcinomas (esophagus:2, stomach:7, colon:5, liver:4, gallbladder and biliary tract:5, pancreas:3, lung:4, urinary tract:2) and one adult T cell leukemia which is prevalent in the southern part of Japan. There were three occult carcinomas (thyroid:2, kidney:1) and two cured carcinomas (breast and larynx). Amyloidosis were three cases (L:2, T:1). Among the cardiovascular disease, heart disease were 9 cases (9%) and its frequency is less the average (19%) of Japan. Dementia was observed in 14 cases (vascular dementia:6, senile dementia of Alzheimer type: 6, mixed:2). There was a hypothesis that long term uptake of DDS might cause the increase of cancers, but our data indicate that frequency of cancer is almost the same as that of whole Japanese death registry. In our leprosarium, rate of biliary or gallbladder carcinoma is extremely higher than that of Japan (age-adjusted rate per 100,000 people is 17.2 vs. 4.6). DDS is mainly excreted via bile juice, which may be correlated increase of bile duct carcinoma.

#### PA24

##### SECONDARY AMYLOIDOSIS IN LEPROSY

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Postmortem examinations were performed on 35 leprosy patients at Eversley Childs Sanitarium Cebu, Philippines during the period 1964 to 1990. There were 29 males and 6 females ranging in age from 12 to 88 years. At autopsy, 28 patients had lepromatous leprosy, 3 borderline lepromatous, 1 borderline, 1 tuberculoid leprosy and 2 had arrested disease.

Amyloid deposits were noted in 18 patients [51%] and observed in the following organs; kidney 94%, liver 78%, spleen 72%, adrenal gland 56%, GI tract 50%, heart 39%, pancreas 33%, testis 33%. Other organs involved included the lymph nodes, urinary bladder, gallbladder, thyroid gland, lungs, blood vessels, prostate gland, skin and nerves.

Erythema nodosum leprosum [ENL] was associated with amyloidosis in 17 patients. The role played by ENL and other factors in the pathogenesis of secondary amyloidosis in leprosy will be presented and discussed.

#### PA25

##### ACTIVITY OF THE PROTECTIVE ENZYME SUPEROXIDE DISMUTASE AND THE LEVELS OF LIPID PEROXIDE IN THE SKIN SITES OF LEPROMATOUS LEPROSY WITH TYPE II REACTIONS

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The activity of the oxygen radical scavenging enzyme superoxide dismutase (SOD) and lipid peroxide (LP) levels in the skin biopsy specimens of Type II reactions (erythema nodosum leprosum) in lepromatous leprosy patients were examined. Interestingly our studies revealed that SOD levels ranged from 0-20, 20-40 and more than 40 units/mg protein in patients with or without ENL episodes i.e. uninvolved skin. The lipid peroxide levels were not significantly different between the ENL and uninvolved skin (US) site. However, the lower and higher ranges of SOD and LP of ENL and US biopsies were significantly different from non-lepromatous controls.

#### PA26

##### SIGNIFICANCE OF CELLULAR MORPHOLOGY OF MITSUDA LEPRONIN RESPONSE

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The late lepromin reaction with Mitsuda Lepromin is known to reflect the cell mediated immunity in leprosy. An effort has been made in the present study to find out if the cellular morphology of late lepromin response indicates the spectrum of leprosy. 32 patients were skin tested with standard Mitsuda Lepromin. The nodule of late lepromin reaction and a representative skin lesion were biopsied. The study was conducted by the double blind method, the pathologist being completely unaware of the clinical details. The nature of granuloma, the presence of distinguishing cells as also their number and distribution were carefully studied. It was found that in 18 patients of TT/BT type, lepromin histology consistent with tuberculoid granuloma was seen in 16 cases. Likewise in 8 BL/LL patients, macrophage granuloma was seen in 6 cases. In mid-borderline patients, the histological picture of lepromin granuloma was similar to that seen in skin lesions of BB leprosy. The study has shown that histology of Mitsuda lepromin reaction gives good indication of underlying immune status of individual to M. leprae infection.

#### PA27

##### PATTERN AND SPREAD OF OCULAR LESIONS IN MULTI-BACILLARY LEPROSY A HISTOPATHOLOGICAL STUDY

M Jacob

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This study investigates, by light microscopy, the pattern of involvement and the mode of spread of ocular lesions in lepromatous leprosy. Five eyes from four patients were examined.

A spectrum of pathological changes are seen. These range from a minimal inflammatory response, to florid lepromas in the anterior segment, and varying degrees of posterior segment involvement.

The spread of bacilli is predominantly through blood vessels, neurovascular complexes and by infiltrating granulomas from the conjunctiva into the cornea, ciliary body, iris, anterior choroid and anterior ciliary nerves. The second route of dissemination is from the conjunctiva to the sclera and episclera. Macrophages with bacilli were seen around the optic nerve and sheath in one eye. The third mode is the spillage of macrophages into the



vitreous and the inner surface of the retina, when there is heavy lepromatous infiltration of the anterior uveal tract. One eye showed changes in the posterior ciliary nerves without involvement of the adjacent tissue.

The significance of the study in understanding ocular leprosy will be discussed.

## PA28

ULTRASTRUCTURAL ALTERATIONS OF DERMAL NERVES IN EARLY CUTANEOUS LEPROUS MACULES.

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The early mechanisms of nerve lesion in leprosy is unclear. We examined 25 dermal nerves of 15 early hypochromic, hypoesthetic cutaneous macules from leprosy patients by Transmission Electron Microscopy. Eight nerves showed nearby inflammatory cells. Three of them had perineural hyperplasia and one of them increased amorphous substance between perineural layers. Unidentified elongated mononuclear cells were found crossing the perineurium of one nerve. A decrease of unmyelinated axons and replacement of the lacking fibers by collagen deposition were found in three nerves. Thin fibroblast cytoplasmic processes partially surround bundles of myelinated and unmyelinated fibers of 5 nerves. Inflammatory infiltrate is restricted to the neural surrounding region and should not be implicated as the cause for the described changes. In addition, six nerves were unaffected by neuritis but presented important morphological changes. All of them were found to contain few or no axons in cross-section profiles and Schwann cell cytoplasmic processes devoid of axons were observed. Collagen deposition fills the empty endoneurium. One nerve showed long perineural cytoplasmic projections into the endoneural compartment. It is possible that the nerve damage in leprosy occurs by mechanisms other than inflammatory ones. The onset of leukocytic infiltration of a nerve may occur upon a previously impaired neural structure so that hypoesthesia rather than painful symptoms appear as the main early clinical manifestations of the disease.

## PA29

PRESENCE OF HANSEN'S BACILLI IN CONJUNCTIVE, VITREOUS BODY AND RETINA IN AN EYE OF A PATIENT BEARING THE VIRCHOWIANE FORM OF HANSEN'S DISEASE.

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Histopathological study of an enucleated eye from a patient bearing Hansen's disease, Virchowian form, being the disease in activity and in which were found Hansen's bacilli in the following structures: conjunctive, sclera, cornea, ciliary body, vitreous body and retina.

## PA30

HISTOPATHOLOGICAL EVOLUTION OF PB PATIENTS UNDER WHO REGIMEN.

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Several published papers argue the efficacy of paucibacillary regimen proposed by WHO in

1982. Some authors propose an addition of six months dapsone monotherapy. Histopathological examination in one criteria adopted by them to ascertain disease activity.

In the present work a group of patient was studied on clinical, immunological, bacteriological and histopathological basis. Biopsies specimens were collected at the beginning of treatment, 6 months and two years after released from treatment. It was observed that even after interruption of specific treatment, there was a tendency to clinical and histopathological healing of lesions, leading to the conclusion that WHO regimens for PB patients are, when used in correctly classified cases, perfectly adequate.

## PA31

THE EFFECT OF TREATMENT ON LEPROSY PATHOLOGY

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Longitudinal studies of leprosy pathology are rare. In this study, we have looked at a series of 28 patients from whom biopsies were taken at two-weekly intervals before and during treatment for histological evaluation. 16 of the patients had paucibacillary (PBL) and 12 multibacillary (MBL) leprosy. In all cases, granuloma fraction (GF) and bacteriological index (BI) fell during treatment, although BI was less sensitive marker of response. Since the biopsies were fixed in buffered formaldehyde and processed through to paraffin wax, immunohistochemistry was limited. However, there was strong evidence of immune activation with increased HLA-DR expression in the granulomas of MBL cases as well as PBL cases. The epidermis also expressed HLA-DR within four weeks of WHO multidrug therapy commencing in a number of patients. The results suggest that enhanced activation of cell-mediated immunity in leprosy lesions occurs in all treated patients and is not restricted to those with clinically apparent upgrading reaction.

## PA32

HISTOPATHOLOGICAL EVALUATION OF CHEMOTHERAPY AND CHEMO-IMMUNOTHERAPY IN MB LEPROSY.

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Under the immunotherapeutic trial being conducted at New Delhi with Mycobacterium w., 257 out of the 380 originally inducted patients have now completed 2 years of treatment. Skin biopsies collected at 0, 6, 12, 18, and 24 months were available from 255 patients for analysis. Each biopsy is graded along the Ridley scale and also evaluated for Granuloma Fractions and Histological Bacillary indices. The 255 patients comprise 130 (68-LL, 41-BL & 21-BB) from the group receiving MDT and vaccine and 127 (73-LL, 34-BL & 20-BB) from the control group receiving MDT only. The results show a significantly greater degree of granuloma clearance and histological upgrading in the vaccine group. Attainment of bacillary negativity is higher and

residual mycobacterial antigen ( as seen by anti-BCG Ab) is less in the vaccine group at the end of 2 years. A higher degree of lepromin conversion is seen in the vaccine group with the lepromin site biopsies showing well developed DTH reactions. The histopathological observations correlate well with the clinical and

bacteriological data. Nerve biopsies from 8 skin BI negative LL cases done for persisting organisms showed granular AFB in 2 control group cases only. The results indicate a significant additive effect of chemo-immunotherapy as compared to chemotherapy alone.

## PSYCHO-SOCIAL

### PS1

A STUDY TO ASSESS SOCIAL DISABILITY AND ECONOMIC LOSS TO LEPROSY PATIENTS ON MDT IN NORTH INDIA -- PRELIMINARY STUDY

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Leprosy with its sequelae gives rise to two major consequences for the patients: 1. Social disruption and 2. Economic loss. This study aims at measuring and relating the magnitude of socioeconomic consequences.

Data were analysed taking into consideration, loss of respect and position in the family; loss of social stature; separation from spouse and displacement from home and community as the major social consequences. Cost analysis was done for change or loss of occupation. Loss of man-hours at work in order for the patient to take outpatient and inpatient treatment was also analysed.

Preliminary results indicated that the social consequences contributed significantly to economic losses. The loss of man-hours due to treatment was also significant. Affluent and upper caste patients appear to be less affected while young adult male manual workers with disabilities seem to incur greater losses.

It is suggested that well integrated socioeconomic measures within the MDT Programme will have maximum beneficial effect for the patients.

### PS2

A STUDY ON THE NON-DEHABILITATED AND DEHABILITATED LEPROSY PATIENTS

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**ABSTRACT:** Community Based Rehabilitation is replacing the costly model of institution-based long term care of leprosy patients. It mostly refers to the social and economic rehabilitation of the individual.

The objectives of the study are: (1) To identify the various factors involved in the process of debilitation of persons afflicted with leprosy. (2) To find out the causes why certain patients were not debilitated inspite of their deformities (3) To bring out the social and economic elements in the life of leprosy afflicted persons. (4) To find out the ways and means to enable the leprosy patients to continue their normal life without any interruption. (5) To help to reduce the number of patients who would require rehabilitation through prevention of debilitation.

Fifty non-dehabilitated patients and 50 debilitated patients were taken as samples for the study. The findings of the study is very useful for programme implementing agencies in social and economic rehabilitation of leprosy patients.

### PS3

COMMUNITY PERCEPTION OF LEPROSY IN KERALA (SOUTH INDIA)

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Kerala is known for its better health status as compared with other States in India, as indicated by a low infant mortality, a low birth rate and higher literacy rate.

The study is aimed to document the baseline data on knowledge and attitudes of the community towards leprosy, with a view to modify the strategy of leprosy control. It will also help evaluation of the programmes after few years.

Both qualitative methods such as focussed group discussions and quantitative methods such as interview schedules were used for data collection. The study has been conducted at Manjeri sub-district and Kollam Urban pockets in Kerala.

The preliminary findings indicate that there is fear about the deformity and high infectivity associated with leprosy. The community prefers to retain the confidentiality of the disease. Knowledge about the signs and symptoms, about the causation, transmission and cure has also been studied. Higher literacy has shown direct co-relation with high stigma and prejudices about leprosy. Intervention is planned to see whether appropriate Health Education will result in a change in knowledge, attitude and practice.

### PS4

COMMUNICATION FOR LEPROSY AWARENESS IN A COUNTRY OF TRANSITION

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In a country of transition, like India, where a relentless war against leprosy is fought with limited and scarce resources, the role of communication for creating awareness about the disease is a pivotal one. Technological advancements have brought about tremendous changes in the methods and means of communication through innovations.

With the objective to study the effectiveness of cartoon strips as a medium for the dissemination of scientific facts on leprosy to the literate and younger sections of the society, within the age group of 10-20 yrs, a study was conducted in two urban and two rural areas covered by GLRA/ALES projects in two states, in South India. 1000 persons each from the urban and rural areas were interviewed.